**FRIENDLY AMENDMENT**

**Proposed by the HBCU College of**

**Plant-Based Lifstyle Medicine**

Expedited Bill No. 34-21
Concerning: Personnel and Human Resources - COVID-19 Vaccination Required
Revised: 09/24/2021 Draft No. 3
Introduced: _____
Expires: _____
Enacted: _____
Executive: _____
Effective: _____
Sunset Date: _____
Ch. _____, Laws of Mont. Co. _____

# COUNTY COUNCIL
# FOR MONTGOMERY COUNTY,

Lead Sponsors: Councilmembers Riemer and

**AN EXPEDITED ACT** to:

(1) require the vaccination of County employees against COVID-19; or alternatively
(2) require THE TEN LAWS of Plant-Based Lifestyle Medicine 28-day mandatory online training option
(32) permit medical accommodations to the COVID-19 vaccination requirements;
(43) exempt the COVID-19 vaccination requirements from collective bargaining; and

By amending

Montgomery County Code
Chapter 33, Personnel and Human Resources

| | |
|---|---|
| **Boldface** | *Heading or defined term.* |
| Underlining | *Added to existing law by original bill.* |
| **[**Single boldface brackets**]** | *Deleted from existing law by original bill.* |
| Double underlining | *Added by amendment.* |
| **[[**Double boldface brackets**]]** | *Deleted from existing law or the bill by amendment.* |
| * * * | *Existing law unaffected by bill.* |

*The County Council for Montgomery County, Maryland approves the following*

**Sec 1. Section 33-22 is amended as follows:**

**33-22. [Reserved.] COVID-19 Vaccination**

(a) *Definitions*. For purposes of this section, the following words have the meanings indicated.

*COVID-19 Vaccine* means a vaccine authorized or approved by the federal Food and Drug Administration to prevent or reduce the transmission of SARS-CoV-2.

*Employee* means an individual employed by the County, regardless of the individual's merit system status or representation by an employee organization.

*Fully vaccinated* means having received all doses of a COVID-19 vaccine.

(b) *Vaccination Required*. As a condition of employment by the County, an

(1) be fully vaccinated and provide to the County proof of vaccination

(2) under subsection (c); or complete the 28-day THE TEN LAWS of Plant-based Lifestyle Medicine online course

(c) *Procedures; remedies for*

(1) Within 7 days after notification by the County to an employee of the requirements of this section, the employee must:

(A) provide to the County proof that the employee is fully vaccinated; or attend the first online THE TEN LAWS of Plant-based Lifestyle Medicine Course and complete the course

(B) apply for an accommodation under subsection (d).

(2) An employee who fails to comply with paragraph (1) must be

See rest of additional language on last page.

(3) Within 7 days after being placed on unpaid leave under paragraph

(A) provide to the County proof that the employee has received

(B) at least one dose of a COVID-19 vaccine; or

(4) An employee under subparagraph (3)(A) must provide to the County, within 40 days of being placed on unpaid leave, proof that the employee is fully vaccinated.

(5) An employee who fails to comply with paragraphs (3) or (4) of this subsection, or with paragraph (3) of subsection (d),

(d) *Health-based*

(1) An employee may apply for an accommodation to the requirements of this section based on the health of the employee.

(2) The Director of Human Resources, or the Director's designee, must approve an application for an accommodation if the accommodation is required for the health of the employee, as documented by a licensed physician.

(3) Within 7 days after the denial of an application for an accommodation under paragraph (1), the employee must provide to the County proof that the employee has received at least one dose of a COVID-19 vaccine. Within 40 days after the denial of the application, the employee must provide to the County proof

(~~e~~) *Exemption from Collective Bargaining.* The requirements and implementation of this section:

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(c)(1)(B) [Continued]

B. All employees enrolled in the online THE TEN LAWS of Plant-based Lifestyle Medicine are required to:

i) test once a week for Covid-19 using free services provided by the County;

ii) provide electronic proof of course attendance

iii) within thirty (30) from completing the course, submit monthly grocery receipts to the Human Resources Department to show compliance with the plant-based dietary plans learned in the course; and

iii) at the option of the employee, disclose any positive medical condition changes as a result of participating in the training by submitting a video, photos or written narrative.

C. The Director of Department of Health and Human Services shall approve all instructors that will provide THE TEN LAWS of Plant-Based Lifestyle Medicine training, which minimum requirements shall be that the instructor lives the whole food plant-based lifestyle and is either a licensed physician in any state, a PhD in Nutrition, Dietitics, Naturalpath, Preventative health, or Naturopath MD, a registered nurse or certified plant-based lifestyle medicine coach.

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# BAXTER DELWORTH MONTGOMERY, MD

The Plant-Based Physician
Montgomery Heart & Wellness
Video Bio

**EXPERIENCE:**

Clinical Assistant Professor
The University of Texas Health Science Center
Department of Medicine
Division of Cardiology/Clinical Cardiac Electrophysiology

President and CEO
Houston Associates of Cardiovascular Medicine, PA.
(1997-Present)

Executive Director
The Johnsie and Aubary Montgomery Institute of Medical Education and Research (a 501(c) 3 nonprofit organization)

**BIRTHPLACE:**

Houston, Texas
United States of America

**OFFICE ADDRESS:**

10480 South Main Street
Houston, Texas 77025
(713) 599-1144 phone
(713) 599-1199 fax
bmontgomery@drbaxtermontgomery. com

**UNDERGRADUATE EDUCATION:**

William Marsh Rice University
Houston, Texas
Bachelor's Degree in Biochemistry (1986)

**GRADUATE EDUCATION:**

The University of Texas Medical Branch at Galveston
Galveston, Texas
Doctor or Medicine

**RESIDENCY:**

Baylor College of Medicine
Houston, Texas
Internal Medicine

**FELLOWSHIP:**

The University of Texas Health Science Center at Houston
Houston, Texas
Cardiovascular Diseases
Clinical Cardiac Electrophysiology

**CERTIFICATION:**

Diplomate of the American Board of Internal Medicine, Cardiovascular Diseases

Diplomate of the American Board of Internal Medicine, Clinical Cardiac Electrophysiology

**LICENSURE:**

Texas State Board of Medical Examiners (Since 1999)
Permit Number H9549

**HOSPITAL APPOINTMENTS:**

Attending Physician
Memorial Hermann Hospital - The Texas Medical Center
Houston, Texas

Attending Physician
The Heart and vascular Institute
Memorial Hermann Hospital - The Texas Medical Center
Houston, Texas

Consulting Physician
Select Specialty Hospital - Heights
Houston, Texas

**TEACHING RESPONSIBILITES:**

Teaching Faculty for Cardiology Fellows and Clinical Advanced Nurse Practitioners
The Heart and Vascular Institute
Memorial Hermann Hospital - The Texas Medical Center
1997 - Present

Cardiovascular Disease Lecturer
GlaxoSmithKline, Inc.
2000 - Present

Cardiovascular Disease Lecturer
Novartis, Inc.
2006 - Present

Cardiovascular Disease Lecturer
Boston Scientific, Inc.
2006 - Present

Co-Director and Lecturing Faculty
Cardiology Concepts for Non-Cardiologists
(An Annual Houston Area Educational Symposium)

JAM Institute, Inc.
2006 - 2008

Steering Committee Member and Lecturing Faculty
*Close the Gap*
Boston Scientific, Inc.
2006 - Present

**RESEARCH:**

**CLINICAL STUDIES:**

**ALLHAT: Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial.** ALLHAT ALLHAT was a blinded, randomized trial that investigated the relative efficacy of different classes of antihypertensive agents in reducing stroke, illness and death from cardiovascular diseases. A subgroup of patients with hyperlipidemia was randomized comparing Pravastatin compared to usual care.
**A Houston Site - Principal Investigator (1998)**

**INVEST: The International Verapamil SR/Trandolapril Study.** INVEST was a randomized controlled clinical trial comparing a calcium antagonist treatment strategy (Isoptin® SR) with a non calcium antagonist treatment strategy for the control of hypertension in a primary care coronary artery disease patient population.
**A Houston Site - Principal Investigator (2000)**

**INVEST SUB-STUDY:** This study was a sub-study of the INVEST patient population designed to evaluate the impact of genetic differences on pharmacokinetics.
**A Houston Site - Principal Investigator (2000)**

**The Safety and Efficacy of PNU-182716 Versus Rosiglitazone:** This was a one-year, randomized, double blind, parallel group, and active comparator study.
**A Houston Site - Principal Investigator (2000)**

**FACTOR: Fenofibrate and Cerivastatin Trial Optimizing Response.** FACTOR was a multicenter, randomized, double blind, placebo controlled, parallel group, study of the safety and efficacy of Cerivastatin in combination with Fenofibrate compared to Cerivastatin alone, Fenofibrate alone and placebo in a population of Type 2 Diabetic Men and Women.
**Grant Sponsor - Bayer 2001**
**A Houston Site - Principal Investigator**

**ADHERE:** ADHERE was a national registry of patients admitted to hospitals with acute decompensated congestive heart failure.
**A Houston Site - Principal Investigator (2001)**

**STELID TM AND STELIX TM LEADS STUDY:** This study was a
safety and efficacy study of steroid-eluting cardiac pacing leads.
**Grant Sponsor - Ella Medical 2002**

**ARRHYTHMIA PATHWAY STUDY:** This was a patient registry study designed to assess the efficacy of a clinical algorithm for identifying and assessing patients at risk of sudden cardiac arrest.
**Grant Sponsor - Medtronic, Inc. 2002**
**A Houston Site - Principal Investigator**

**RAPIDO CATHETER STUDY:** This study was to evaluate the efficacy of a left ventricular defibrillator-pacemaker lead delivery system.
**Grant Sponsor - Guidant, Inc. 2003**
**A Houston Site - Principal Investigator**

**PROTOS HEART RATE DISTRIBUTION STUDY:** This was a clinical study designed to compare the heart rate distribution in patients undergoing pacemaker implants requiring heart rate response therapy. This study compared the heart rate distribution of accelerometer rate response therapy to the BIOTRONIK Closed Loop System therapy.
**Grant Sponsor - Biotronik, Inc. 2003**
**A Houston Site - Principal Investigator**

**CSPP100A2404** - A 54 week, randomized, double-blind, parallel-group, multicenter study evaluating the long-term gastrointestinal (GI) safety and tolerability of Aliskiren (300 mg) compared to Ramipril (10 mg) in patients with essential hypertension.
Sponsored by Novartis, since April 4, 2008.
**A Houston Site - Principal Investigator**

**CSPP100AUS03** - An 8 week Prospective, Multicenter, Randomized, Double-Blind, Active Control, Parallel Group Study to Evaluate the Efficacy and Safety of Aliskiren HCTZ versus Amlodipine in African American Patients with Stage 2 Hypertension.
Sponsored by Novartis, since August 2008.
**A Houston Site - Principal Investigator**

**CSPP100A2409**- An 8 week randomized, double-blind, parallel-group, multicenter, active-controlled dose escalation study to evaluate the

efficacy and safety of Aliskiren HCTZ (300/25 MG) compared to Amlodipine (10 mg) in patients with satage 2 systolic hypertension and diabetes mellitus.
Sponsored by Novartis, since December 2008.
**A Houston Site - Principal Investigator**

**SPAlOOAUSOl -** An 8 week randomized, double-blinded, parallel-group, multicenter, active-controlled dose escalation study to evaluate the efficacy and safety of Aliskiren Administered in Combination with Amlodipine (150/5 mg, 300/10 mg) versus Amlodipine alone (5 mg, 10 mg) in African American patient with Stage 2 Hypertension.
Sponsored by Novartis, since February 2009.

**CLAF237B22Ol**- A multicenter, randomized, double-blind study to evaluate the efficacy and long-term safety of vildagliptin modifies release (MR) as monotherapy in patients with type 2 diabetes.
Sponsored by Novartis, since February 2009.
**A Houston Site - Principal Investigator**

**CLAF237B2224** - A multi-center, randomized, double-blind study to evaluate the efficacy and long-term safety of vildagliptin modified release (MR) as add-on therapy to metformin in patients with type 2 diabetes.
Sponsored by Novartis, since February 2009.
**A Houston Site - Principal Investigator**

**Galaxy study**: An aftermarket registry of one of the Biotronik implantable cardioverter defibrillators ICD leads (2009 to present)
**A Houston Site - Principal Investigator**

**Paradigm study:** A multicenter, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of LCZ696 compared to enalapril on morbidity and mortality in patients with chronic heart failure and reduced ejection fraction. 2009 -2014
**A Houston Site - Principal Investigator**

**BASIC RESEARCH:**

**In Rapid Separation of Mitochondria from Extra- mitochondrial Space Applied to Rat Heart Mitochondria.** An abstract presented at an NIH sponsored student research poster session, Univ. of Texas Medical Branch, Galveston, TX, June 17, 1987.

**Regulation of the Adenine Nucleotide Pool-Size of Heart Mitochondria by the ADP/ATP Translocase.** Abstract and poster presented at the Galveston-Houston Conference for Cardiovascular

Research, Univ. of Texas, Medical Branch, Galveston, TX, February 26, 1988.

**The Adenine Nucleotide Pool-Size of Heart Mitochondria is Regulated by the ADP/ATP Translocase.** Abstract presented at the 29th Annual National Student Research Forum, University of Texas Medical Branch, Galveston Texas, April 6-8, 1988.

**Increased Frequency of the Deletion Allele of the ACE Gene in African-Americans Compared to Caucasians**. This study evaluated the prevalence of the deletion allele of the ACE gene in a population of African Americans compared to Caucasians. The findings were presented at the annual meeting of the American College of Cardiology in March of 1996.

**Determination of the effect of Calcium infusion on CGRP mRNA Production.** A pilot study investigating a possible mechanism by which calcium supplementation may increase CGRP (Calcitonin gene-related peptide, a potent peripheral vasodilator) content in afferent neurons of Sprague Dawley rats, 1990.

**PUBLICATIONS:**

**Montgomery, B, D**, MD. A Review of Microanatomy for Medical Students, 1987, chapter 1-8.

**Baxter D. Montgomery, MD**, Elizabeth A. Putnam, Ph.D., John Reveille, MD, Dianna M. Milewicz. MD, Ph.D.: Increased Frequency of the Deletion Allele of the ACE Gene in African-Americans Compared to Caucasians. (Abstract) J. American College of Cardiology March, 1996

Doyle, N.M., Monga, M., **Montgomery, B.**, Dougherty, A.H.: Arrhythmogenic right ventricular cardiomyopathy with implantable cardioverter defibrillator placement in pregnancy. J Mat Fetal Neo Med 18:141-4, 2005

**Baxter D. Montgomery, MD Co-Author of Dreams of the nation Book:** "Improving Health" with focus on strengthening the food and health connection and replacing unnatural foods from our diet and replacing them with natural foods as a way of reversing illness. 2009

**Montgomery, Baxter D**: The Food Prescription for Better Health, Houston: Delworth Publishing, 2011

**Montgomery,B.D**, MD, Effects of the Montgomery Food Prescription on Clinical Biomarkers of Cardiovascular Disease. Plant-based diet can improve clinical biomarkers associated with cardiovascular disease. This study was submitted to the 10th annual Texas A&M University System Pathways Student Research Symposium 2012.

**Baxter D. Montgomery, MD Co-Author of the book Rethink Food:** About the need for revolutionary change in how to address chronic illness with optimal nutrition.2014

**CLINICAL PRESENTATIONS:**

Clinical Concepts for Non Cardiologist, Director and Faculty. An educational symposium held for primary care and other non-cardiology specialists in the Houston area. October 2006

Patients at Risk for Sudden Cardiac Arrest Dinner Symposium at the Houston Forum June, 2007

Clinical Concepts for Non Cardiologist, Director and Faculty. An educational symposium held for primary care and other non-cardiology specialists in the Houston area. October 2007

Clinical Concepts for Non Cardiologist, Director and Faculty. An educational symposium held for primary care and other non-cardiology specialists in the Houston area. October 2008

Houston Town Hall Meeting, Director and Faculty. Health summit on the benefits of a healthy nutritional lifestyle for the management of chronic illnesses held for both health care professional and the general public in the Houston area. 2009

Houston Town Hall Meeting, Director and Faculty. Health summit on the benefits of a healthy nutritional lifestyle for the management of chronic illnesses held for both health care professional and the general public in the Houston area. 2010

Houston Health Summit (Town Hall Meeting), Director and Faculty. Health summit on the benefits of a healthy nutritional lifestyle for the management of chronic illnesses held for both health care professional and the general public in the Houston area. 2011

Houston Health Summit (Town Hall Meeting), Director and Faculty. Health summit on the benefits of a healthy nutritional lifestyle for the management of chronic illnesses held for both health care professional and the general public in the Houston area. 2012

Houston Health Summit (Town Hall Meeting), Director and Faculty. Health summit on the benefits of a healthy nutritional lifestyle for the management of chronic illnesses held for both health care professional and the general public in the Houston area. 2013

**PROFESSIONAL APPOINTMENTS:**

Clinical Assistant Professor of Medicine, University of Texas Health Science Center - Houston 1996 - Present

Steering Committee Member, Boston Scientific Close the Gap Initiative 2005 - Present
Scientific/Medical Board of Advisors, Nutritional Excellence, Inc. 2007 - Present

Medical Board of Directors, Twelve Oaks Medical Center Independent Physician's Association 2005 - Present

Medical Executive Committee (Twelve Oaks Hospital), Member at Large 2002 - 2006

Patient Safety Committee (Twelve Oaks Hospital), Chairman 2002 - 2004

Physician Peer Review Committee (Twelve Oaks Hospital) 2002 - 2005

Medical Director, SCCI (Specialized Complex Care) Hospital, 2003 - 2005

Physician Relation Council Advisory Board, Unicare, 2002 - 2004

Aldine Education Foundation: The mission of the Aldine Education Foundation is to provide community-based support to the Aldine Independent School District in pursuit of excellence in teaching, innovation in the classroom and superior learning opportunities for all students.

**CLINICAL INTERESTS:**

Nutritional Lifestyle Interventions for the Management of Chronic Illnesses
Cardiac Pacing and Electrophysiology

Diastolic and Systolic Heart Failure
Hypertensive Heart Disease
Cardiovascular Exercise Physiology
Basic Echocardiography
Nuclear Cardiology
Diagnostic Cardiac Catheterization
Cardiovascular Wellness and Nutrition

**PROFESSIONAL ASSOCIATIONS:**

American College of Cardiology (Elected as Fellow of the College in January, 1999)
American Heart Association
Heart Rhythm Society (North American Society of Pacing and Electrophysiology, NASPE)
American College of Physicians
Harris County Medical Society
Houston Medical Forum

**HONORS AND AWARDS:**

Benjamin Spock Award for Compassion in Medicine - 2010

America's Top Physicians - 2007

Cumulative evaluation of "Superior" performance by senior house staff and faculty during first year of residency (Baylor College of Medicine), 1990

Outstanding Young Men of America, 1988

Kempner Award (University of TX Medical Branch) 1986-87 and 1987-88

Academic Scholarship (University of TX Medical Branch) 1986-87

Who's Who Among American Colleges and Universities (Rice University) 1986

Franz Brotzen Outstanding Senior Award (Rice University) 1986

Jones College Service Award (Rice University) 1986 and 1985

100 Black Men of Metropolitan Houston (Awarded in 2012) for the dedication to the improvement of the community.

Physicians Committee for Responsible Medicine- Member of Advisory Board- Current.

**ACTIVITIES:**

Gardening
Scouting
Physical Conditioning

Complementary Therapies in Medicine 45 (2019) 211–214

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# A defined, plant-based diet as a potential therapeutic approach in the treatment of heart failure: A clinical case series

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Complementary therapies

ABSTRACT

*Background:* Individuals diagnosed with congestive heart failure (CHF) have a 50% five-year mortality rate and approximately 650,000 new cases of CHF are diagnosed annually. Plant-based diets are known to improve plasma lipid concentrations, reduce blood pressure, and as part of a lifestyle intervention, lead to the regression of atherosclerotic lesions. However, a paucity of data exists with regards to plant-based diets in the treatment of CHF.

*Methods:* Three patients diagnosed with CHF opted to undergo a dietary intervention consisting of a defined plant-based diet as an adjunct to standard medical treatment for CHF. Cardiac magnetic resonance imaging was performed. Patients' consumed the defined plant-based diet for an average of ˜79 days.

*Results:* Follow-up cardiac magnetic resonance images revealed a 92% increase in ejection fraction [mean ± standard deviation for all data] (22.0 ± 6.9% vs 42.2 ± 18.4%), 21% reduction in left ventricular mass (214 ± 90 g vs 170 ± 102 g), 62% increase in stroke volume (55.8 ± 24.3 cc vs 90.3 ± 30.6 cc) and a 17% increase in cardiac output (3.6 ± 1.2 L/min vs 4.2 ± 1.6 L/min). In patient 1, 90–95% ostial stenosis of the left anterior descending artery nearly completely regressed following the dietary intervention. All patients subjectively reported significant clinical improvements, including less angina, shortness of breath and fatigue.

*Conclusion:* As an adjunct treatment, a defined plant-based diet may contribute to the reversal of cardiac morphological and functional abnormalities in the setting of CHF.

## 1. Introduction

Congestive heart failure (CHF) independently increases the risk of mortality by 50% within the first five years of diagnosis.[1] Cardiac remodeling due to increased left ventricular pressure, increased reactive oxygen species (ROS), decreased antioxidant enzymatic activity, and decreased nitric oxide (NO), may also contribute to structural remodeling of the myocardium, promoting the development of CHF.[2]

Plant-based diets have emerged as effective therapeutic interventions to treat and even reverse coronary atherosclerosis.[3,4] Both interventional and observational evidence suggests that plant-based diets may decrease the incidence and severity of CHF.[5] These positive effects may be due to decreased saturated fat and dietary cholesterol intakes, which may reduce serum cholesterol,[6,7] as well as increased phytonutrient consumption, such as antioxidants, which can reduce oxidative stress and inflammation. Indeed, previous investigations utilizing plant-based diets have demonstrated reduced inflammation, body weight and blood pressure.[8,9]

Current pharmacological therapies to treat CHF rely on modifying hemodynamics to reduce cardiac work as well as modifying cardiac signaling via neurohormonal means.[10] While these drugs prolong survival and decrease hospitalizations, these therapies have not definitely been shown to improve cardiac function and morphology. Despite compelling evidence suggesting that plant-based diets may be beneficial in the treatment of CHF, it has yet to be demonstrated in the clinical setting.[5] Presented are a case series of 3 patients with CHF and reduced ejection fraction (EF) who underwent a defined, plant-based dietary intervention to treat CHF without surgical interventions.

## 2. Methods

### 2.1. Patient presentations

A 46-year-old female (Patient 1) presented with complaints of mild

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Available online 29 June 2019

**Table 1**
Baseline characteristics.

| Patient | Patient 1 | Patient 2 | Patient 3 |
|---|---|---|---|
| Gender | Female | Male | Male |
| Ethnicity | African American | African American | African American |
| Age (y) | 46 | 58 | 70 |
| Smoking status | No | Quit 1–5 y | Quit > 20 y |
| Alcohol consumption | Occasional | No | Occasional |
| Diet | Regular | Regular | Regular |
| Exercise | No | No | No |
| BMI (kg/m$^2$) | 37.9 | 30.1 | 33.7 |
| SBP (mmHg) | 149 | 174 | 128 |
| DBP (mmHg) | 85 | 94 | 84 |
| HR (beats/min) | 74 | 69 | 57 |
| Medical history | None | Hypertension<br>Type II diabetes<br>Kidney disease | Hypertension<br>Hypercholestrolemia<br>Cardiac arrythmia |
| Medications | None | furosemide 40 mg, 1 tablet 2x/day<br>Tribenzor [olmesartan medoxomil, amlodipine & hydrochlorothiazide] 5 mg-25 mg-40 mg, 1 tablet 1x/day<br>One-A-Day Men 50 Plus, 1 tablet 1x/day | amiodarone 200 mg, 1 tablet 1x/day<br>furosemide 20 mg, 4 tablets 2x/day<br>metoprolol tartrate 50 mg, 0.5 tablets 2x/day<br>potassium chloride 8 mEq, 4 tablets 1x/day<br>simvastatin 80 mg, 0.5 tables 1x/day<br>finasteride 5 mg, 1 tablet 1x/day<br>isosorbide dinitrate 40 mg, 1 tablet 3x/day<br>lisinopril 20 mg, 1 tablet 2x/day<br>ferrous sulfate 325 mg, 1 tablet 2x/day |

Abbreviations: BMIbody mass index; SBPsystolic blood pressure; DBPdiastolic blood pressure; HRheart rate.

**Table 2**
Clinical and pharmacological changes.

| | Baseline | Final |
|---|---|---|
| BMI (kg/m$^2$) | | |
| Patient 1 | 37.9 | 34.2 |
| Patient 2 | 30.1 | 26.1 |
| Patient 3 | 33.7 | 32 |
| SBP (mmHg) | | |
| Patient 1 | 149 | 123 |
| Patient 2 | 174 | 158 |
| Patient 3 | 128 | 124 |
| DBP (mmHg) | | |
| Patient 1 | 85 | 82 |
| Patient 2 | 94 | 92 |
| Patient 3 | 84 | 73 |
| HR (beats/min) | | |
| Patient 1 | 74 | 61 |
| Patient 2 | 69 | 50 |
| Patient 3 | 57 | 64 |
| Ejection Fraction (%) | | |
| Patient 1 | 24.9 | 50 |
| Patient 2 | 27.1 | 55.6 |
| Patient 3 | 14.2 | 21.2 |
| LV Mass (g) | | |
| Patient 1 | 117.4 | 94 |
| Patient 2 | 295.18 | 286 |
| Patient 3 | 231 | 130 |
| Stroke Volume (cc) | | |
| Patient 1 | 46.6 | 100 |
| Patient 2 | 83.5 | 115 |
| Patient 3 | 37.5 | 56.1 |
| Cardiac output (L/min) | | |
| Patient 1 | 4.7 | 4.6 |
| Patient 2 | 4 | 5.6 |
| Patient 3 | 2.2 | 2.4 |
| Perscription medications (n) | | |
| Patient 1 | 0 | 6 |
| Patient 2 | 2 | 2 |
| Patient 3 | 8 | 9 |

Abbreviations: BMI, body mass index; SBP, systolic blood pressure.

chest pain, fatigue, night palpitations and shortness of breath induced by physical activity. She was not taking any medications at the time of her office visit and had no previous medical diagnoses as indicated in Table 1 detailing baseline patient characteristics. A baseline physical examination revealed a normal heart rate, normal first and second heart sounds and normal cardiac amplitude. The heart rhythm was regular and no murmurs, gallops or rubs were identified. An electrocardiogram (EKG) revealed nonspecific ST and T wave abnormalities. Based on the presented symptoms and abnormal EKG findings, cardiac magnetic resonance imaging (MRI) and a coronary angiogram were ordered. Findings from the cardiac MRI revealed a left ventricular (LV) mass of 117 g and an EF of 22.1% (Table 2). The coronary angiogram revealed a 90%–95% ostial left anterior descending coronary artery (LAD) stenosis with diffuse left main disease. The left main coronary artery was notably small compared to the LAD and circumflex arteries. This finding was consistent with the likelihood of diffuse atherosclerosis in the left main coronary artery.

A 58-year-old male (Patient 2) complained of chest pain, shortness of breath, low energy levels and edema of the lower extremities. Patient 2 reported taking furosemide (40 mg), tribenzor [olmesartan medoxomil, amlodipine & hydrochlorothiazide] (5 mg–25 mg-40 mg) and a multivitamin (Table 1). He had been previously diagnosed with hypertension, diabetes, and kidney disease. At the time of his office visit, his heart rate was normal with no abnormal sounds. An echocardiogram was performed which indicated an estimated EF of 20–25%, mild to moderate LV hypertrophy, severe LV dilation, left and right atrial enlargement and mild pulmonary and tricuspid valve regurgitation. A cardiac MRI was ordered which revealed an EF of 27.1%, and an LV mass of 295 g.

Lastly, a 70-year-old male (Patient 3) presented with complaints of shortness of breath at rest, dyspnea with minimal physical exertion, orthopnea, profuse diaphoresis, fatigue and chest pain at rest and with exertion. Patient 3 had been previously diagnosed with hypertension, hypercholesterolemia and cardiac arrhythmia. He had been prescribed 8 different medications (Table 1) to manage these conditions. His EKG showed sinus bradycardia with occasional premature ventricular complexes. The QRS duration on EKG was mildly increased. His echocardiogram estimated his EF to be 20–25% in addition to LV

enlargement, mild-moderate LV hypertrophy, restrictive diastolic dysfunction, moderate left atrial enlargement, thickened aortic and mitral valves as well as mild to moderate mitral and tricuspid valve regurgitation. A cardiac MRI also revealed an LV mass of 231 g and an EF of 14.2%.

### 2.2. Intervention

Each patient was prescribed a defined, plant-based dietary intervention (DPBD) within levels 0-4b in The Food Classification System described elsewhere.[6] The composition of the DPBD consisted of raw fruits, vegetables, avocado, seeds, with small amounts of raw oats and buckwheat. Patients were advised to eliminate the consumption of all animal products, cooked foods, free oils, soda, alcohol, and coffee.

Patient 1 was prescribed nebivolol 5 mg (1 tablet once per day), valsartan 160 mg (1 tablet once per day). ranolazine 500 mg (1 tablet twice per day), rosuvastatin 10 mg (1 tablet once per day), clopidogrel bisulfate 75 mg (1 tablet once per day) and diazepam 5 mg (1 tablet twice per day). Patient 2 was prescribed nebivolol 5 mg (1 tablet once per day) in place of furosemide. Patient 3 was prescribed spironolactone 25 mg (tablet once per day) and remained on his current medications.

## 3. Results

The DPBD was followed for 53, 88 and 95 days by Patient 1, Patient 2 and Patient 3, respectively. Each patient was mostly compliant with the nutritional intervention without adverse reactions. Overall, morphological and functional parameters of the heart improved for all 3 patients (Fig. 1). Patient 1 reported having more energy and less chest discomfort within 2 weeks of the intervention, and greater exercise tolerance within 4 weeks with full compliance. Her body mass index, blood pressure and heart rate (Table 2) dramatically improved. Her EF improved by 100%, cardiac stroke volume improved by 115%, LV mass decreased by 20% and her cardiac output was relatively unchanged. Cardiac MRI footage for Patient 1 demonstrated a clear visual improvement in LV function (Supplementary video file 1).

Additionally, stenosis of the ostial LAD coronary artery nearly completely regressed after initiating the DPBD (Fig. 2). Patient 2 reported feeling better within 4 weeks of the DPBD. He was mostly compliant and did not require any significant medication changes during his course of treatment. He experienced complete resolution of his symptoms within 5 weeks, including resolution of angina and shortness of breath. His EF improved by 105%, LV mass regressed by 3%, stroke volume improved by 38%, and cardiac output improved by 40%.

Patient 3 experienced a more complex clinical course. He was admitted to the hospital with decompensated heart failure 4 days after his initial evaluation in our clinic prior to starting the dietary intervention. He started the nutritional intervention during this hospitalization. He had decreased shortness of breath and chest discomfort and continued to have subjective improvements until 6 weeks after initiation of his dietary treatment; he suffered a clinical stroke with resolution of his symptoms in 48 h and a subsequent transient ischemic attack 2 days later. His follow-up cardiac MRI was performed during this hospitalization. In addition to having sustained improvement in his heart failure symptoms, he was found to have a 50% improvement in EF, a 44% regression in LV mass, a 19% improvement in cardiac stroke volume, and a 9% improvement in his cardiac output.

## 4. Discussion

This dietary intervention has previously been shown to significantly reduce blood pressure, heart rate and systemic inflammation.[8,9] These hemodynamic and biochemical changes suggest a possible mechanisms by which the DPBD improves cardiac function. There was a significant reduction in LV mass observed in each subject, including a 101 g regression seen in Patient 3. This large reduction in LV mass could be due

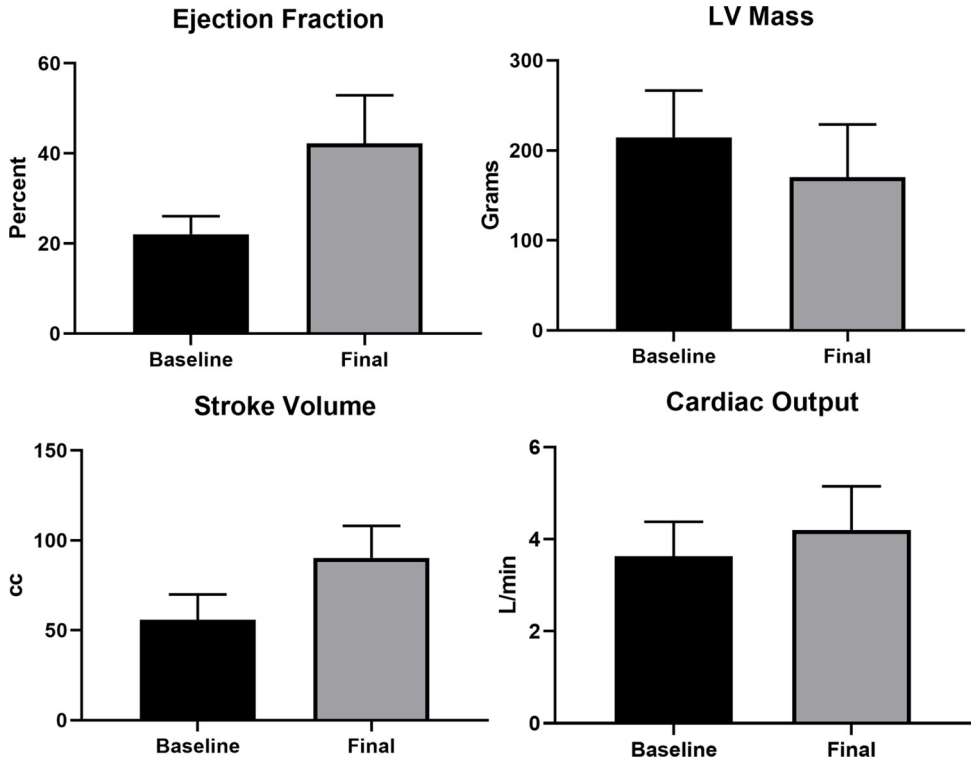


**Fig. 1.** Cardiac function and morphological changes of all patients.
Legend: Mean cardiac function and morphology of all 3 patients at baseline and final as determined by cardiac magnetic resonance imaging. Error bars are standard error of the mean.

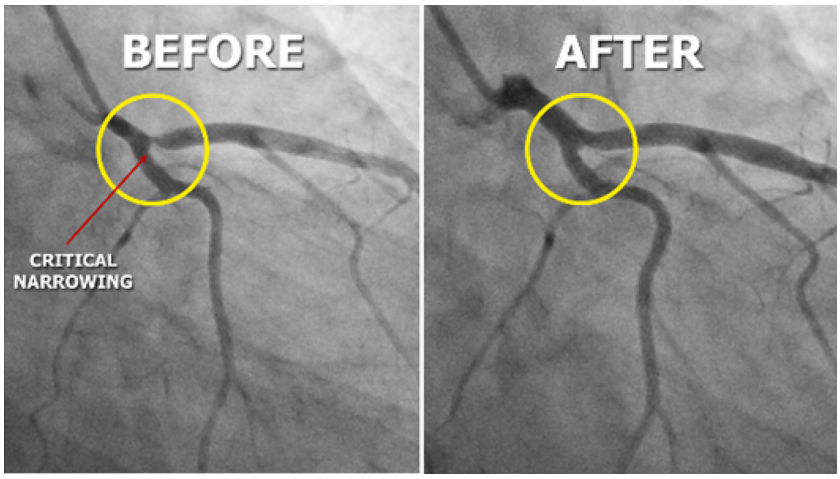


**Fig. 2.** Coronary angiogram changes for Patient 1.
Legend: Baseline coronary angiogram (left) showing diffusely small left main coronary artery with a 90–95% ostial stenosis of the left anterior descending artery. Follow up angiogram (right) showing increased luminal size of left main coronary artery with a near-total regression of ostial left anterior descending artery lesion.

to a reduction in intramyocardial edema, possibly due to reduced leukocyte infiltration causing a decrease in reactive oxygen and nitrogen species which may have ameliorated the degradation of the extracellular matrix and decreased collagen deposition.[11]

In general, the consumption of animal based foods are associated with increased oxidative stress and inflammation in humans, while plant-based foods have an inverse association.[12] These positive redox effects associated with consuming plants could result in the higher bioavailability of nitric oxide, resulting in vasodilation and a reduction in blood pressure likely due to reduced systemic vascular resistance (SVR).[13] With a reduction in SVR, stroke volume would increase, improving cardiac output and possibly reducing heart rate. None of these clinical improvements would be expected to occur with the standard medical treatments for CHF. Multicenter drug trials have not definitely shown improvements in EF, nor have these investigations demonstrated changes in physiological function of the heart to the extent that was examined here.[10,14] Hence, the DPBD resulted in both stabilization and partial reversal of advanced cardiovascular disease across a broad age spectrum of patients with differing clinical courses. Indeed, previous investigations have demonstrated that a plant-based diet can reverse coronary atherosclerosis, however, a paucity of data exists with regards to plant-based diets in the treatment of CHF.[3,4]

## 5. Conclusion

In the standard treatment of CHF, such dramatic and rapid improvements in heart morphology and function would be deemed highly improbable. However, the findings in this case series demonstrate that a plant-based diet as an adjunct to standard medical therapies may reverse certain pathophysiologic processes in heart failure. This intervention provides an outline for a potential novel therapy for heart failure with reduced ejection fraction. A larger case series or a prospective clinical trial utilizing this plant-based dietary intervention is needed to confirm these findings.

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## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ctim.2019.06.010.

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PREVENTION WILEY CLINICAL CARDIOLOGY

CLINICAL INVESTIGATIONS

# A defined, plant-based diet utilized in an outpatient cardiovascular clinic effectively treats hypercholesterolemia and hypertension and reduces medications

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**Background:** Cardiovascular disease (CVD) is a major economic burden in the United States. CVD risk factors, particularly hypertension and hypercholesterolemia, are typically treated with drug therapy. Five-year efficacy of such drugs to prevent CVD is estimated to be 5%. Plant-based diets have emerged as effective mitigators of these risk factors.

**Hypothesis:** The implementation of a defined, plant-based diet for 4 weeks in an outpatient clinical setting may mitigate CVD risk factors and reduce patient drug burden.

**Methods:** Participants consumed a plant-based diet consisting of foods prepared in a defined method in accordance with a food-classification system. Participants consumed raw fruits, vegetables, seeds, and avocado. All animal products were excluded from the diet. Participant anthropometric and hemodynamic data were obtained weekly for 4 weeks. Laboratory biomarkers were collected at baseline and at 4 weeks. Medication needs were assessed weekly. Data were analyzed using paired-samples *t* tests and 1-way repeated-measures ANOVA.

**Results:** Significant reductions were observed for systolic (−16.6 mmHg) and diastolic (−9.1 mmHg) blood pressure ($P < 0.0005$), serum lipids ($P \leq 0.008$), and total medication usage ($P < 0.0005$). Other CVD risk factors, including weight ($P < 0.0005$), waist circumference ($P < 0.0005$), heart rate ($P = 0.018$), insulin ($P < 0.0005$), glycated hemoglobin ($P = 0.002$), and high-sensitivity C-reactive protein ($P = 0.001$) were also reduced.

**Conclusion:** A defined, plant-based diet can be used as an effective therapeutic strategy in the clinical setting to mitigate cardiovascular risk factors and reduce patient drug burden.

KEYWORDS

Biomarkers, General Clinical Cardiology/Adult, Hypertension, Preventive Cardiology, Vegetarian Diet

## 1 | INTRODUCTION

Cardiovascular disease (CVD) is a major economic burden to the United States. Currently, 17% of all healthcare expenditures go toward CVD care.[1] Projections are expected to rise, as 40.5% of the US population may have some form of CVD by 2030, leading to a near tripling in medical care costs, from $273 billion to $818 billion. CVD has been the leading cause of death in the United States since 1950.[2] The standard of clinical care in the primary prevention of CVD is to reduce CVD risk factors, particularly through lipid-lowering and antihypertensive drug therapy.[3] It has been estimated that nearly 40% of the population has high serum low-density lipoprotein cholesterol (LDL-C).[4] In addition, approximately one-third of individuals age 40 to 59 years are estimated to be hypertensive.[5] Of those with hypertension (HTN), 76% are on medications to reduce blood pressure, but only 52% achieve blood-pressure control. The highest drug prices in the world are found within the United States. On average, per capita spending on prescription drugs in the United States is $858, compared with an average of $400 in 19 other industrialized countries.[6]

Patients' opinion of the efficacy of drug therapy in CVD prevention is often inflated multifold.[7,8] It has been estimated that high-risk

  

patients have a < 5% chance of benefiting from cardioprotective drugs within the next 5 years. Moreover, most patients wish to take drugs at a benefit threshold of ≥20% over 5 years.[9] Thus, if patients were aware of the actual benefit of cardioprotective drugs, many patients may not be willing to take such medications.

Based on growing evidence,[10–15] it has been recommended that physicians encourage patients to consume plant-based diets.[16] The aim of this investigation was to evaluate the effectiveness of a defined, plant-based diet as an adjunct to or replacement of prescription drugs in the treatment of hypercholesterolemia and HTN in an outpatient clinical setting.

## 2 | METHODS

### 2.1 | Study population

All subjects were registered new patients of a cardiovascular center. The study intervention was carried out in an outpatient clinical setting. All participants provided written informed consent after the study protocol and procedure had been fully explained. The study was approved by the Texas Woman's University Institutional Review Board.

Baseline characteristics of the patients are shown in Table 1. All participants were age 32 to 69 years with HTN, elevated LDL-C, and excess body weight. HTN was defined as systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg. Elevated LDL-C was considered to be a serum LDL-C concentration ≥ 100 mg/dL, and excess body weight was defined as a body mass index ≥25 kg/m$^2$.

Exclusion criteria included current tobacco use, current drug abuse, excessive alcohol use (defined as >2 glasses of wine or alcohol equivalent per day for men or >1 glass of wine or alcohol equivalent for women), a current cancer diagnosis, an ongoing clinically defined infection, a mental disability that would prevent the participant from following the study protocol, an estimated glomerular filtration rate < 60 mg/dL, current pregnancy or lactation, a hospitalization within the past 6 months, and previous exposure to the nutrition program.

### 2.2 | Screening

Eligibility was determined through initial screening of participants who expressed interest in participating in the intervention. Demographics, lifestyle habits, anthropometrics, and hemodynamics were used to determine the eligibility of participation for each subject. A trained medical assistant measured blood pressure, heart rate, and body weight. Medical history and lifestyle habits were obtained by the medical assistant and/or nurse practitioner. Fasting blood was collected by a licensed phlebotomist. The clinical care of all patients was overseen by a board-certified cardiologist.

### 2.3 | Weekly visits

After subjects were screened for study inclusion, follow-up appointments were arranged for study enrollment. Participants were instructed to attend 4 follow-up weekly office visits in addition to a baseline assessment. Baseline weight, blood pressure, heart rate,

**TABLE 1** Baseline patient demographics and clinical diagnoses

| | Participants, n = 31 |
|---|---|
| Mean age, y | 53.4 (32–69) |
| Sex | |
| M | 10 (33) |
| F | 21 (67) |
| Race/ethnicity | |
| African American | 25 (80) |
| Hispanic | 3 (10) |
| White | 3 (10) |
| BMI, kg/m$^2$ | 37.5 ± 8.3 |
| 25–29.9 (overweight) | 6 (19) |
| 30–34.9 (obese class 1) | 6 (19) |
| 35–39.9 (obese class 2) | 10 (33) |
| ≥40 | 9 (29) |
| Current diagnoses | |
| CAD | 10 (33) |
| T2DM | 8 (27) |
| Arthritis | 7 (23) |
| Prediabetes | 5 (17) |
| Medications, n | |
| BP medications, total | 49 |
| ACEI | 5 |
| ARB | 11 |
| Central antiadrenergic | 1 |
| Cardioselective (β1)-blocker | 6 |
| Noncardioselective (β1)-blocker | 2 |
| CCB | 9 |
| Potassium-sparing diuretic | 1 |
| Thiazide diuretic | 14 |
| Other prescription drugs, total | 33 |
| Biguanide | 2 |
| Sulfonylurea | 3 |
| Dipeptidylpeptidase-4 inhibitor | 1 |
| Insulin | 2 |
| NSAID | 1 |
| Biologic immune suppressant | 1 |
| Statin | 2 |
| Bronchodilator/steroid inhaler | 5 |
| Thyroid drugs | 3 |
| Xanthine oxidase inhibitor | 2 |
| PPI | 1 |
| Antiplatelet | 1 |
| Antianginal | 2 |
| Digitalis glycoside | 1 |
| Vasodilator | 1 |
| Other | 5 |
| Total medications | 82 |

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; BMI, body mass index; BP, blood pressure; CAD, coronary artery disease; CCB, calcium channel blocker; F, female; M, male; NSAID, nonsteroidal anti-inflammatory drug; PPI, proton pump inhibitor; SD, standard deviation; T2DM, type 2 diabetes mellitus. Unless otherwise noted, data are presented as n (%) or mean ± SD (range).

waist circumference, medications, and biochemical indicators were documented. A baseline 24-hour dietary recall was conducted by a trained nutritionist with the utilization of food models to verify portion sizes of foods and beverages consumed. Nutrient intake was analyzed by the Nutrition Data System for Research software, version 2016 (University of Minnesota, Minneapolis).

Follow-up visits (weeks 1–4) consisted of obtaining weight, blood pressure, heart rate, and waist circumference. Medications were assessed and adjusted as needed by the medical doctor or nurse practitioner during the follow-up visits. The final visit (week 4) consisted of a second 24-hour dietary recall and a second collection of fasting blood to assess biochemical measures.

## 2.4 | Medications

Medications were documented following the conclusion of each office visit. All medications listed at baseline were chronic stable medications (>3 months), except for medications changed during the baseline office visit as outlined in the protocol below. All other medication changes were documented in the medication tracking of this study. No lipid-lowering medications were added at the onset or during the study. The medication needs-assessment protocol is as follows:

- Baseline: All nonessential medications and supplements were discontinued. Additionally, diuretics were discontinued in patients who were clinically euvolemic. Insulin, sulfonylureas, and other potential glucose-lowering medications were either removed or the dosage was decreased in patients whose glucose levels were routinely below 250 mg/dL. All baseline medications are indicated in Table 1.
- Week 1 follow-up: If a patient's blood pressure was low and the patient had symptoms of dizziness or fatigue associated with low blood pressure, then blood pressure medications were decreased by 25% to 50%. Other medications were reviewed with consideration of removal based on patient needs (eg, hypoglycemics).
- Week 2 follow-up: The patients' clinical response to the diet was reevaluated and medication adjustments were made according to their clinical response. Medications primarily prescribed for symptom management were assessed (eg, sleep, allergies, mood disorders, pain) and discontinued if necessary.
- Weeks 3 and 4 follow-up: Based on the patients' clinical response to the dietary intervention, changes were made to the medications as needed for the remainder of the intervention.

## 2.5 | Dietary protocol

Participants were instructed to follow a defined plant-based dietary intervention for 4 weeks. A food classification system using a scale of 0 to 10 was devised to create a simple, reproducible way of prescribing a nutritional regimen to patients in the clinical setting (Table 2). Participants were instructed to consume foods within this food classification system. Food levels 0 through 4B were permitted, whereas all other food levels were excluded. Briefly, food levels 0 through 4B exclude all animal products, with the exception of honey. Cooked foods, free oils, soda, alcohol, and coffee were also excluded. Emphasized were raw fruits and vegetables, with avocado and raw seeds

**TABLE 2** The food classification system

| Food Level | Description |
|---|---|
| 0 | Liquids including water, tea, unpasteurized fruit and vegetable juices, and blended fruit and vegetable smoothies. These foods would be consumed raw, except for tea, which can be steeped in hot water. |
| 1 | Raw fruits and vegetables with a low glycemic index (<56) |
| 2 | Raw fruits and vegetables with a medium to low GI (56–70) |
| 3 | Raw fruits and vegetables with a high GI (>70) |
| 4A | Plant foods that are raw with a high fat content (≥20% of caloric content from fat), such as raw seeds and avocados |
| 4B | Plant foods that are dehydrated to temperatures ≤160°F |
| 4C | Plant foods that are dried, dehydrated, or warmed (dry-heat cooking) at 160°F–175°F, or steamed or boiled for a short duration (steaming, <4 min; boiling, <10 min). Includes lightly steamed, soaked, sprouted, dehydrated, or warmed fruits, vegetables, legumes or beans, and grains. Heated foods with >20% of calories from fat are excluded. |
| 5 | Foods that are warmed, dried, or dehydrated at 175°F to 200°F, and steamed or boiled for a medium duration (steaming, 4–10 min; boiling, 10–45 min). Typical foods include greens, beans and legumes, and starches, including grains, bean or mixed-vegetable soups, and other fruit and vegetables boiled for up to 45 min or oven-warmed (at 155°F–200°F). Heated foods with >20% of calories from fat are excluded. |
| 6 | Foods that are baked, warmed, dried, or dehydrated at >200°F, or steamed or boiled for a long duration (steaming, >10 min; boiling, >45 min). Heated foods with >20% of calories from fat are excluded. |
| 7 | Fish with low mercury content lightly steamed or poached for ≤8 min. Processed plant foods with preservatives or additives, free oils, and heated foods with >20% calories from fat are included. |
| 8 | Same as level 7, except also includes wild-game meats, low-mercury fish lightly steamed or poached for >8 min, and plant-based foods that are grilled or heavily processed. May also include carbohydrates with white flour or white rice, or natural foods that have been stripped of their natural components. |
| 9 | Animal-based foods that include domestically raised animals (excluding beef and pork) and plant-based foods that are sautéed, stir-fried, medium-fried or deep-fried in oil. Other animal-based foods include all other types of fish. May also include foods containing dairy products. |
| 10 | All other types of animal-based foods, and plant-based foods prepared in any way. May include processed foods of any kind. |

Abbreviations: F, Fahrenheit; GI, glycemic index. Food classification levels 0 through 4B were permitted for consumption during the dietary intervention; levels >4B were excluded from the intervention. Sodium consumption was low, although the food provided to patients contained small amounts of sea salt.

provided as condiments. All meals and snacks were provided at no cost to the participants for the full duration of the 4-week intervention. Vitamin, herbal, and mineral supplements were to be discontinued unless otherwise clinically indicated. Participants were not advised to alter their exercise habits, nor were exercise habits monitored.

Participants were free to consume foods outside of what was provided, as long as the foods fell within food levels 0 through 4B. No caloric targets were prescribed, nor were any macronutrient restrictions advocated; participants were free to consume food ad libitum. Participants were also instructed to track dietary adherence with a daily adherence-assessment tool. Participants indicated in writing each day whether they were "100% on the diet" or "ate anything off of the diet." The number "1" was assigned to an adherent day, and "0" was assigned to a nonadherent day. Scores after 4 weeks could therefore range from 0 to 28 points for each participant. Evaluation of the adherence-assessment tool was conducted during each weekly follow-up visit by a trained nutritionist.

### 2.6 | Biochemical measures

After a 12-hour fast during the baseline and final office visits, the following serum biomarkers were obtained: total cholesterol, LDL-C, high-density lipoprotein cholesterol, triglycerides, insulin, glucose, glycated hemoglobin ($HbA_{1c}$), and high-sensitivity C-reactive protein (hs-CRP). These specific biomarkers of interest were analyzed by either True Health Diagnostics (Frisco, TX) or Singulex (Alameda, CA), depending on the subject's insurance. The same company that analyzed the baseline laboratory tests for a participant was used for the follow-up testing to ensure assay consistency.

Serum lipids were measured by enzymatic colorimetric assay, and insulin was measured by a no-competitive sandwich-type enzyme-linked immunosorbent assay with electrochemical detection for both True Health Diagnostics and Singulex. Glucose was measured by an enzymatic reference method with hexokinase using colorimetric detection, and hs-CRP was measured by a particle-enhanced immunoturbidometric assay for both Singulex and True Health Diagnostics. $HbA_{1c}$ was measured by a turbidometric inhibition immunoassay for Singulex. Boronate affinity chromatography was used by True Health Diagnostics for $HbA_{1c}$.

### 2.7 | Statistical analysis

Paired-samples *t* tests were used for the analysis of biochemical and nutrient intake means. A one-way repeated-measures ANOVA was used to analyze the means for anthropometric, hemodynamic, and medication data. Significance was set at a $P$ value of $< 0.05$. SPSS version 24 (IBM Corp., Armonk, NY) was used for data analysis.

## 3 | RESULTS

### 3.1 | Demographics

During screening, a total of 65 patients showed interest in participating in the study; however, 30 patients did not meet inclusion criteria or were excluded. Two individuals were unable to participate due to scheduling conflicts. Although 33 participants initially enrolled into the study, 2 participants were either lost to contact (n = 1) or no longer wished to follow the dietary protocol (n = 1). One participant refused to complete the final 24-hour dietary recall during week 4 due to time availability. Thus, a total of 31 participants provided clinical data and 30 participants provided nutrient intake data.

Based on clinical diagnoses and medical history, 33% of participants had coronary artery disease and 44% were either prediabetic ($HbA_{1c}$ 5.7%–6.4%) or had diabetes mellitus ($HbA_{1c} \geq 6.5\%$; (Table 1). The average body mass index was 37.5 $kg/m^2 \pm 8.3$ $kg/m^2$, and approximately 81% of the participants were obese.

### 3.2 | Nutrient intake

Nutrient intake of participants on the defined, plant-based diet significantly changed after 4 weeks (Table 3). Significant reductions in energy intake, saturated fat as a percent of energy, dietary cholesterol, protein as a percent of energy, total fat, monounsaturated and polyunsaturated fat as a percent of energy, trans fat, vitamin D, vitamin B12, calcium, zinc, and sodium were observed after 4 weeks. Carbohydrate intake as a percent of energy, vitamin A, vitamin C, folate, dietary fiber, magnesium, and potassium intake increased significantly after 4 weeks. Patients anecdotally reported overall satisfaction with the food provided during the clinical follow-ups, and no significant symptoms of increased hunger were reported.

### 3.3 | Clinical variables

Anthropometric and hemodynamic characteristics, as well as medications, changed significantly ($P \leq 0.018$) from baseline to 4 weeks (Table 4). Adherence was well maintained over the 4-week period. Overall, participants were noncompliant for 3.6 out of 28 days. There were no significant differences between subjects with 100% adherence and lower-adherent subjects. Participants lost on average a total of 6.7 kg (14.7 lbs.) after 4 weeks on the defined plant-based diet (Table 4). SBP and DBP decreased by 16.6 mmHg and 9.1 mmHg, respectively. The reduction in blood pressure was accompanied with a decreased use of blood pressure medications (decreased 33% by week 4). Additionally, those taking hypoglycemic drugs, including insulin, reduced medication usage by 87%. Overall, total medication usage decreased 40% by week 4.

### 3.4 | Biomarkers

All biochemical changes were significant ($P \leq 0.037$) at 4 weeks compared with baseline, with the exception of the total cholesterol to high-density lipoprotein cholesterol ratio ($P = 0.068$) and glucose ($P = 0.25$; Table 5). Although fasting glucose was not significantly reduced, $HbA_{1c}$ was significantly reduced ($P = 0.002$).

The distribution of high-interest clinical variable changes during the intervention are displayed in Supporting Information, Figure, in the online version of this article.

**TABLE 3** Nutrient intake[b]

| | Baseline | Final | Change, %[a] | *P* Value[c] |
|---|---|---|---|---|
| Energy, Kcal | 2053 ± 873 | 1369 ± 488 | −33 (−683 ± 808) | <0.0005 |
| Fat, % of energy | 36.4 ± 10.4 | 19.0 ± 8.9 | −48 (−17.3 ± 12.8) | <0.0005 |
| Saturated fat, % of energy | 11.6 ± 4.5 | 3.8 ± 2.7 | −67 (−7.7 ± 5.5) | <0.0005 |
| Monounsaturated fat, % of energy | 13.2 ± 4.8 | 7.0 ± 3.9 | −47 (−6.2 ± 5.4) | <0.0005 |
| Polyunsaturated fat, % of energy | 8.4 ± 5.6 | 5.4 ± 2.7 | −36 (−3.0 ± 3.5) | <0.0005 |
| Omega-6, g | 18.5 ± 11.1 | 6.0 ± 4.7 | −67 (−12.4 ± 10.6) | <0.0005 |
| Omega-3, g | 2.11 ± 1.60 | 2.14 ± 1.95 | 1 (0.03 ± 2.16) | 0.92 |
| Omega-6/omega-3[d] | 9.8 ± 3.7 | 4.3 ± 3.0 | −56 (−5.5 ± 3.8) | <0.0005 |
| Trans fat, g | 2.25 ± 1.97 | 0.04 ± 0.09 | −99 (−2.21 ± 2.00) | <0.0005 |
| Cholesterol, mg | 295.4 ± 211.7 | 12.2 ± 56.2 | −96 (−283.2 ± 214.8) | <0.0005 |
| Carbohydrate, % of energy | 46.3 ± 14.0 | 72.6 ± 11.3 | 57 (26.3 ± 17.0) | <0.0005 |
| Protein, % of energy | 16.5 ± 6.4 | 7.5 ± 2.1 | −54% (−9.0 ± 6.1) | <0.0005 |
| Total fiber, g | 20.4 ± 11.9 | 51.0 ± 17.7 | 150 (30.6 ± 17.8) | <0.0005 |
| Total vitamin A activity, IU | 8265 ± 9258 | 33387 ± 19052 | 303 (25 121 ± 21 876) | <0.0005 |
| Vitamin D, IU | 159.1 ± 154.3 | 12.3 ± 30.4 | −92 (−146.8 ± 161.8) | <0.0005 |
| Vitamin E, mg | 9.9 ± 6.3 | 10.5 ± 5.6 | 6 (0.6 ± 6.4) | 0.60 |
| Vitamin C, mg | 87.7 ± 108.8 | 412.7 ± 164.7 | 370 (325.0 ± 197.3) | <0.0005 |
| Vitamin B12, μg | 4.0 ± 1.9 | 0.3 ± 0.8 | −92 (−3.6 ± 2.3) | <0.0005 |
| Folate, μg | 298 ± 229 | 741 ± 298 | 115 (343 ± 329) | <0.0005 |
| Iron, mg | 15.4 ± 7.2 | 15.3 ± 6.9 | −1 (−0.1 ± 9.9) | 0.97 |
| Calcium, mg | 796 ± 438 | 566 ± 279 | −29 (−229 ± 527) | 0.024 |
| Sodium, mg | 3730 ± 1783 | 839 ± 778 | −76 (−2891 ± 1776) | <0.0005 |
| Magnesium, mg | 288.1 ± 119.9 | 488.1 ± 186.0 | 69 (200.0 ± 178.0) | <0.0005 |
| Zinc, mg | 12.2 ± 5.9 | 7.8 ± 3.4 | −76 (−4.4 ± 7.0) | 0.002 |
| Potassium, mg | 2668 ± 1190 | 5078 ± 1758 | 90 (2410 ± 1764) | <0.0005 |

Data are presented as mean ± standard deviation unless otherwise indicated.

[a] Data are presented as percent change (mean ± standard deviation).

[b] Data are for subjects who completed 24-hour recalls at both baseline and 4 weeks and do not include dietary supplements (n = 30).

[c] Paired samples *t* tests for within-group comparisons of changes from baseline to final values.

[d] Values indicate a ratio.

**TABLE 4** Change of anthropometrics, hemodynamics, medications, and adherence over 4 weeks

| | Baseline | Week 1 | Week 2 | Week 3 | Week 4 | *P* Value[a] |
|---|---|---|---|---|---|---|
| Weight, kg, mean ± SE | 108.1 ± 5.1 | 105.4 ± 4.8[b] | 103.9 ± 4.8[b] | 102.6 ± 4.7[b] | 101.4 ± 4.7[b] | <0.0005 |
| BMI, kg/m$^2$ | 37.5 ± 1.4 | 36.5 ± 1.4[b] | 36.0 ± 1.4[b] | 35.6 ± 1.4[b] | 35.2 ± 1.4[b] | <0.0005 |
| WC, cm | 111.9 ± 2.5 | 109.2 ± 2.5[b] | 107.6 ± 2.5[b] | 106.3 ± 2.5[c] | 105.3 ± 2.5[b] | <0.0005 |
| SBP, mm Hg | 146.6 ± 2.8 | 131.9 ± 2.8[b] | 127.0 ± 2.4 | 129.5 ± 1.9 | 130.0 ± 2.3 | <0.0005 |
| DBP, mm Hg | 91.2 ± 1.3 | 81.5 ± 1.4[b] | 79.0 ± 1.3 | 82.1 ± 1.2 | 82.1 ± 1.2 | <0.0005 |
| BP medications | 1.6 ± 1.1 | 1.6 ± 1.0 | 1.4 ± 1.0[d] | 1.1 ± 1.0[d] | 1.0 ± 0.1 | <0.0005 |
| Heart rate, bpm | 69.8 ± 1.8 | 71.8 ± 1.9 | 68.4 ± 1.7 | 68.1 ± 1.7 | 66.2 ± 1.2 | 0.018 |
| Other prescription drugs | 1.0 ± 1.4 | 1.0 ± 1.4 | 0.9 ± 1.5 | 0.6 ± 0.9 | 0.5 ± 0.9 | 0.008 |
| Total medications | 2.6 ± 2.0 | 2.7 ± 2.0 | 2.3 ± 2.0[d] | 1.8 ± 1.6 | 1.6 ± 1.3 | <0.0005 |
| Adherence, d/wk[e] | — | 6.32 ± 0.19 | 6.03 ± 0.25 | 6.06 ± 0.27 | 5.96 ± 0.27 | 0.531 |

Abbreviations: ANOVA, analysis of variance; BMI, body mass index; BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure; SE, standard error; WC, waist circumference.

[a] Repeated-measures 1-way ANOVA with a Greenhouse–Geisser correction due to violation of Mauchly's test of sphericity ($P > 0.05$).

[b] $P \leq 0.001$ compared with previous week.

[c] $P \leq 0.01$ compared with previous week.

[d] $P \leq 0.05$ compared with previous week (all pairwise comparisons were determined by post hoc analysis with a Bonferroni adjustment).

[e] Measured by weekly adherence-assessment tool. Values represent the number of days on average that adherence was 100% out of 1 week (7 days).

## 4 | DISCUSSION

Four weeks of a defined, plant-based dietary intervention resulted in clinically significant reductions in SBP, DBP, blood pressure medication usage, total medication usage, and serum lipids. Statistically significant reductions were also observed for other CVD risk factors, including body weight, heart rate, waist circumference, insulin, $HbA_{1c}$, and hs-CRP. This intervention demonstrated that a plant-based diet can be used effectively in the clinical setting with profound results. Additionally, subjects were able to transition from a standard American diet to the plant-based diet outlined in this intervention with good adherence. Physician advice can significantly impact the dietary choices of patients,[17] as demonstrated in this trial.

Although weight was reduced, this likely did not contribute fully to the reduction in blood pressure. A recent Cochrane review of randomized trials lasting ≥24 weeks examined the effects of weight loss on blood pressure and concluded that a 4-kg reduction in weight resulted in a 4.5-mmHg and 3-mmHg reduction in SBP and DBP, respectively.[18] Results from this review would underestimate expected outcomes of this trial. In comparison, participants in the present study lost 6.7 kg and reduced SBP and DBP by 16.6 mmHg and 9.1 mmHg, respectively. These findings are striking considering that blood pressure medications were reduced by 33% by week 4 and blood pressure nearly normalized. Participants' blood pressure was better even when discontinuing medications, which may indicate superiority of the dietary intervention over drug therapy. The reduction in blood pressure by this nutritional intervention was due to a variety of contributing factors, which may include a reduction in hs-CRP (−2.4 ± 3.7 mg/L)[19] and increased consumption of nitrates,[20] potassium,[21] and magnesium.[22] Increased dietary fiber,[23] phytosterols,[24] and polyphenols[25] also likely contributed to reduced serum lipids in addition to the exclusion of animal-based foods.[26]

It is interesting to note that fasting blood glucose was not significantly reduced ($P = 0.25$), yet $HbA_{1c}$ was significantly reduced ($P = 0.002$). It is likely that reduced postprandial glucose fluctuations accounted for this decrease in $HbA_{1c}$, although this was not directly tested. It has been previously demonstrated that $HbA_{1c} < 7\%$ is mostly influenced by postprandial glucose.[27] The average $HbA_{1c}$ of this sample was 5.9%; therefore, postprandial blood glucose would likely play a more significant role.

Other similar plant-based dietary trials have also demonstrated reduced CVD risk factors. In a 4-week randomized trial comparing a low-fat, plant-based diet to an American Heart Association diet, Macknin et al[28] reported significant reductions in weight (3.64 ± 3.41 kg), SBP (7.96 ± 12.28 mmHg), and LDL-C (27.00 ± 26.72 mg/dL) compared with baseline in adults on the plant-based diet. Bloomer et al[29] conducted a trial in which subjects consumed a plant-based diet for 3 weeks. Despite normal baseline clinical indicators, large reductions were observed in LDL-C (22.3 mg/dL), SBP (8.8 mmHg), and DBP (5.2 mmHg).

Jenkins et al[30] fed 3 weight-maintaining diets for 2 weeks that were low in saturated fat to participants with elevated LDL-C (~115 mg/dL at baseline). The dietary groups included a conventional low-fat diet, a vegetarian diet high in complex carbohydrates, and a raw vegan diet similar to that of the present study. Significant differences in changes of serum LDL-C were observed between these dietary groups. The conventional low-fat diet reduced LDL-C by 8 mg/dL, the starch-based vegetarian diet reduced LDL-C by 27 mg/dL, and the raw vegan diet reduced LDL-C by 38 mg/dL ($P < 0.001$). Thus, a raw plant-based diet may result in greater reductions in serum lipids than one that includes cooked complex carbohydrates.

**TABLE 5** Change in biochemical variables after 4 weeks

| | Baseline | Final | Change | *P* Value[a] |
|---|---|---|---|---|
| TC, mg/dL | 216.6 ± 34.2 | 182.7 ± 29.9 | −33.8 ± 25.9 | <0.0005 |
| LDL-C, mg/dL | 143.0 ± 28.9 | 118.4 ± 26.4 | −24.6 ± 21.3 | <0.0005 |
| HDL-C, mg/dL | 54.8 ± 9.4 | 49.5 ± 10.6 | −5.2 ± 6.2 | <0.0005 |
| TC/HDL[b] | 4.04 ± 0.88 | 3.81 ± 0.88 | −0.22 ± 0.64 | 0.068 |
| TG, mg/dL | 124.1 ± 58.1 | 104.5 ± 53.6 | −19.6 ± 38.4 | 0.008 |
| Insulin, uIU/mL | 14.6 ± 7.6 | 10.3 ± 7.6 | −4.2 ± 5.1 | <0.0005 |
| Glucose, mg/dL | 90.1 ± 12.0 | 87.1 ± 4.7 | −2.9 ± 14.0 | 0.25 |
| $HbA_{1c}$, % | 5.9 ± 0.5 | 5.7 ± 0.3 | −0.2 ± 0.3 | 0.002 |
| hs-CRP, mg/L | 7.8 ± 6.4 | 5.3 ± 4.7 | −2.4 ± 3.7 | 0.001 |

Abbreviations: $HbA_{1c}$, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; hs-CRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; SD, standard deviation; TC, total cholesterol; TG, triglycerides. Data are presented as mean ± SD; n = 31.

[a] Paired-samples *t* tests for within-group comparisons of changes from baseline to final values.

[b] Values indicate a ratio.

### 4.1 | Study strengths and limitations

Several strengths of the present study should be noted. First, the utilization of the food classification system allows for reproducibility in other clinical practices and trials, as the food selection type, preparation, and degree of processing is detailed. Second, the utilization of a prescribed nutrition program in an outpatient cardiovascular clinic allows for the close assessment of the patient's clinical response to the diet. This was facilitated by weekly office visits that allowed for medication weaning as needed. In addition, the provision of food to participants helped facilitate adherence to the dietary protocol. Although there were no statistical differences between high- and low-adherent subjects, a lack of statistical power may be present due to a reduced sample size when groups were divided based on adherence. Additionally, strict adherence standards may also have required a larger sample size for statistical significance to be apparent between groups. A single bite or drink of any food outside of the prescribed diet counted against adherence for the day, even if the remainder of the day represented complete dietary compliance. Lastly, the range of reported dependent variables represents meaningful clinical indicators often evaluated in cardiology practices across the United States. These clinical indicators are most commonly used in the assessment of CVD risk. Thus, this study has real-world applicability in the clinical setting.

Limitations of the current study include the small sample size, lack of a control group, and short duration of follow-up. Although the sample size was small, the large effect sizes indicate that the sample size was more than sufficient for adequate power of the primary endpoints. Further research is needed to determine whether medications,

serum lipids, and blood pressure would continue to decrease if the diet were consumed for an extended period of time. In addition, extended trials are needed to assess long-term adherence to the diet. Lastly, inclusion of periodic postprandial glucose testing during the intervention may help establish a potential relationship between postprandial glucose fluctuations and reduced $HbA_{1c}$.

## 5 | CONCLUSION

A defined plant-based diet can be used as an effective therapeutic approach in the clinical setting in the treatment of HTN, hypercholesterolemia, and other cardiovascular risk factors while simultaneously reducing overall medication usage. Patients may find this therapeutic approach preferable to conventional and costly drug therapy. Further replication trials are needed with larger sample sizes, control groups, and other dietary comparison groups.

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### Conflicts of interest

The authors declare no potential conflicts of interest.

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## SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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WILEY CLINICAL CARDIOLOGY

CLINICAL INVESTIGATIONS

# Consumption of a defined, plant-based diet reduces lipoprotein(a), inflammation, and other atherogenic lipoproteins and particles within 4 weeks

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**Background:** Lipoprotein(a) [Lp(a)] is a highly atherogenic lipoprotein and is minimally effected by lifestyle changes. While some drugs can reduce Lp(a), diet has not consistently shown definitive reduction of this biomarker. The effect of consuming a plant-based diet on serum Lp(a) concentrations have not been previously evaluated.

**Hypothesis:** Consumption of a defined, plant-based for 4 weeks reduces Lp(a).

**Methods:** Secondary analysis of a previous trial was conducted, in which overweight and obese individuals ($n$ = 31) with low-density lipoprotein cholesterol concentrations >100 mg/dL consumed a defined, plant-based diet for 4 weeks. Baseline and 4-week labs were collected. Data were analyzed using a paired samples $t$-test.

**Results:** Significant reductions were observed for serum Lp(a) (−32.0 ± 52.3 nmol/L, $P$ = 0.003), apolipoprotein B (−13.2 ± 18.3 mg/dL, $P$ < 0.0005), low-density lipoprotein (LDL) particles (−304.8 ± 363.0 nmol/L, $P$ < 0.0005) and small-dense LDL cholesterol (−10.0 ± 9.2 mg/dL, $P$ < 0.0005). Additionally, serum interleukin-6 (IL-6), total white blood cells, lipoprotein-associated phospholipase A2 (Lp-PLA2), high-sensitivity c-reactive protein (*hs*-CRP), and fibrinogen were significantly reduced ($P \leq 0.004$).

**Conclusions:** A defined, plant-based diet has a favorable impact on Lp(a), inflammatory indicators, and other atherogenic lipoproteins and particles. Lp(a) concentration was previously thought to be only minimally altered by dietary interventions. In this protocol however, a defined plant-based diet was shown to substantially reduce this biomarker. Further investigation is required to elucidate the specific mechanisms that contribute to the reductions in Lp(a) concentrations, which may include alterations in gene expression.

KEYWORDS

general clinical cardiology/adult, lipoproteins, preventive cardiology, vegetarian diet

## 1 | INTRODUCTION

Lipoprotein(a) [Lp(a)] is an atherogenic lipoprotein structurally similar to low-density lipoprotein cholesterol (LDL-C), although synthesis occurs through independent pathways. Key differences include the linkage of apolipoprotein B100 (Apo-B) to apolipoprotein(a) on the LDL surface.[1,2] It has been estimated that expression of the genomic region encoding apolipoprotein(a) (*LPA* gene) accounts for approximately 90% of plasma Lp(a) concentrations.[3] Elevated Lp(a) is independently associated with cardiovascular disease,[4] and the LPA gene was observed to have the strongest genetic link to cardiovascular disease.[5] Individuals with Lp(a) plasma concentrations >20 mg/dL have twice the risk of developing cardiovascular disease and approximately 25% of the population may have this plasma concentration.[6] The mode of action by which Lp(a) exerts its atherogenic effect is likely similar to that of LDL-C, by deposition in the sub-endothelial space and uptake by macrophages mediated via the VLDL receptor.[7] Lp(a) is particularly atherogenic due to its unique property of being a carrier of oxidized phospholipids, in addition to its higher binding affinity to negatively charged endothelial proteoglycans.[8] Lp(a) can facilitate

  

endothelial dysfunction when concentrations are elevated likely due to this effect.[9]

While PCSK9 inhibitors, high dose atorvastatin, ezetimibe and niacin have resulted in significant reductions in Lp(a),[10–12] lifestyle interventions have not reliably demonstrated reduced Lp(a) to a clinically significant degree. Interestingly, even high saturated fat and high cholesterol diets known to induce hypercholesterolemia have had little influence on plasma Lp(a) concentrations.[13] Despite the lack of evidence in the literature indicating a relationship between diet and Lp(a) concentrations, a defined, plant-based has not been previously evaluated with respect to its potential effect to reduce Lp(a). Previous investigations have found that a very-high fiber diet comprised of vegetables, fruits and nuts can reduce LDL-C by 33% and Apo-B by 26%,[14] although Lp(a) was not measured. Since such a diet can result in dramatic reductions in LDL-C and Apo-B, secondary analysis of a previously published investigation[15] employing a similar plant-based diet were analyzed to evaluate if Lp(a) could be significantly reduced after 4 weeks among other inflammatory indicators and atherogenic lipoproteins and particles.

## 2 | METHODS

### 2.1 | Study population

Participants were subjects of a previous study in which written informed consent was obtained to draw blood for analysis.[15] Laboratory reports for each subject included biomarkers used for clinical purposes, and selected biomarkers are included in the present investigation. The study protocol was approved by the Texas Woman's University Institutional Review Board, Houston.

The study protocol has been previously described.[15] Briefly, all participants were registered new patients of a cardiovascular center and were hypertensive (systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg), had elevated LDL-C (≥100 mg/dL) and excess body weight (body mass index ≥25 kg/m$^2$) at baseline. Exclusionary criteria included current tobacco use, current drug abuse, excessive alcohol use (>2 glasses of wine or equivalent for men or > 1 glass of wine or equivalent for woman), a current cancer diagnosis, an ongoing clinically defined infection, a mental disability that would prevent a participant from following the study protocol, an estimated glomerular filtration rate < 60 mg/dL, current pregnancy or lactation, a hospitalization within the past 6 months, and previous exposure to the nutrition program.

### 2.2 | Intervention

Participants were instructed to consume a defined, plant-based diet for 4 weeks ad-libitum which included the consumption of foods within a food classification system.[15] These foods fell within food levels 0 to 4b of the food classification system (Table S1, Supporting information). Briefly, excluded were animal products, cooked foods, free oils, soda, alcohol, and coffee. Allowed for consumption were raw fruits, vegetables, seeds, and avocado. Small amounts of raw buckwheat and oats were also permitted. Vitamin, herbal, and mineral supplements were to be discontinued unless otherwise clinically indicated. All meals and snacks were provided to subjects, although they were free to consume food on their own within food levels 0 to 4b. In addition, subjects were not advised to alter their exercise habits. Adherence was measured daily as previously described[15] with an adherence assessment tool. Participants indicated in writing each day whether they were adherent. Dietary recalls (24-hour) were conducted by a trained nutritionist at baseline and at 4 weeks. Nutrient intake was analyzed by the Nutrition Data System for Research software (University of Minnesota, version 2016). No lipid lowering medications were altered throughout the intervention.

### 2.3 | Measures

After a 12-hour fast, the following plasma biomarkers were obtained at baseline and after 4-weeks: total cholesterol (Total-C), LDL-C, high-density lipoprotein cholesterol (HDL-C), triglycerides, LDL particles (LDL-P), small-dense low-density lipoprotein cholesterol (sdLDL-C), Apo-B, high-density lipoprotein 2 cholesterol (HDL2-C), apolipoprotein A-1 (Apo A-1), and Lp(a). Additionally, high-sensitivity c-reactive protein (*hs*-CRP), endothelin, interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-a), lipoprotein-associated phospholipase A2 (Lp-PLA2), myeloperoxidase, fibrinogen, troponin-I, N-terminal pro b-type natriuretic peptide (NT-proBNP), total white blood cell count (WBC), neutrophil count, lymphocyte count, monocyte count, eosinophil count, and basophil count were documented. These specific biomarkers of interest were analyzed by either True Health Diagnostics (Frisco, Texas) or Singulex (Alameda, California) depending on the subject's health insurance. The same company that analyzed the baseline labs for a participant was used for the follow-up labs to ensure consistency.

### 2.4 | Data analysis

Paired samples t-tests were used for the analysis of biochemical measures at baseline and 4-weeks, and significance was confirmed with non-parametric tests. Significance was determined to be a $P$ value less than 0.05. SPSS (version 24) was used for data analysis.

## 3 | RESULTS

Baseline demographics are indicated in Table 1. Subjects represent a sample that was 81% obese with multiple clinical diagnoses. Two-thirds of subjects were women and 80% were African American.

Adherence to the dietary intervention was approximately 87% over the course of the 4 weeks as measured by the daily adherence assessment tool. Food group consumption is indicated in Table 2 at baseline and 4-weeks. Notably, total fruit consumption increased from 1.3 ± 2.0 servings to 11.8 ± 10.4 servings (808% increase, $P < 0.0005$) and total vegetable consumption increased 2.7 ± 2.0 servings to 16.0 ± 9.2 servings (493% increase, $P < 0.0005$). Additionally, total animal product consumption decreased from 7.9 ± 4.7 servings to 0.4 ± 1.4 servings (95% decrease, $P = 0.001$). The consumption of avocados, dark-green vegetables, deep-yellow vegetables, tomatoes,

**TABLE 1** Baseline characteristics and clinical diagnoses

| | Participants[a] |
|---|---|
| *n* | 31 |
| Age (years) | 53.4 (32-69) |
| Sex | |
| Male | 10 (33%) |
| Female | 21 (67%) |
| Race, ethnicity | |
| African American | 25 (80%) |
| Hispanic | 3 (10%) |
| White | 3 (10%) |
| Mean BMI (kg/m$^2$) | 37.5 ± 8.3 |
| Overweight (25-29.9 kg/m$^2$) | 6 (19%) |
| Obesity class 1 (30-34.9 kg/m$^2$) | 6 (19%) |
| Obesity class 2 (35-39.9 kg/m$^2$) | 10 (33%) |
| Obesity class 3 (≥40 kg/m$^2$) | 9 (29%) |
| Current diagnoses | |
| Coronary artery disease | 10 (33%) |
| Type II diabetes mellitus | 8 (27%) |
| Arthritic condition | 7 (23%) |
| Pre-diabetes | 5 (17%) |

Abbreviation: BMI, body mass index.
[a] Data are mean (range) unless otherwise indicated.

and other vegetables also significantly increased ($P \leq 0.006$). A decreased consumption of white potatoes, fried potatoes, total grains, refined grains, whole grains, added oils, added animal fat, red meat, white meat, eggs, and dairy were also observed ($P \leq 0.027$). The consumption of sweets (5% decrease, $P = 0.90$) and the consumption of nuts/seeds (17% increase, $P = 0.736$) did not significantly change between baseline and 4-weeks.

Body weight, BMI, total cholesterol, LDL-C, HDL-C, and triglycerides (Table 3) were significantly reduced after 4-weeks of the dietary intervention ($P \leq 0.008$). Lp(a) was also significantly reduced (−32.0 ± 52.3 nmol/L, $P = 0.003$). In addition, LDL-P, sdLDL-C, Apo-B, HDL2-C, and Apo A-1 were significantly reduced ($P \leq 0.03$). Of the atherogenic lipoproteins, sdLDL-C had the greatest relative reduction of approximately 30% (Figure 1). Lp(a) reduced 16% which was proportional to the decrease in Total-C, triglycerides and LDL-P.

Of the inflammatory indicators, *hs*-CRP, IL-6, Lp-PLA2, and fibrinogen significantly decreased ($P \leq 0.004$) (Table 4). The WBC, neutrophil, lymphocyte, monocyte, eosinophil and basophil count also significantly decreased ($P \leq 0.033$). Interestingly, no statistically significant changes were observed for endothelin-1, TNF-a, myeloperoxidase, troponin-I, or NT-proBNP ($P \geq 0.056$) between baseline and 4-weeks.

**TABLE 2** Number of food group servings at baseline and 4-weeks[a]

| Food group | Serving size | Baseline[b] | Final[b] | Change[c] | *P*[d] |
|---|---|---|---|---|---|
| Fruits, total | 1/2 cup chopped, 1/4 cup dried or 1 medium piece | 1.3 ± 2.0 | 11.8 ± 10.4 | 808% (10.5 ± 10.8) | <0.0005 |
| Avocado | 1/2 cup chopped | 0.1 ± 0.2 | 0.9 ± 0.9 | 800% (0.8 ± 0.9) | <0.0005 |
| Vegetables, Total | 1/2 cup chopped or 1 cup raw leafy | 2.7 ± 2.0 | 16.0 ± 9.2 | 493% (13.3 ± 9.2) | <0.0005 |
| Dark-green vegetables | 1/2 cup chopped or 1 cup raw leafy | 0.7 ± 1 | 5.2 ± 3.8 | 643% (4.5 ± 4.0) | <0.0005 |
| Deep-yellow vegetables | 1/2 cup chopped | 0.2 ± 0.4 | 1.2 ± 1.1 | 500% (1.0 ± 1.3) | <0.0005 |
| Tomatoes | 1/2 cup chopped | 0.4 ± 0.5 | 1.7 ± 2.4 | 325% (1.3 ± 2.4) | 0.006 |
| Other vegetables | 1/2 cup chopped | 1.4 ± 1.2 | 7.9 ± 6.6 | 464% (6.5 ± 6.3) | <0.0005 |
| White Potatoes[e] | 1/2 cup chopped or 1 medium baked potato | 0.3 ± 0.7 | 0.0 ± 0.0 | −100% (−0.3 ± 0.7) | 0.03 |
| Fried potatoes | 1/2 cup chopped or 70 g french fries | 0.5 ± 0.9 | 0.1 ± 0.3 | −80% (−0.4 ± 0.9) | 0.027 |
| Grains, Total | 1 slice of bread or halfcup cooked cereal | 5.7 ± 3.5 | 0.7 ± 0.9 | −88% (−5.0 ± 3.6) | <0.0005 |
| Refined grains | 1 slice of bread or half cup cooked cereal | 3.8 ± 2.7 | 0.2 ± 0.7 | −95% (−3.6 ± 3.0) | <0.0005 |
| Whole grains | 1 slice of bread or half cup cooked cereal | 1.9 ± 2.6 | 0.5 ± 0.7 | −74% (−1.4 ± 2.7) | 0.007 |
| Sweets[f] | 4 g of sugar, 1 tbsp honey or 2 tbsp syrup | 1.8 ± 2.3 | 1.7 ± 1.5 | −5% (−0.1 ± 2.7) | 0.90 |
| Nuts/seeds | 1/2 oz | 1.2 ± 3.0 | 1.4 ± 1.6 | 17% (0.2 ± 3.4) | 0.736 |
| Added oils | 1 tsp | 3.2 ± 3.5 | 0.1 ± 0.2 | −97% (−3.1 ± 3.5) | <0.0005 |
| Added animal fat | 1 tsp | 1.3 ± 2.3 | 0.0 ± 0.1 | −100% (−1.3 ± 2.3) | 0.005 |
| Animal products, Total[g] | 1 oz | 7.9 ± 4.7 | 0.4 ± 1.4 | −95% (−7.5 ± 5.3) | 0.001 |
| Red meat | 1 oz | 2.1 ± 2.9 | 0.1 ± 0.2 | −95% (−2.0 ± 3.0) | <0.0005 |
| White meat | 1 oz | 3.9 ± 3.7 | 0.2 ± 1.1 | −95% (−3.7 ± 4.1) | <0.0005 |
| Eggs | 1 large egg | 0.5 ± 0.7 | 0.0 ± 0.1 | −100% (−0.5 ± 0.7) | 0.002 |
| Dairy | 1 cup of milk/yogurt or 1.5 oz of cheese | 1.5 ± 1.6 | 0.1 ± 0.3 | −93% (−1.4 ± 1.7) | <0.0005 |

[a] Data are for subjects who completed 24-h recalls at both baseline and 4-weeks ($n = 30$).
[b] Data are listed in serving size and are presented as mean ± SD.
[c] Data indicated as % change (mean ± SD).
[d] Paired samples *t*-tests for within-group comparisons of changes from baseline to final values.
[e] Excludes fried potatoes.
[f] Includes honey, candy, or other added sugars.
[g] Excludes added animal fat.

**TABLE 3** Atherogenic lipoproteins and particles at baseline and 4-weeks

| | Baseline[a] | Final[a] | Change[b] | *P*[c] |
|---|---|---|---|---|
| Weight (kg) | 108.1 ± 28.6 | 101.4 ± 26.3 | −6% (−6.6 ± 3.6) | <0.0005 |
| BMI (kg/m$^2$) | 37.5 ± 8.3 | 35.2 ± 7.8 | −6% (−2.2 ± 1.1) | <0.0005 |
| Total-C (mg/dL) | 216.6 ± 34.2 | 182.7 ± 29.9 | −16% (−33.8 ± 25.9) | <0.0005 |
| LDL-C (mg/dL) | 143.0 ± 28.9 | 118.4 ± 26.4 | −17% (−24.6 ± 21.3) | <0.0005 |
| HDL-C (mg/dL) | 54.8 ± 9.4 | 49.5 ± 10.6 | −9% (−5.2 ± 6.2) | <0.0005 |
| Triglycerides (mg/dL) | 124.1 ± 58.1 | 104.5 ± 53.6 | −16% (−19.6 ± 38.4) | 0.008 |
| Lp(a) (nmol/L)[d] | 200.7 ± 150.0 | 168.8 ± 126.7 | −16% (−32.0 ± 52.3) | 0.003 |
| Apo-B (mg/dL) | 115.2 ± 24.5 | 101.9 ± 17.7 | −11% (−13.3 ± 18.3) | <0.0005 |
| LDL-P (nmol/L)[e] | 1891 ± 586 | 1586 ± 508 | −16% (−305 ± 363) | <0.0005 |
| *sd*LDL-C (mg/dL) | 33.7 ± 11.5 | 23.7 ± 8.7 | −30% (−10.0 ± 9.2) | <0.0005 |
| HDL2-C (mg/dL) | 17.4 ± 9.8 | 15.6 ± 9.9 | −10% (−1.8 ± 4.5) | 0.030 |
| Apo A-1 (mg/dL) | 189.7 ± 150.7 | 160.2 ± 126.5 | −14% (−27.0 ± 19.6) | <0.0005 |

Abbreviations: Apo A-1, apolipoprotein A-1; Apo-B, apolipoprotein B100; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; HDL2-C, high-density lipoprotein-2 cholesterol; LDL-C, low-density lipoprotein cholesterol; LDL-P, low-density lipoprotein particles; Lp(a), lipoprotein(a); sdLDL-C, small-dense low-density lipoprotein cholesterol; total-C, total cholesterol.
[a] Mean ± SD (*n* = 31 unless otherwise indicated).
[b] Data indicated as % change (mean ± SD).
[c] Paired samples *t*-tests for within-group comparisons of changes from baseline to final values.
[d] *n* = 28 due to premature coagulation of sample (*n* = 1) and incompatible units (mg/dL) when merging laboratory results (*n* = 2).
[e] *n* = 29 due to premature coagulation of samples.

## 4 | DISCUSSION

The consumption of a defined, plant-based diet resulted in a significant reduction in Lp(a) after 4 weeks; thus, the study hypothesis was accepted. The reduction in Lp(a) was profound and is one of the largest reductions due to lifestyle reported in the literature. The magnitude of change was comparable to other leading medical therapies, such as niacin (~20% reduction) and PCSK9 inhibitors (~25% reduction).[12] It is important to note that this dietary intervention rapidly reduced Lp(a) by 16% in only 4 weeks, whereas shorter duration niacin and PCSK9 inhibitor drug trials typically lasted 8 to 12 weeks. It should also be noted that niacin may reduce inflammation, such as *hs*-CRP, by 15% after 3 months, although PCSK9 inhibitors do not.[16,17] After 4 weeks, the dietary intervention reduced *hs*-CRP by 30.7%. In addition, IL-6, Lp-PLA2, fibrinogen, and white blood cells were significantly reduced, as were sdLDL-C, LDL-P, and Apo-B, all of which represent a systemic, cardio-protective effect.[18–24] Thus, the use of this single dietary approach in the clinical setting, vs multiple drug therapy, may be an appropriate tool in treating complex patients with a myriad of elevated CVD-related biomarkers.

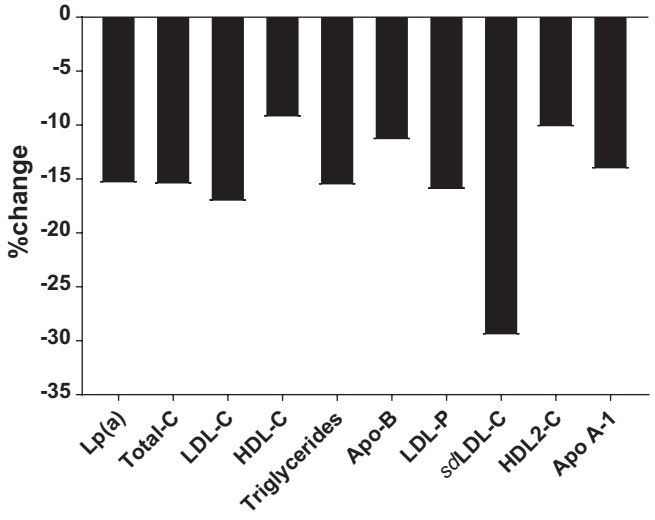


**FIGURE 1** Percent change of atherogenic lipoproteins and particles from baseline to 4-weeks. All variable changes indicated are significant ($P < 0.05$). Lp(a), lipoprotein(a); Total-C, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; Apo-B, apolipoprotein B100; LDL-P, low-density lipoprotein particles; sdLDL-C, small-dense low-density lipoprotein cholesterol; HDL2-C, high-density lipoprotein-2 cholesterol; Apo A-1, apolipoprotein A-1

Elevated Apo A1, HDL-C, and HDL2-C are associated with reduced cardiovascular disease risk.[24,25] While these HDL fractions were significantly reduced in this trial, this is a common phenomenon observed when consuming plant-based diets. A systematic review and meta-analysis of plant-based observational and clinical trials found that while HDL-C was significantly reduced compared to those consuming non-vegetarian diets, LDL-C and total-C were also reduced.[26] Despite reductions in HDL-C, those who consumed plant-based diets had a 25% reduced incidence of ischemic CVD compared with non-vegetarian counterparts.[27]

Lp(a) concentrations in the present study represent a high-risk population.[28] This may be explained by the higher proportion of African Americans in this sample, as African Americans may have higher Lp(a) concentrations compared with Caucasians.[29] An evaluation of 532 359 patients found that an Lp(a) concentration > 50 mg/dL was common among patients.[30] This range roughly corresponds to the mean nmol/L Lp(a) concentration observed in the present study.

### 4.1 | Effect of weight loss on plasma Lp(a) concentrations

An energy restricted diet was found to independently reduce serum Lp(a) in those with baseline concentrations >20 mg/dL, but not <20 mg/dL.[31] Further studies have found that weight loss may not

**TABLE 4** Inflammatory and other cardiovascular indicators at baseline and 4-weeks

| | Baseline[a] | Final[a] | Change[b] | P[c] |
|---|---|---|---|---|
| *hs*-CRP (mg/dL) | 7.8 ± 6.4 | 5.4 ± 4.7 | −30.7% (−2.4 ± 3.7) | 0.001 |
| Endothelin (pg/mL)[d] | 2.2 ± 0.7 | 2.2 ± 0.8 | 0% (0.0 ± 0.7) | 0.916 |
| IL-6 (pg/mL)[d] | 2.6 ± 1.4 | 2.0 ± 1.0 | −23.1% (−0.6 ± 1.0) | 0.001 |
| TNF-α (pg/mL)[d] | 2.0 ± 0.9 | 2.2 ± 0.9 | 10.0% (0.2 ± 0.6) | 0.096 |
| Lp-$PLA_2$ (ng/mL)[d] | 252.3 ± 136.3 | 210.7 ± 119.1 | −16.4% (−41.6 ± 64.6) | 0.001 |
| Myeloperoxidase (pmol/L)[e] | 124.1 ± 58.1 | 104.5 ± 53.6 | −23.0% (−28.5 ± 66.1) | 0.056 |
| Fibrinogen (mg/dL)[f] | 561.4 ± 112.2 | 530.1 ± 102.9 | −5.6% (−31.3 ± 50.7) | 0.004 |
| NT-proBNP (pg/mL)[d] | 65.2 ± 71.2 | 69.4 ± 75.9 | 6.2% (4.1 ± 23.2) | 0.337 |
| Total WBC (K/μL)[d] | 6.3 ± 2.0 | 4.8 ± 1.3 | −22.2% (−1.4 ± 1.1) | <0.0005 |
| Neutrophils (K/μL)[d] | 3.5 ± 1.4 | 2.5 ± 0.9 | −28.6% (−1.0 ± 0.8) | <0.0005 |
| Lymphocytes (K/μL)[d] | 1.9 ± 0.7 | 1.6 ± 0.6 | −15.8% (−0.3 ± 0.4) | <0.0005 |
| Monocytes (K/μL)[d] | 0.46 ± 0.12 | 0.38 ± 0.09 | −15.2% (−0.07 ± 0.1) | <0.0005 |
| Eosinophils (K/μL)[d] | 0.18 ± 0.11 | 0.15 ± 0.11 | −16.6% (−0.03 ± 0.07) | 0.033 |
| Basophils (K/μL)[d] | 0.029 ± 0.016 | 0.024 ± 0.015 | −17.2% (−0.005 ± 0.010) | 0.016 |

Abbreviations: *hs*-CRP, high-sensitivity c-reactive protein; IL-6, interleukin-6; Lp-$PLA_2$, lipoprotein-associated phospholipase A2; NT-proBNP, N-terminal pro b-type natriuretic peptide; TNF-α, tumor necrosis factor-alpha; WBC, white blood cells.
[a] Mean ± SD (*n* = 31 unless otherwise indicated).
[b] Data indicated as % change (mean ± SD).
[c] Paired samples *t*-tests for within-group comparisons of changes from baseline to final values.
[d] *n* = 30 due to premature coagulation of samples.
[e] *n* = 25 due to premature coagulation of samples.
[f] *n* = 27 due to premature coagulation of samples.

independently reduce Lp(a) concentrations. A pooled analysis of cohorts found that as weight loss ensued, Lp(a) concentrations surprisingly increased.[32] Baseline Lp(a) concentrations on average between the four cohorts analyzed were approximately 40 mg/dL, well above the >20 mg/dL threshold reported in the initial study.[31] Other investigations examining the effect of weight loss on Lp(a) concentration have not demonstrated a relationship between these two variables.[33,34] Interestingly, the emphasis on consuming plant-based foods, even with a calorie restricted diet, did not result in Lp(a) reductions compared with a calorie restricted red meat centered diet.[35] The plant-centered diet in this trial[35] still contained a significant number of calories derived from animal-based sources in addition to processed plant foods. Also, both diets contained similar quantities of dietary fiber, a measure of plant-food intake. Based on these weight loss trials, Lp(a) concentration is likely not influenced by weight reduction.

## 4.2 | Effect of diet on plasma Lp(a) concentrations

Other trials using diets emphasizing plant-based foods have not demonstrated similar results. A low-fat and low-saturated fat diet with an increased intake of fruits and vegetables interestingly increased Lp(a) concentrations.[36] Subjects consumed four to five servings of fruits or berries and five to six servings of vegetables daily for 5 weeks and all food was provided. It is important to note that subjects still consumed animal products throughout the intervention[36] which included dairy products and lean meats. The fiber content (40 g vs 51 g in the present study) was not as high as would be expected when consuming a higher quantity of plant-foods, and the number of fruits and vegetables did not meet the levels observed in the present study (11.8 servings of fruits and 16 servings of vegetables). Based on this data, it is probable that exclusively increasing fruit and vegetable intake is not sufficient to elicit reduced Lp(a) concentrations.

It has also been reported that a low-carbohydrate, high-fat diet (45% carbohydrate, 40% fat) may have a favorable impact on Lp(a) concentrations compared with a high-carbohydrate, low-fat diet (65% carbohydrate, 20% fat), although it is unclear as to what precisely was consumed on either of these diets.[37] In addition, the differences were small, as only a 2.17 mg/dL difference was observed between both groups, and baseline Lp(a) concentrations were <20 mg/dL. The Omni Heart Trial also found that replacing calories from carbohydrates and protein with unsaturated fats produced a smaller increase in Lp(a) comparatively, but both diets still elicited increased plasma Lp(a) compared with baseline. The differences between groups were also small at the end of the intervention (<4 mg/dL difference).[38]

In individuals with low baseline Lp(a) concentrations (approximately 5.5 mg/dL), the consumption of copious saturated fat, cholesterol (derived from egg consumption) and polyunsaturated fat did not influence Lp(a) concentrations.[13] Carbohydrate intake was low in this trial as well (39% to 46% carbohydrate as a percent of energy). While fat consumption does not appear to influence serum Lp(a) concentrations in the fasting state, a variety of fats may significantly increase postprandial, transient plasma Lp(a) concentrations over the course of 8 hours.[39] Investigators found that linoleic, oleic, palmitic, and stearic acid all resulted in significant transient increases in Lp(a) concentrations which closely tied to a proportional increase in triacylglycerol concentrations. While saturated fats, stearic acid and palmitic acid, appeared to have the greatest increase in serum Lp(a) compared with oleic acid and linoleic acid, this differing response did not reach statistical significance.

### 4.3 | Mechanisms contributing to reduced plasma Lp(a)

The observed reduction in Lp(a) in the present study may be due to decreased hepatic synthesis of apolipoprotein(a) and Apo-B. This may be in part due to decreased expression of the LPA gene. Since the LPA gene is almost exclusively expressed in the liver,[40] hepatic influences, including the production of *hs*-CRP and inflammatory cytokines, such as IL-6, may upregulate LPA gene expression.[41] Indeed, those with inflammatory conditions may have increased Lp(a) concentrations compared with healthy controls.[42]

Current data in our plant-based study supports this hypothesis, as reduced *hs*-CRP and IL-6 was observed. In contrast, previous studies utilizing plant-centered diets to reduce Lp(a) were unsuccessful, as animal products were still substantially consumed.[35,36] Animal-based foods, including lean meat, can induce a postprandial inflammatory response, including increased *hs*-CRP and IL-6.[43] Pooled data of those consuming non-vegan, plant-based diets have shown reduced *hs*-CRP and IL-6,[44] although to a lesser extent compared with the present study (*hs*-CRP; −0.55 mg/dL vs −2.42 mg/dL, IL-6; −0.25 pg/mL vs −0.64 pg/mL). The elimination of animal products and processed foods completely on a defined, plant-based diet may be a more prudent dietary strategy to avoid potential fluctuations in inflammation. Thus, the fact that there were only minimally processed plant foods consumed during this dietary intervention may account for the observed reduction in serum Lp(a) concentrations that may be associated with reduced LPA gene expression. Further mechanistic research is needed to confirm this hypothesis.

### 4.4 | Strengths and limitations

The high dietary adherence and provision of all food to subjects supports the conclusion that the intervention likely fully accounted for the observed biochemical changes among the subjects. Furthermore, the study took place in an outpatient clinical setting with established patients providing a real-world example of a standard clinical practice. This study provides a model for the implementation of this intervention across other medical practices. In contrast, a limitation in the design of this study was the lack of a control group and the small sample size. A larger sample size and a control group would be needed to strengthen a causal relationship.

## 5 | CONCLUSION

A defined, plant-based diet has a favorable impact on Lp(a) and other atherogenic lipoproteins and particles. Lp(a) concentration was previously thought to be only minimally altered by lifestyle interventions. In this study, however, a defined plant-based diet resulted in a substantial reduction in Lp(a) in only 4 weeks. Further investigations are warranted to elucidate the specific mechanisms that contribute to reduced Lp(a) concentrations, which may include alterations in LPA gene expression mediated via hepatic inflammation.


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### Conflict of interest

The authors declare no potential conflicts of interest.


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## SUPPORTING INFORMATION

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