

North American Artery Fourth Annual Meeting

Arterial Stiffness: If You Don't Measure It, You Can't Manage It

September 5-6, 2014, Hyatt Regency O'Hare, Chicago, IL



FINAL PROGRAM

September 5-6, 2014
Hyatt Regency O'Hare
Rosemont, IL



NORTH AMERICAN ARTERY



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ABOUT THE NORTH AMERICAN ARTERY SOCIETY

Mission Statement

The Mission of North American Artery Society is to:

- Support education on arterial structure and function appropriate to the various medical communities, such as scientific researchers, clinical specialists, primary care specialists, medical students, and pharmaceutical researchers, as well as the patient community;
- Develop mechanisms and venues for disseminating information on the understanding and application of arterial structure and function and its measurement among the various medical communities;
- Participate in and encourage the study of improved application of technologies in the measurement of arterial structure and function;
- Participate in and encourage clinical trials that develop the understanding of how arterial structure and function and its measurement can guide and inform patient selection and treatment;
- Guide and support efforts to standardize arterial structural and functional measurements for clinical practice and clinical/scientific studies;
- Direct efforts to include arterial structure and function measurements in appropriate national guidelines;
- Formulate a consensus statement regarding what is known in regards to arterial structure and function.

Society Objectives

North American Artery is a non-profit, non-partisan professional society dedicated to the encouragement, support, and understanding of vascular structure and function and its application to clinical medicine, research and pharmaceutical and medical device development. The Society Objectives are to:

- Support education on arterial mechanics appropriate to the various medical communities, such as scientific researchers, clinical specialists, primary care specialists, and pharmaceutical researchers, as well as the patient community;
- Develop mechanisms and venues for disseminating information on the understanding and application of arterial mechanics and its measurement among the various medical communities;
- Participate in and encourage the study of arterial mechanics in basic and applied research to further especially the clinical applications derived from an improved understanding of arterial mechanics;
- Participate in and encourage clinical trials that develop the understanding of how arterial mechanics and its measurement can guide and inform patient treatment;
- Guide and support efforts to standardize arterial mechanics measurements for clinical practice and clinical/scientific studies;
- Direct efforts to include arterial mechanics measurements in appropriate national guidelines;
- Provide the knowledge for the critical understanding and application of technologies to measure arterial mechanics.

ACKNOWLEDGEMENT

North American Artery sincerely thanks the following firms for their support of the Fourth Annual Meeting.

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TABLE OF CONTENTS

President’s Welcome	4
Program Committee Chairmen Welcome	5
General Information	6
2014 Program Committee Members	7
Faculty List.....	7
Conflict of Interest Disclosures	8
Takeaway Messages-Friday, September 5, 2014	9
Takeaway Messages-Saturday, September 6, 2014	10
Meeting Agenda-Friday, September 5 2014.....	11
Meeting Agenda-Friday & Saturday, September 5 & 6, 2014	12
Meeting Agenda-Saturday, September 6, 2014	13
Posters.....	14
Faculty Bios	15
Exhibitors	23
Abstracts (Accepted for Oral Presentation).....	26
Abstracts (Accepted for Poster Presentation)	31
NAA Membership Information	63
Membership Application	64

PRESIDENT'S WELCOME



NORTH AMERICAN ARTERY

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*Elaine M Urbina MD,
Cincinnati Children's Hospital
Medical Center
Cincinnati, OH*

North American Artery
12734 Cimarron Path
San Antonio, TX 78249

Dear Colleagues,

I'd like to personally welcome each of you to our Fourth Annual Meeting, "Arterial Stiffness: If You Don't Measure It, You Can't Manage It". The field of arterial hemodynamics is an exciting area and the North American Artery Society will continue to meet and bring inspired people together in forums like this, to ensure the NAA remains at the cutting edge of research and the practical applications for technologies that measure arterial structure and function.

I appreciate the efforts of our Conference Co-Chairs, Bo Fernhall and Gary Pierce, as well as the members of the Program Committee for working tirelessly with me to put together this program. We are also indebted to Hansen Global Event Management for such excellent logistical support.

I look forward to meeting our members, both old and new who will be here. For those of you attending who are not members, there is information about the NAA included within this book, and membership applications are available at the registration desk. I encourage you to think about being a part of our new and exciting organization.

This conference would not be possible without the generous support of our Diamond Dinner sponsor, AtCor Medical, Inc., our Platinum sponsor, Fukuda Denshi, and our Gold sponsors, I.E.M. GmbH, Hitachi Aloka Medical, Itamar Medical, Medical Imaging Applications, and Omron Healthcare. The NAA is grateful to each of them for their support of our organization. Please visit with them in the exhibit area during our breaks.

In closing, I would like to thank each of you for attending the conference and bringing your expertise to our gathering. Your vision, knowledge, and experience will help us pave the way for future developments in arterial studies. Throughout this conference, you are encouraged to engage faculty and sponsors. My personal respect and thanks to all!

Sincerely,

Raymond R. Townsend, M.D.
NAA President

WELCOME FROM THE CO-CHAIRS



NORTH AMERICAN ARTERY

North American Artery Fourth Annual Meeting

Arterial Stiffness: If You Don't Measure It, You Can't Manage It

September 5-6, 2014, Hyatt Regency O'Hare, Chicago, IL

Program Committee

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Dear Colleagues,

On behalf of the North American Artery Society (NAA), it is our distinct pleasure to welcome you to the 4th Annual meeting of NAA, "Arterial Stiffness: If You Don't Measure It, You Can't Manage It". The NAA is a multidisciplinary society dedicated to understanding vascular structure and function and its application to clinical medicine, basic/translational research, and pharmaceutical and medical device development. The breadth of this year's program clearly reflects these objectives with presentations focusing on clinical perspectives and prognosis, impact of drugs on blood pressure and arterial hemodynamics, new devices for determining central arterial hemodynamics, lifestyle interventions, reimbursement issues, and basic and translational science.

The Program Committee worked tirelessly to create a dynamic program that has continued to build on the success of last year's meeting. This is demonstrated by the more than 30 abstract presentations that are included in this year's meeting, as well as the exciting main lectures, debates, and exhibits.

We truly hope you will enjoy the 2014 NAA meeting at the Hyatt Regency O'Hare and that you take the opportunity to meet our speakers, exhibitors, and delegates from not only the United States, but from Canada, Europe, Asia, and South America as well.

We would especially like to thank our sponsors AtCor Medical, I.E.M., Fukuda Denshi, Hitachi Aloka Medical, Itamar Medical, Medical Imaging Applications, and Omron Healthcare for making this exciting and scientifically enriching conference possible. Thank you for participating and helping to move the NAA forward as our organization continues to grow.

Sincerely,

Bo Fernhall, Ph.D.

Gary Pierce, Ph.D.

GENERAL INFORMATION

Meeting Venue/Headquarters Hotel Hyatt Regency O'Hare

The sophisticated, upscale hotel provides registrants with effortless convenience to downtown Chicago and O'Hare airport. Recently refreshed, the hotel has a long tradition of service and extraordinary convenience and now features new amenities, newly refreshed guestrooms, and contemporary styling. With cutting-edge design and stunning lobby with impressive atrium, the hotel offers a striking modern environment.

Attendees staying at the hotel receive complimentary internet access in their rooms.

Airport Shuttle

The Hyatt Regency O'Hare offers 24 hour, complimentary shuttle service, which runs every 15 minutes. Follow the red Shuttle signs at the airport to the designated pick-up area, O'Hare Bus / Shuttle Center Door One. Shuttle buses are blue with white signage that reads Hyatt Regency O'Hare.

Valet and Self-Parking

Self-Parking – \$22 daily or \$29 overnight.

Valet Parking – \$32 daily or \$35 overnight.

Hotel Amenities

- StayFit Fitness Center—24/7 state of the art gym
- Perks Coffee & Gift Shop—On-site convenience/gift shop that is open 22 hours/day
- Room Service available from 6:00 AM to Midnight
- Full Service FedEx Office & Business Center open 24 hours daily
- Complimentary high-speed wireless access in all public spaces

Restaurants

- O'H American Grill – American Cuisine
- Red Bar – Sushi Bar; Innovative cocktails & food

Conflict of Interest Disclosure

The North American Artery Society strives to ensure balance, independence, objectivity, and scientific rigor in its educational activities. Faculty members and Program Committee Chairpersons have disclosed to the Society financial relationships with commercial interests or manufacturers with products associated with or discussed in their presentation, in existence over the past 12 months. All Disclosure Statements are available to meeting attendees in the Program Book.

Meeting Registration – Grand Ballroom Foyer

All Conference materials including badges can be picked up from the registration desk during the following hours:

September 5, 2014 1:00 PM - 7:00 PM

September 6, 2014 6:30 AM - 4:00 PM

Badges are required for entry to all functions.

Sessions – Grand Ballroom H (Lower Level)

All sessions will take place in Grand Ballroom H except for the Dinner, which will take place in the United Room (lower level).

Posters on Display—Grand Ballroom E

Posters will be on display throughout the conference. Presenters will be available to discuss their posters during the Lunch on Saturday.

Exhibits—Grand Ballroom E

All meal functions and refreshment breaks, except the dinner, will be held in the exhibit hall as shown below.

Friday, September 5, 2014

Opening Reception	2:00 to 2:45 PM
Refreshment Break	4:20 to 4:35 PM
Refreshment Break	5:25 to 6:15 PM
Dinner (Int'l Ballroom DEF)	7:35 to 9:00 PM

Saturday, September 6, 2014

Breakfast	7:15 to 8:00 AM
Refreshment Break	9:00 to 9:15 AM
Refreshment Break	10:15 to 11:15 AM
Lunch/Poster Presentations	12:30 to 2:00 PM

Fourth Annual Meeting Sponsors

The North American Artery Society wishes to acknowledge the following Corporate Sponsors for their generous support of the Fourth Annual Meeting.

We encourage all participants to visit with our sponsors' exhibit booths during the breaks

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Wales Heart Research Institute
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Professor, Preventive Medicine,
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Eileen M. Foell Professor of Heart
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David B. Rubin, MD

Director, Clinical Development
GlaxoSmithKline
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Patrick Segers, PhD

Institute of Biomedical Technology
Ghent University
Ghent, Belgium

Sanjiv J. Shah, MD

Division of Cardiology, Department
of Medicine
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Raymond R. Townsend, MD

Hypertension Program - Hospital of
the University of Pennsylvania
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Ronald G. Victor, MD

Burns and Allen Chair
in Cardiology Research
Director, Hypertension Center
Director of Clinical Research &
Associate Director, The Heart
Institute
Cedars-Sinai Medical Center
Los Angeles, CA

CHAIRPERSONS AND FACULTY DISCLOSURES

Michael D. Brown, PhD, Department of Kinesiology and Nutrition, University of Illinois, Chicago, has no conflict of interests to disclose.

Julio A. Chirinos, MD, PhD, Penn Cardiovascular Institute, University of Pennsylvania School of Medicine

Consultant: Fukuda-Denshi

Grant/Research Support: NIH, ACRIN, VA

Other: Named as inventor on patent application for the use of inorganic nitrates in HFPEF

John Cockcroft, MD, Wales Heart Research Institute, University of Wales College of Medicine

Consultant: Novartis

Speaker's Bureau: Menarini

Grant/Research Support: GlaxoSmithKline

Honoraria: Menarini

William C. Cushman, MD, Chief, Preventive Medicine Section, Veterans Affairs Medical Center and Professor, Preventive Medicine, Medicine, and Physiology, University of Tennessee Health Science Center, has no conflict of interests to disclose.

Peter U. Feig, MD, President of PF Pharmaceutical Development, LLC, has no conflict of interests to disclose.

Bo Fernhall, PhD, Dean, College of Applied Health Sciences, Professor of Kinesiology, University of Illinois at Chicago, has no conflicts of interest.

Stanley S. Franklin, MD, University of California, Irvine, has no conflict of interests to disclose.

Donald M. Lloyd-Jones, MD, ScM, Senior Associate Dean for Clinical and Translational Research, Chair, Department of Preventive Medicine, Director, Northwestern University Clinical and Translational Sciences (NUCATS) Institute, Eileen M. Foell Professor of Heart Research, Northwestern University Feinberg School of Medicine, has no conflict of interests to disclose.

Gary F. Mitchell, MD, President of Cardiovascular Engineering Inc.

Consultant: Novartis, Merck, Servier

Stock Shareholder (self-managed): Cardiovascular Engineering Inc.

Honoraria: Novartis, Servier

Full-time/part-time Employee: Cardiovascular Engineering Inc.

Gary L. Pierce, PhD, Assistant Professor, Department of Health and Human Physiology, University of Iowa, has no conflict of interests to disclose.

David B. Rubin, MD, Director, Clinical Development, GlaxoSmithKline

Full-time/part-time Employee: GlaxoSmithKline

Patrick Segers, PhD, Institute of Biomedical Technology, Ghent University, has no conflict of interests to disclose.

Sanjiv J. Shah, MD, Division of Cardiology, Department of Medicine, Northwestern University Feinberg School of Medicine

Consultant: Novartis, Bayer, DC Devices

Grant/Research Support: Novartis, Gilead, Bayer, Pfizer

Honoraria: American Board of Internal Medicine, Pulmonary Hypertension Association

Raymond R. Townsend, MD, Hypertension Program - Hospital of the University of Pennsylvania, Clinical & Translational Research Center, University of Pennsylvania

Consultant: Medtronic, Janssen Pharmaceuticals

Grant/Research Support: NIH

Ronald G. Victor, MD, Burns and Allen Chair in Cardiology Research, Director, Hypertension Center, Director of Clinical Research & Associate Director, The Heart Institute, Cedars-Sinai Medical Center

Consultant: Northwind

Grant/Research Support: Eli Lilly

Other: Steering Committee – Medtronic

TAKEAWAY MESSAGES - FRIDAY, SEPTEMBER 5, 2014

3:00 - 3:30 pm Why Should We Measure Arterial Stiffness?—Gary F. Mitchell, MD

At the end of my presentation, participants will be able to:

- 1) *Differentiate various measures of arterial stiffness, central pressure-flow relations and wave reflection*
- 2) *Read and critically evaluate the arterial stiffness literature*
- 3) *Use validated measures of arterial stiffness to stratify risk and examine pathophysiologic correlates or aortic stiffening and excessive pressure pulsatility*

3:30 - 3:55 pm Percutaneous Intervention for Hypertension? Update on Baroreceptor Pacing and Renal Denervation Ronald G. Victor, MD

More rigorous science needs to be done to determine whether or not either of these intervention methods is efficacious in treating hypertension.

3:55 - 4:20 pm Inflammation and Calcification—John Cockcroft, MD

Following my presentation delegates should understand the difference between atherosclerosis and arteriosclerosis and that the factors driving them are different.

In addition, I will focus on the role of inflammation and calcification as major driving factors for arteriosclerosis and the implications this has for improved treatment of arteriosclerosis in clinical practice.

4:35 - 5:00 pm Stiffness Treatment Target: Aldosterone (receptor antagonists, synthase inhibitors)—Peter U. Feig, MD

There is strong current evidence for the effect of mineralocorticoid receptors beyond those traditionally ascribed to their renal effects encompassing direct effects on arterial function and stiffness. Aldosterone antagonism may be improved via more selective antagonists, which may reduce the risk of hyperkalemia while enhancing their arterial protective effects.

5:00 - 5:25 pm Nitrate-Nitrite-NO Pathway: An Opportunity to Enhance Arterial Hemodynamic Function Julio A. Chirinos, MD, PhD

- *An alternative to the eNOS pathway, the nitrate-nitrite-NO pathway may be important for the generation of NO and exercise-induced vasodilation*
- *This pathway is enhanced in hypoxic conditions, which inhibit the classic NOS pathway of NO generation*
- *Nitrate also have beneficial effects on skeletal muscle mitochondria and can reduce late systolic pressure*
- *These peripheral effects appear ideal to target exercise intolerance in Heart Failure with preserved ejection fraction, a condition for which effective pharmacologic therapies are not available.*

8:10 - 8:40 pm Dinner Lecture—Patrick Segers, PhD Future Directions in Arterial Stiffness Measurement

Carotid-femoral pulse wave velocity (PWV) has, especially in Europe, established its position as pragmatic and clinically applicable phenotype of arterial stiffness. PWV, however, still has its shortcomings, and its strong position should not impede and discourage the further development and use of novel techniques, with in particular new, emerging ultrasound-based technologies (still under research), for the assessment of the local stiffness of superficial arteries.

8:40 - 9:00 pm AtCor Medical Sponsored Lecture—David B. Rubin, MD Aortic Pulse Wave Velocity as a Potential Target for Respiratory Drug Development

While definitive studies are yet required, clinical trials suggest that long acting bronchodilators might lower cardiovascular events in COPD patients by reducing aortic pulse wave velocity.

TAKEAWAY MESSAGES - SATURDAY, SEPTEMBER 6, 2014

8:00 - 8:30 am Arterial Stiffness in Vascular Dementia/Cognitive Decline—Gary F. Mitchell, MD

At the end of my presentation, participants will be able to:

- 1) *Define unique aspects of the cerebral circulation that contribute to enhanced susceptibility of the brain to aortic stiffness*
- 2) *Differentiate vascular type versus Alzheimer type dementia*

8:30 - 9:00 am Arterial Stiffness and Heart Failure—Sanjiv J. Shah, MD

- 1) *Ventricular-arterial interactions are integral to the pathogenesis of the heart failure syndrome, particularly heart failure with preserved ejection fraction (HFpEF).*
- 2) *Increases in both systemic and pulmonary arterial stiffness promote and exacerbate the HFpEF syndrome.*
- 3) *In heart failure syndromes, there is a dynamic interplay between reflected arterial waves and myocardial wall stress that likely results in disruption of myocyte T-tubules, thereby leading to abnormalities in calcium cycling within the myocyte and ultimately abnormal ventricular mechanics.*
- 4) *In patients with heart failure or who are at risk for heart failure, improved understanding of measures of arterial stiffness and ventricular-arterial coupling can help the clinician understand the pathogenesis of heart failure in an individual patient, and may help tailor therapy.*

9:15 - 9:45 am Effect of Currently Available Drug Therapies on Aortic Stiffness—Stanley S. Franklin, MD

Aldosterone plays an important role in the regulation of both peripheral vascular resistance and arterial stiffness—two important factors in the development and progressive increased severity of hypertension and of cardiovascular disease.

9:45-10:15 am Designing the Arterial Stiffness Clinical Trial—William C. Cushman, MD

A clinical trial testing whether reducing arterial stiffness should be treated in clinical practice should be conducted on a background of appropriate evidence-based treatment for hypertension and other risk factors in a high-risk population and ask whether implementing an intervention that reduces and/or prevents progression of arterial stiffness further reduces major cardiovascular outcomes.

11:15-11:45 am Destiffening the Aorta with Habitual Exercise in Aging and Hypertension: Fact or Fallacy?

Gary L. Pierce, PhD

- 1) *Moderate intensity aerobic exercise or frequent light physical activity should be recommended for a minimum of 2-4 days/week for 30-45 min/day for middle-aged and older normotensive adults to alter aortic stiffness, although de-stiffening effects on the aorta may not be observed until at least 3-4 months in middle-aged, and >1 year in older, normotensive adults.*
- 2) *In middle-aged and older adults with hypertension, a minimum of >4 days/week, >40 minutes/day of moderate aerobic exercise for more than 6 months that results is likely required to achieve any potential de-stiffening effects on the aorta, but more studies are needed to determine the exact dose of aerobic exercise required.*

12:15-12:30 pm Platinum Sponsor Presentation—Christopher Broadbridge

A Clinical and Technical Background on VaSera and the CAVI Measurement

VaSera, with its CAVI measurement, is a reasonable and effective solution to the challenge of bringing research-quality stiffness measurements to typical medical practices for the management of CVD.

2:00 - 2:30 pm AHA Arterial Stiffness Summary Statement Update—Raymond R. Townsend, MD

Learners will recognize that conducting research using measurements of arterial stiffness that are intended to be generalizable these measurements need to be obtained by attention to details of distance measurement, surroundings, and procedural competence.

2:30 - 3:15 pm Arterial Stiffness Should Not be a Part of CVD Risk Assessment—Donald M. Lloyd-Jones, MD, ScM

- *The addition of novel biomarkers to risk assessment is not simply a function of finding independent associations.*
- *A number of statistical and practical considerations far beyond mere association and biologic plausibility (or even causation) determine the clinical utility of a test for prognostication.*
- *Measurement of arterial stiffness has not yet met the criteria necessary to demonstrate clinical utility for CVD risk assessment.*

- 2:00 - 2:45 pm** **Opening Reception in Exhibit Hall (Grand Ballroom E)**
- 2:45 - 2:50 pm** **Welcome Remarks**
Bo Fernhall, PhD, University of Illinois at Chicago
Gary L. Pierce, PhD, University of Iowa
- 2:50 - 3:00 pm** **President's Opening Statement**
Raymond R. Townsend, MD, University of Pennsylvania
- 3:00 - 3:30 pm** **Opening Plenary Lecture**
Moderator: Raymond R. Townsend, MD, University of Pennsylvania
 Why Should We Measure Arterial Stiffness?
Gary F. Mitchell, MD, Cardiovascular Engineering, Inc.
- 3:30 - 5:25 pm** **Clinical/Translational Lectures: Biological Targets in Arterial Stiffness**
Moderator: Gary L. Pierce, PhD, University of Iowa
- 3:30 - 3:55 pm Percutaneous Intervention for Hypertension? Update on Baroreceptor Pacing and Renal Denervation
Ronald G. Victor, MD, Cedars Sinai Medical Center
- 3:55 - 4:20 pm Inflammation and Calcification
John Cockcroft, MD, University of Wales College of Medicine
- 4:20 - 4:35 pm** **Refreshment Break in Exhibit Hall (Grand Ballroom E)**
- 4:35 - 5:00 pm Stiffness Treatment Target: Aldosterone (receptor antagonists, synthase inhibitors)
Peter U. Feig, MD, PF Pharmaceutical Development, LLC
- 5:00 - 5:25 pm Nitrate-Nitrite-NO Pathway: An Opportunity to Enhance Arterial Hemodynamic Function
Julio A. Chirinos, MD, PhD, University of Pennsylvania School of Medicine
- 5:25 - 6:15 pm** **Refreshment Break in Exhibit Hall (Grand Ballroom E)**
- 6:15 - 7:30 pm** **Oral Abstract Presentations**
Moderators: Bo Fernhall, PhD, University of Illinois at Chicago
Gary L. Pierce, PhD, University of Iowa
- 6:15 pm
 OR-01 Central Artery Stiffness, Baroreflex Sensitivity, and Brain White Matter Integrity in Older Adults
Takashi Tarumi^{1,2}, David C. Zhu⁴, Daan L.K. de Jong⁵, Rutger L. Meijers⁵, Rong Zhang^{1,2,3}
¹Institute for Exercise and Environmental Medicine, Texas Health Presbyterian Hospital Dallas, Dallas, TX, USA; ²Department of Internal Medicine, ³Department of Neurology and Neurotherapeutics, University of Texas Southwestern Medical Center, Dallas, TX, USA; ⁴Department of Psychology and Radiology, and Cognitive Imaging Research Center, Michigan State University, East Lansing, MI, USA; ⁵Department of Geriatric Medicine, Radboud University Medical Center, Nijmegen, Netherlands

(Continued on page 12)

AGENDA—SEPTEMBER 5 & 6, 2014

- 6:30 pm
OR-02 Saxagliptin Prevents Increased Coronary Arterial Stiffness and Advanced Glycation End Product Expression in a Miniature Swine Model of Heart Failure with Preserved Ejection Fraction
Bradley S. Fleenor¹, An Ouyang¹, Melissa S. Cobb², Emily Dehn², Jessica A. Hiemstra², Jan R. Ivey², and *Craig A. Emter*²
¹University of Kentucky, Lexington, KY, USA, ²University of Missouri-Columbia, Columbia, MO, USA
- 6:45 pm
OR-03 Cardio-Respiratory Interactions Immediately following Dynamic Leg Cycling: Influences of the Muscle Pump
Daniel W. White, Gilbert Morales, Victoria L. Kay, Wendy L. Eubank, Peter B. Raven
The University of North Texas Health Science Center at Fort Worth, Fort Worth, TX, USA
- 7:00 pm
OR-04 Importance of Time Delay Estimation Methods for Aortic Pulse Wave Velocity Assessment with Phase-Contrast MRI
*Priyanka Bhattacharya*¹, Chandrasa Sharabu², Deepa Rawat³, Scott Akers^{2,3}, Anjaneyulu Dunde², Prithvi Shivakumar², Prasad Konda², Walter Witschey², Payman Zamani², Julio A Chirinos²
¹Mercy Hospital of Philadelphia, an Affiliate of Drexel University College of Medicine, Philadelphia, PA, USA ; ²University of Pennsylvania, Philadelphia, PA, USA; ³Philadelphia VA Medical Center, Philadelphia, PA, USA
- 7:15 pm
OR-05 Relationship of Common Carotid Artery Perivascular Adipose Tissue, Arterial Stiffness, and Intima-Medial Thickness, in Adult Humans
H. L. Choi, J. S. Au and M. J. MacDonald
Department of Kinesiology, McMaster University, Hamilton, Ontario, Canada
- 7:35 - 9:00 pm Dinner & Presentations (International Ballroom DEF)**
Moderator: Raymond R. Townsend, MD, University of Pennsylvania
- 8:00 - 8:10 pm Business Meeting
- 8:10 - 8:40 pm Future Directions in Arterial Stiffness Measurement
Patrick Segers, PhD, Institute of Biomedical Technology, Ghent University
- 8:40 - 9:00 pm Diamond Dinner Lecture**
Aortic Pulse Wave Velocity as a Potential Target for Respiratory Drug Development
David B. Rubin, MD, GlaxoSmithKline

The Dinner and the Diamond Dinner Lecture is sponsored by AtCor Medical, Inc. (USA)

SATURDAY, SEPTEMBER 6, 2014

- 7:15 - 8:00 am Breakfast in Exhibit Hall (Grand Ballroom E)**
- 8:00 - 9:00 am Target Organ Lectures**
Moderator: Stanley S. Franklin, MD, University of California, Irvine
- 8:00 - 8:30 am Arterial Stiffness in Vascular Dementia/Cognitive Decline
Gary F. Mitchell, MD, Cardiovascular Engineering, Inc.
- 8:30 - 9:00 am Arterial Stiffness and Heart Failure
Sanjiv J. Shah, MD, Northwestern University Feinberg School of Medicine

AGENDA—SEPTEMBER 6, 2014

9:00 – 9:15 am Refreshment Break in Exhibit Hall (Grand Ballroom E)

9:15 -10:15 am Clinical Translational Lectures in Risk Assessment and Management

Moderator: Peter U. Feig, MD, PF Pharmaceutical Development, LLC

9:15 - 9:45 am Effect of Currently Available Drug Therapies on Aortic Stiffness

Stanley S. Franklin, MD, University of California, Irvine

9:45-10:15 am Designing the Arterial Stiffness Clinical Trial

William C. Cushman, MD, University of Tennessee Health Science Center

10:15-11:15 am Coffee/Refreshment Break and Poster Viewing (Grand Ballroom E)

11:15-12:15 pm Clinical Lectures in Exercise and Racial Disparities

Moderator: Bo Fernhall, PhD, University of Illinois at Chicago

11:15-11:45 am Destiffening the Aorta with Habitual Exercise in Aging and Hypertension: Fact or Fallacy?

Gary L. Pierce, PhD, University of Iowa

11:45-12:15 pm Racial Disparities in Arterial Stiffness and Function: Potential Mechanisms

Michael D. Brown, PhD, University of Illinois at Chicago

12:15-12:30 pm Platinum Sponsor Presentation

Moderator: Elaine M. Urbina, MS, MD, Cincinnati Children's Hospital Medical Center

12:15-12:30 pm A Clinical and Technical Background on VaSera and the CAVI Measurement

Christopher Broadbridge, Fukuda Denshi USA

12:30 - 2:00 pm Poster Abstract Presentations & Lunch (Grand Ballroom E)

2:00 - 2:30 pm AHA Arterial Stiffness Summary Statement Update

Raymond R. Townsend, MD, University of Pennsylvania

2:30 - 3:15 pm Debate/Counterpoint Presentation

Moderator: Raymond R. Townsend, MD, University of Pennsylvania

Arterial Stiffness **Should** be a Part of CVD Risk Assessment

John Cockcroft, MD, University of Wales College of Medicine

Arterial Stiffness **Should Not** be a Part of CVD Risk Assessment

Donald M. Lloyd-Jones, MD, ScM, Northwestern University Feinberg School of Medicine

3:15 - 3:30 pm Awards Presentations

Best Abstract and Young Investigator Awards

3:30 - 3:40 pm Concluding Remarks and Future Direction of NAA

POSTERS

- PO-01 Longitudinal and Circumferential Strain of the Proximal Aorta
- PO-02 Effects of Acute Induced Inflammation on Pressure Waveforms: Does Age Matter?
- PO-03 Sex Differences in Stiffness Parameters following Maximal Exercise
- PO-04 Correlations between Arterial Stiffness/Central Hemodynamics and Serum Cardiac Troponin T and Natriuretic Peptide Levels
- PO-05 Buffering of Carotid Artery Pressure and Flow Pulsatility during Cognitive Engagement in Healthy Adults
- PO-06 Effects of Systemic Niacin Infusion on Sympathetic Activity, Arterial Stiffness and Aortic Wave Reflection: A Pilot Study
- PO-07 Racial Differences in Circulating csRAGE and Alternatively Spliced esRAGE in Healthy Adolescents: Relation with Aortic Stiffness
- PO-08 Effects of Acute Dietary Nitrate Supplementation on Aortic Wave Reflection in Young Adults
- PO-09 Spironolactone as Add-On Therapy to Chlorthalidone Improves Endothelial Function, Arterial Stiffness and Insulin Resistance in European and African American Patients with Essential Hypertension – A Double-Blind Placebo-Controlled Randomized Study
- PO-10 A Multi-Modality 4D system for Analysis of the Aortic Morphology and Function from MR or CT
- PO-11 Sex Differences in the Development of Abnormal Endothelium-Dependent Vasodilation in Aorta from Type 2 Diabetic Rats: Possible Role of Nitric Oxide
- PO-12 Racial Differences of eNOS Expression Respond to C-reactive Protein
- PO-13 Arterial Hemodynamics in Overweight Young Adult Males Following Maximal Exercise
- PO-14 Relationship between Carotid Artery Stiffness and Altered Cerebrovascular Hemodynamics in South Asian Indian Older Adults
- PO-15 The Temporal Relationship between Metabolically Healthy Obesity and Carotid Atherosclerosis in Men
- PO-16 Reduced Cardiac Baroreflex Sensitivity Is Associated with Greater Aortic Stiffness in Middle-Aged/Older Humans: Beneficial Effect of Habitual Aerobic Exercise
- PO-17 A New Arterial Stiffness Index Permitting Isobaric Comparisons
- PO-18 Ultrasound Biomicroscopic Study of Arteries in Detection of Doxorubicin-induced Disorders
- PO-19 Significant Basal and Stimulated Variations in Inflammatory Gene Expression Profiles in African American and Caucasian HUVECS
- PO-20 Aortic Hemodynamics following Discontinuation of Menopausal Hormone Therapy in Postmenopausal Women
- PO-21 Racial Differences in Vascular Function
- PO-22 Higher Aortic Stiffness and Carotid Systolic and Pulse Pressure are Selectively Associated with Lower White Matter Integrity in the Genu and Frontal Cortex in Older Healthy Adults
- PO-23 Dependency of Arterial Stiffness Indicators on Acute Blood Volume Changes
- PO-24 Sex Differences in Hemodynamic Responses following Acute Inflammation: Wave Separation Analysis
- PO-25 Left Ventricular End-Systolic Elastance (Ecavi) Estimated with CAVI
- PO-26 The Implications of Poor Sleep Quality on Arterial Health in Persons with Multiple Sclerosis
- PO-27 Higher Central Augmentation Pressure/Index Is Associated with Tension-Type Headache but Not Migraine in Middle-Aged/Older Obese Humans
- PO-28 Changes in Cerebrovascular Pulsatility during Aerobic Exercise Are Unrelated to Brachial-Ankle Pulse Wave Velocity in Chronic Stroke
- PO-29 Creation of a Fixed Central Arterial-Venous Anastomosis on Arterial Stiffness and Central Haemodynamics: A Treatment for Hypertension Targeting the Physical Properties of the Arterial Vasculature
- PO-30 Carotid Strain Does Not Explain Sex Differences in Blood Pressure
- PO-31 Sex-Specific Differences in Cardiovascular Parameters in Spinal Cord Injured Individuals

CHRISTOPHER BROADBRIDGE is the US National Sales & Marketing Manager at Fukuda Denshi USA for the VaSera™ product. Mr. Broadbridge has worked for 10 years managing and developing a diagnostic and research laboratory for Autonomic Nervous System research in the Department of Clinical Neurophysiology at Harvard University's teaching hospital, Beth Israel Deaconess Medical Center, Boston, Massachusetts. He has been a contributor to several multi-site diabetes studies, including the D.I.A.D.* study, and served as a senior coordinator on the NIH** Stroke Team, Washington, D.C. He has authored 14 peer-reviewed medical articles and abstracts. He has also worked for 5 years in the design and marketing of medical devices, and performed market research for new medication concepts for Johnson & Johnson and Pfizer.

*--Detection of Ischemia in Asymptomatic Diabetics; **--National Institutes of Health

MICHAEL D. BROWN, PhD, is a Professor in the Department of Kinesiology and Nutrition at the University of Illinois, Chicago. Dr. Brown received his Ph.D. in Exercise Physiology from the

University of Maryland. He then completed a Postdoctoral Fellowship in the Department of Internal Medicine, Geriatrics Division and the Institute of Gerontology at the University of Michigan where he studied age-associated hypertension. Following his Postdoctoral Fellowship, he returned to the University of Maryland as an Assistant Professor in the Department of Kinesiology. After being promoted to Associate Professor, Dr. Brown relocated to Temple University. In 2012, Dr. Brown joined the esteemed faculty of the Department of Kinesiology and Nutrition at the University of Illinois, Chicago.

Dr. Brown is a Fellow in of the American Heart Association Council for High Blood Pressure Research and the American College of Sports Medicine. He serves on various national level committees, is a regular grant reviewer for the National Institutes of Health and the American Heart Association, and is an Associate Editor for Exercise and Sport Science Reviews and the World Journal of Hypertension. Dr. Brown is Director of the Vascular Health Lab and the Integrative Physiology Lab.

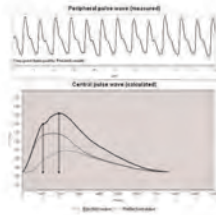
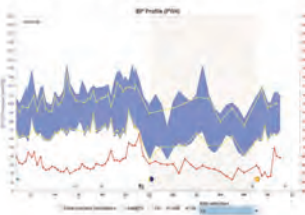
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His research program focuses on hypertension, vascular health, and exercise in African Americans. His research uses complementary human and cell models to address research questions.

JULIO A. CHIRINOS, MD, PhD is an Assistant Professor of Medicine at the University of Pennsylvania and Director of Non-Invasive Cardiac Imaging at the Philadelphia VA Medical Center.

Dr. Chirinos' research interests include the role of arterial hemodynamics in left ventricular remodeling and failure and the cardiovascular consequences of obstructive sleep apnea.

JOHN R. COCKCROFT, MD is Professor of Cardiology at the Wales Heart Research Institute in Cardiff. He is also visiting Professor in the Department of Cardiology at Columbia Presbyterian Hospital New York and adjunct Professor in the Australian School of Advanced Medicine at Macquarie University, Sydney, Australia.

His major research interests focus on endothelial function and arterial stiffness, and vascular ageing in health and disease, and recently, Professor Cockcroft has become interested in the relationship between COPD and cardiovascular disease and the mechanisms involved in the increased CV risk associated with COPD. He is a founding member and past president of the Association for Research into Arterial Structure and Physiology (ARTERY) and is past Secretary of the European Association of Clinical Pharmacology and Therapeutics (EACPT). He is principal investigator of the Assessment of Risk in Chronic Airways Disease Evaluation (ARCADE) Study. He is Editor-in-Chief of Artery Research and on the editorial board of Hypertension, the American Journal of Hypertension and the American Journal of Nephrology, and has published over 350 peer-reviewed articles and has co-authored books on hypertension and coronary heart disease.

Professor Cockcroft's clinical interests focus on hypertension and cardiovascular disease prevention, and he was a member of the committee, which produced the Welsh National Service Framework for cardiovascular disease. He is especially interested in patient empowerment and the promotion of more informed involvement with their care and treatment. He has lectured widely to patient groups on hypertension and cardiovascular disease; established the first patient self-referral clinic in the UK; and has run mobile cardiac vascular risk factor screening clinics throughout Wales and England.

Professor Cockcroft is a member of the British, European, American, and International societies of Hypertension, the British Pharmacology Society, the British Cardiac Society, and the European Association for the Study of Diabetes.

WILLIAM C. CUSHMAN, MD, FACP, FAHA, FASH, is Chief of the Preventive Medicine Section at the Veterans Affairs (VA) Medical Center in Memphis, Tennessee, Professor of Preventive Medicine, Medicine, and Physiology at the University of Tennessee Health Science Center, and the Lead Hypertension Consultant to Medical Service in Central Office of the Department of Veterans Affairs. He is the VA Champion for the 2013-14 VA-DoD (Department of Defense) Hypertension Clinical Practice Guideline committee, was a member of the Executive Committee for the Seventh (2003) Joint National Committee Report on Prevention, Detection, Evaluation, and Treatment of Hypertension (JNC 7) and was on the JNC 8 (2008-2014) Panel.

In 2010, Dr. Cushman received the John Blair Barnwell Award (Barnwell Award) for outstanding achievement in clinical science, the Department of Veterans Affairs Clinical Science Research and Development's (CSR&D) highest honor for scientific achievement.

Dr. Cushman graduated Magna cum Laude from the University of Mississippi School of Medicine, where he was also selected in his third year to Alpha Omega Alpha honorary society. He completed his residency training at the University of Mississippi in Jackson, Mississippi, and served on the faculty from 1977-1988, when he moved to the University of Tennessee in Memphis.

He has been an investigator in many clinical studies relating to hypertension, diabetes, and lipid therapy. He has been the chairman for three VA Cooperative Studies: 1) PATHS (Prevention and Treatment of Hypertension Study), 2) the VA participation (70 VA sites) in the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), and 3) The Diuretic Comparison Project. He is also Principal Investigator for the VA Clinical Center Network and Chair of the Blood Pressure Working Group of the NHLBI-sponsored Action to Control Cardiovascular Risk in Diabetes (ACCORD/ACCORDION) trial (2000-) and Principal Investigator for the VA Clinical Center Network and Chair of the Intervention Subcommittee of the NHLBI-sponsored Systolic Blood Pressure Intervention Trial (SPRINT) (2009-).

PETER U. FEIG, MD is currently a consultant to the Pharmaceutical and Biotech Industry and President of PF Pharmaceutical Development, LLC. He provides expertise in drug development, regulatory strategy, and translational science to the health care and venture capital industry.

Formerly, Dr. Feig was a Senior Director at Merck Research Laboratories, where he built and mentored a strong clinical

(Continued on page 17)

team and established a strong clinical program for new antihypertensive drugs development, in close conjunction with basic science and commercial teams. In addition, he headed the company's safety boards. Prior to that, while serving as a consultant to the Pharmaceutical Industry, Dr. Feig was also a partner at Pharmaceutical Development Initiatives, a company with the goal of developing drugs and out licensing them. He also served as vice-president for clinical development of drugs and vaccines in the US for Medeva Pharmaceuticals; and at Bayer in leading roles in cardiovascular and metabolic drug development, developing numerous compounds and achieving regulatory approval worldwide of three new molecular entities.

Since 2008, Dr. Feig has been a faculty member of the Columbia University College of Physicians and Surgeons. He has been an outpatient physician at Columbia Presbyterian Hospital and a teaching faculty member in the Nephrology Division. In addition, he developed a comprehensive course in drug development as a model of translational science, a program that has reached numerous medical schools through

NIH's CTSA program. Previously, Dr. Feig was a faculty member of the Schools of Medicine at the University of Pennsylvania, the University of Connecticut, and the University of Pittsburgh.

Dr. Feig earned his MD degree from the University of Sao Paulo School of Medicine, Sao Paulo, Brazil and did his post-graduate training in internal medicine nephrology at Hospital das Clinicas, University of Sao Paulo School of Medicine, Newton-Wellesley Hospital, and Tufts University School of Medicine, and in nephrology at Beth Israel Hospital, Harvard Medical School, Boston, Massachusetts.

He is board certified in Internal Medicine and Nephrology, has been a member of numerous professional societies, and is a fellow of the Council for High Blood Pressure Research of the American Heart Association and of the American Society of Hypertension.

STANLEY S. FRANKLIN, MD, FACP, FACC, FAHA, FASN, FASH, is clinical professor of medicine and Associate Director for the

(Continued on page 18)



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FACULTY BIOS

Heart Disease Prevention Program at the University of California, Irvine. He previously served as consulting physician at the Long Beach VA and Wadsworth VA Medical Center in Los Angeles, California. He has been an investigator with the Framingham Heart Study from 1995 to the present.

Dr. Franklin received a degree in biology and chemistry Summa Cum Laude from the University of California at Los Angeles, his M.D. degree from Harvard Medical School, and did his post-graduate training in nephrology at Peter Bent Brigham in Boston and in clinical pharmacology at Royal Postgraduate Medical School, London.

His research interests have been in the epidemiology of hypertension; the effect of aging on blood pressure; arterial stiffness; the importance of ambulatory blood pressure monitoring in the clinical assessment of cardiovascular disease risk: white-coat and masked hypertension.

Dr. Franklin is a Fellow of the American College of Physicians, the American College of Cardiology, the American Society of Nephrology, the American Society of Hypertension, the High Blood Pressure Council, the Council on Geriatric Cardiology, and the American Heart Association.

The contributor of more than 200 scientific papers and chapters to the medical literature, he has served on the editorial boards of the Journal of Hypertension, the Journal of Human Hypertension, Blood Pressure, and the Journal of Clinical Hypertension.

The European Society for Artery Research has honored him with their 2013 "Lifetime Research Achievement Award" for his pioneering work on the importance of pulse pressure as a marker of arterial stiffness in the prediction of cardiovascular disease risk and as a metric for pathologic ageing, based on his many publications from the Framingham Heart Study.

DONALD M. LLOYD-JONES, MD, SCM, FACC, FAHA, earned his BA from Swarthmore College in 1986, his MD degree from Columbia University College of Physicians and Surgeons in 1991, and a Master of Science degree in Epidemiology from the Harvard School of Public Health in 2001. He was an intern and resident in Internal Medicine at Massachusetts General Hospital in Boston, and served as Chief Medical Resident in 1995-1996. After his cardiology fellowship at MGH, he joined the staff as an attending cardiologist, and was an Instructor and then Assistant Professor of Medicine at Harvard Medical School. He joined the National Heart, Lung, and Blood Institute's Framingham Heart Study as a research fellow in 1997, and became a staff research associate in 1999.

He moved to Northwestern University in 2004, and was appointed the Chair of the Department of Preventive

Medicine in 2009. He is also Senior Associate Dean for Clinical and Translation Research, Director of the Northwestern University Clinical and Translational Sciences (NUCATS) Institute and the Eileen M. Foell Professor of Preventive Medicine and Medicine.

Dr. Lloyd-Jones' research interests include cardiovascular disease epidemiology, risk estimation, and prevention. A main focus of his research has been investigation of the lifetime risks for various cardiovascular diseases, and factors that modify those risks. Other areas of interest include CVD risk estimation using novel biomarkers, imaging of subclinical atherosclerosis, and the epidemiology of hypertension. His clinical and teaching interests lie in general cardiology, with a focus on prevention. He chaired the committee and authored the monograph that defined and set the American Heart Association's Strategic Impact Goals for 2010-2020, including a bold new focus on cardiovascular health promotion. He was co-chair of the Risk Assessment Work Group and a member of the Cholesterol Treatment Guidelines Panel for the 2013 ACC/AHA Guidelines for Cardiovascular Disease Risk Reduction. In 2014, he was named by Thomson Reuters as a Highly Cited Researcher, a distinction reserved for investigators in the top 1% by total citations of highly cited papers in their scientific field during the period 2002-2012.

He is a Fellow of the American College of Cardiology and the American Heart Association, and is an inducted member of the American Society for Clinical Investigation. In 2010, he was awarded the American Heart Association's annual Chairman's Award, recognizing the volunteer who has performed outstanding service to further the AHA's strategic goals. He is a recipient of numerous teaching awards, including the Patterson Award for Teacher of the Year from the Department of Medicine and the Teacher of the Year from the Division of Cardiology at Northwestern. In 2013, he was awarded Northwestern's Tripartite Legacy Award in recognition of his achievements as a mentor, leader, and translational physician-scientist.

GARY F. MITCHELL, MD, founder and President of Cardiovascular Engineering, Inc., is a cardiologist and internationally acknowledged leader in the field of vascular stiffness and pulsatile hemodynamics. He received his medical degree from Washington University in St. Louis and completed his training in Medicine and Cardiology at Brigham and Women's Hospital in Boston, where he served as a staff cardiologist until 1998.

(Continued on page 19)

Dr. Mitchell left the Brigham in 1998 to become founder and president of Cardiovascular Engineering, Inc., which is an NIH-funded small business that designs and develops innovative devices for measuring arterial stiffness and uses those devices to examine genetic and environmental correlates of arterial stiffness and the role that arterial stiffness plays in the pathogenesis of hypertension and target organ damage.

He joined the Framingham Heart Study as a Framingham Investigator in 1999 and became a collaborator on the AGES-Reykjavik study in 2006 and the Jackson Heart Study in 2010. Using devices designed and built by Cardiovascular Engineering, Dr. Mitchell has performed detailed assessments of arterial stiffness and pulsatile hemodynamics in more than 20,000 research participants, including participants in all 3 generations of the Framingham Heart Study as well as participants in the AGES-Reykjavik study, the REFINE study, and the Jackson Heart Study.

GARY L. PIERCE, PHD is an Assistant Professor in the Department of Health and Human Physiology at the University of Iowa and a faculty member of the Institute for Clinical and

Translational Science and Fraternal Order of Eagles Diabetes Research Center at the University of Iowa. He received an M.S. in Clinical Exercise Physiology from Northeastern University and PhD in Exercise Physiology from the University of Florida in 2005. He performed postdoctoral training in Vascular Aging in the Department of Integrative Physiology at the University of Colorado at Boulder, and has been at the University of Iowa since 2011.

The goal of his research is to understand the mechanisms that contribute to vascular endothelial dysfunction and large elastic artery stiffness with aging, obesity, prediabetes, and hypertension in humans. His lab uses an integrative experimental approach, including non-invasive and semi-invasive approaches to assess vascular function in human subjects and complementary studies in cells/tissues from humans to investigate the cellular and molecular mechanisms involved in abnormal vascular function. His lab also conducts small randomized, controlled pharmacological and lifestyle intervention studies to determine effectiveness of these

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1- Rubinshtein et al, European Heart Journal 2010
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interventions on arterial stiffness, endothelial function and autonomic function and the cellular mechanisms involved.

DAVID B. RUBIN, MD is Director, Clinical Development at GlaxoSmithKline (GSK) in Research Triangle Park, North Carolina.

Born and raised in Chicago (and still a Cub fan), he attended pre-medical school at University of Illinois, Champaign, Rush Medical College in Chicago, Duke for Internship and Residency in Internal Medicine and Pulmonary Fellowship at University of California, San Francisco and at University of Geneva, Switzerland. He chose to become a lung doctor because the lungs have the largest collection of endothelial cells.

Dr. Rubin was on faculty at Northwestern (1980-1985) and Rush Medical Schools (1985-2004) and Attending in Pulmonary and Critical Care at both of these institutions and at Cook County Hospital. His academic focus was on the radiation biology of endothelial cells.

Dr. Rubin Joined the pharmaceutical industry 10 years ago, first with Pfizer in Ann Arbor and since 2007, with GSK Respiratory R&D in Research Triangle, NC, where he currently is Physician Lead for developing IL-5 inhibitor, Mepolizumab, for COPD patients.

PATRICK SEGERS, PhD is a Professor at Ghent University, Ghent, Belgium. His research involves modelling and simulation of the hemodynamics and mechanics of the cardiovascular system making use of computer and experimental models, yet always in close collaboration with clinicians and with attention for validation and implementation of new techniques in a clinical setting.

Over the past few years, his research focused on phenotyping large artery stiffness and function, arterial physiology and early non-invasive detection of increased arterial stiffness and wave reflections on the one hand, and the use of advanced computational tools for medical applications on the other.

Professor Segers is one of the “founding fathers” of the Asklepios study, a longitudinal population study on the interplay between ageing, hemodynamics, and cardiovascular disease. He heads the bioMMeda research unit (“Biofluid, tissue and solid mechanics for medical applications”) within the Institute Biomedical Technology (IBiTech) at Ghent University.

Research topics, in which he has expertise, include Artificial Organs and Biofluidics, Medical Device Design (mainly cardiovascular stent-based applications), Cardiovascular Mechanics, Multi-physics modelling, Geometrical modelling, and Skeletal biomechanics. Professor Segers is (co-)author of

over 200 publications in both (biomedical) engineering journals as well as cardiovascular physiology and clinical journals.

SANJIV J. SHAH, MD is Associate Professor of Medicine in the Division of Cardiology, Department of Medicine, at Northwestern University’s Feinberg School of Medicine. He is also Director of the Heart Failure with Preserved Ejection Fraction (HFpEF) Program in the Bluhm Cardiovascular Institute at Northwestern Memorial Hospital, and a member of the Feinberg Cardiovascular Research Institute and Center for Genetic Medicine at Northwestern University.

Dr. Shah’s research interests include understanding the physiology, mechanisms, and epidemiology of heart failure with preserved ejection fraction (HFpEF); the genetics of cardiac structure and function, including ventricular-arterial coupling and cardiac mechanics; and the physiology, mechanisms, and risk prediction of pulmonary hypertension. Dr. Shah has expertise in cardiac mechanics, ventricular-arterial coupling, genetics of complex traits, and cardiovascular epidemiology. In 2007, Dr. Shah won the Jay N. Cohn, MD New Investigator Award from the Heart Failure Society of America. He was also the recipient of an AHA National Scientist Development Grant, and several other career development awards. Dr. Shah is currently principal investigator of an NIH R01 grant to study the acquired and genetic risk factors for abnormal cardiac mechanics in the HyperGEN study, and he is consortium PI on two additional NIH R01 grants. He has published over 85 peer-reviewed research articles.

Dr. Shah has major teaching roles in the Northwestern University Feinberg School of Medicine. In 2010, he was the winner of the George Joost Teacher-of-the-Year Award, the highest teaching award for basic science education at the medical school. Dr. Shah has received multiple teaching awards while at UCSF and Northwestern, most recently the American College of Cardiology W. Proctor Harvey Young Teacher Award.

Dr. Shah specializes in echocardiography, heart failure, and pulmonary hypertension. He is board certified in internal medicine, cardiovascular medicine, echocardiography, and advanced heart failure/transplant. In 2007, he started the Northwestern University HFpEF Program, the first of its kind, now caring for over 1200 patients with HFpEF (diastolic heart failure). Since arriving at Northwestern in 2007, he also obtained funding from the Northwestern Memorial Foundation to co-develop the multidisciplinary Northwestern

(Continued on page 21)

Pulmonary Hypertension Program. Dr. Shah is the cardiologist for the Northwestern Scleroderma Program, the Northwestern Amyloidosis Program, the Northwestern Immunotherapy Program, and the Northwestern Kovler Center for Organ Transplantation.

RAYMOND R. TOWNSEND, MD is a Professor of Medicine in the Renal Division and Associate Director of the Clinical & Translational Research Center (CTSA) at the University of Pennsylvania. He is also the Director of the Penn Hypertension Program.

Dr. Townsend received his MD degree from Hahnemann University Hospital. His formal certifications are in internal medicine (ABIM), nephrology (ABIM), clinical pharmacology (ASCP) and hypertension (ASH). He is a Fellow of the American Heart Association and a Fellow of the Council for High Blood Pressure Research. An empanelled member of the NHLBI Joint National Committee (JNC8), Dr. Townsend is the Principal Investigator of the Pulse Wave Velocity in CKD ancillary project in the Chronic Renal Insufficiency Cohort Study (CRIC), and the Principal Investigator of the Penn Clinical

Center in the CRIC Study.

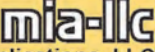
Dr. Townsend's principal research interests focus on the role of hypertension and in particular mechanisms of kidney damage that are related to pulse wave travel and pulse wave reflection in the circulation; and in the role of metabolism, specifically the linkages between insulin resistance and kidney disease progression in people with chronic kidney disease. These two areas (arterial stiffness and metabolism) link the role of hemodynamics (as reflected in both blood pressure and vascular stiffness) to a variety of outcomes in CKD including heart failure, cognitive function changes, retinopathy, CKD progression, and vascular calcification.

RONALD G. VICTOR, MD, serves at Cedars-Sinai Medical Center in Los Angeles, California as Associate Director, Cedars-Sinai Heart Institute; Director, Hypertension Center of Excellence; and Director, Clinical Research, Cedars-Sinai Heart Institute, where he holds the Burns and Allen Chair in Cardiology Research.

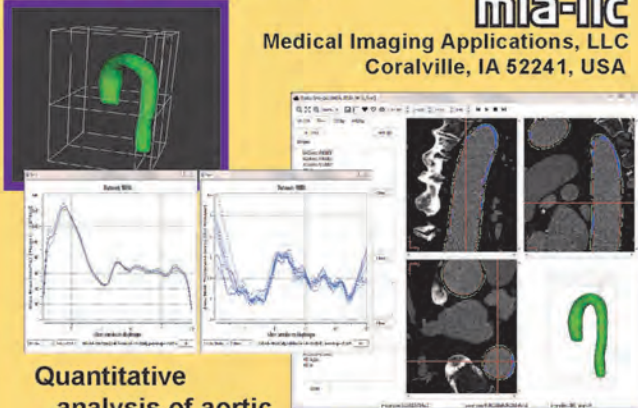
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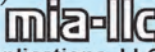


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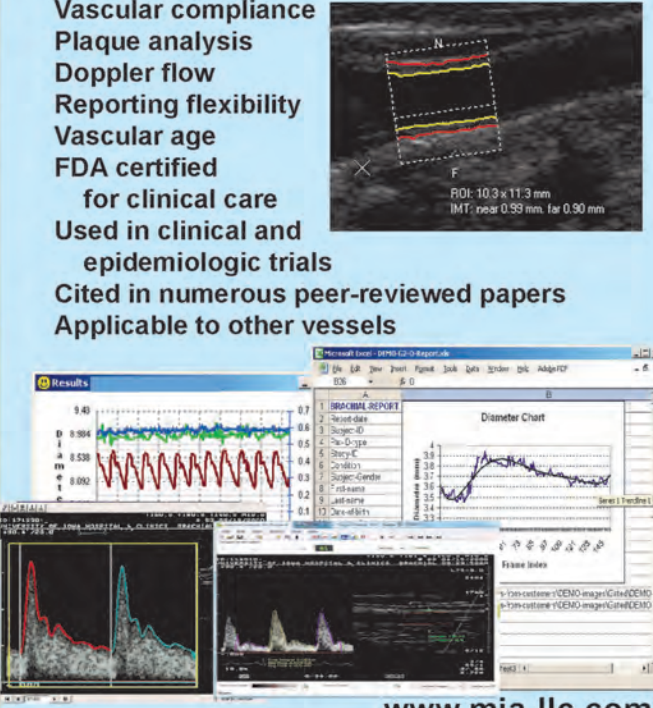
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Dr. Victor is board-certified in internal medicine, with a subspecialty in cardiovascular diseases. His research focuses on the neural mechanisms of hypertension and hypertension in special populations, including African Americans and patients with chronic renal failure. His other research interests include cardiovascular toxicity of cocaine and hookah (water pipe) smoking, cyclosporine-induced hypertension, and metabolic modulation of adrenergic receptor signaling. Dr. Victor has been awarded numerous grants from the National Institutes of Health and other organizations for his studies of heart disease, including the innovative project "Optimizing a Barber Intervention for Hypertension in African American Men." He was Principal Investigator of the Dallas Heart Study, as well as for a specialized center of research on ischemic heart disease in African American men in Dallas. Dr. Victor has published more than 200 articles and book chapters in peer-reviewed publications, and he is co-author of Kaplan's Clinical Hypertension. A sought-after speaker, Dr. Victor has presented at dozens of conferences, nationally and internationally.

Dr. Victor is Past-President of the Association of University Cardiologists, as well as a member of several professional associations, including: the American Society for Clinical Investigation, the Association of American Physicians, the Association of University Cardiologists, and the Executive Committee for the American Society of Hypertension. As an active member of the American Heart Association, Dr. Victor is a member of the Leadership Committee of the Council on High Blood Pressure Research.

Dr. Victor graduated summa cum laude with distinction, Phi Beta Kappa, and Phi Kappa Phi from Cornell University, and he earned his medical degree from Tulane University. He completed his internship and residency in internal medicine at the University of California, Los Angeles, a cardiology fellowship at Duke University, and a special cardiovascular research fellowship at the University of Iowa. He has also completed a visiting fellowship in clinical neurophysiology at the University of Uppsala in Uppsala, Sweden.



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Central Artery Stiffness, Baroreflex Sensitivity, and Brain White Matter Integrity in Older Adults

Takashi Tarumi^{1,2}, David C. Zhu⁴, Daan L.K. de Jong⁵, Rutger L. Meijers⁵, Rong Zhang^{1,2,3}

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Central artery stiffness is associated with greater risk of white matter (WM) lesions and cognitive impairment in older adults, yet the pathophysiological mechanisms remain unclear. Stiffening of central elastic arteries impairs cardiovagal baroreflex, a neurogenic mechanism of short-term blood pressure regulation, and may increase the risk of cerebral hypoperfusion in deep and periventricular WM areas. **Objective:** To determine the associations among central artery stiffness, cardiovagal baroreflex sensitivity (BRS), and cerebral WM microstructural integrity in older adults. **Methods:** Fifty-four older adults (65±6 years) with normal cognitive function (n=18) or mild cognitive impairment (MCI, n=36) were tested. Carotid-femoral pulse wave velocity (cfPWV) via applanation tonometry, cardiovagal BRS via the Modified Oxford technique, and deep and periventricular WM tract integrity via diffusion tensor imaging were measured. Voxelwise and region of interest analyses were performed on fractional anisotropy (FA) and radial diffusivity (RD), indices of axonal integrity and demyelination respectively. **Results:** Participants with MCI showed lower memory and executive function performance whereas cfPWV, cardiovagal BRS, and WM tract integrity were not different from normal subjects. In the pooled data combining all subjects, cfPWV and cardiovagal BRS were inversely correlated (r=-0.34, P=0.01). Across WM, lower FA and higher RD were associated with increasing cfPWV and decreasing BRS with many of the regions showing overlap (Figure 1). Multiple linear regression analysis of FA and RD, including age, sex, and cognitive status as covariates, demonstrated independent contributions of cfPWV and cardiovagal BRS to posterior corona radiata, external capsule, and retrolenticular part of internal capsule. Furthermore, FA and RD measured from these regions were associated with executive function performance (Figure 2). **Conclusion:** Central arterial stiffness and lower cardiovagal BRS are independently associated with deep and periventricular WM microstructural integrity and contribute to executive function performance in older adults.

This study was supported by National Institute on Aging (5R01AG033106-01).

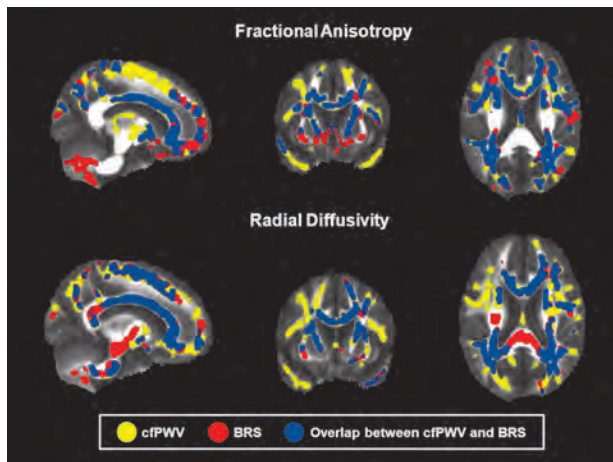


Figure 1: Tract-based spatial statistics maps displaying the regions of fractional anisotropy (FA) and radial diffusivity (RD) which showed associations with carotid-femoral pulse wave velocity (cfPWV) and cardiovagal baroreflex sensitivity (BRS). Lower FA and higher RD were associated with increasing cfPWV (yellow) and decreasing cardiovagal BRS (red). The blue areas represent the overlap where both cfPWV and cardiovagal BRS associated with FA and RD.

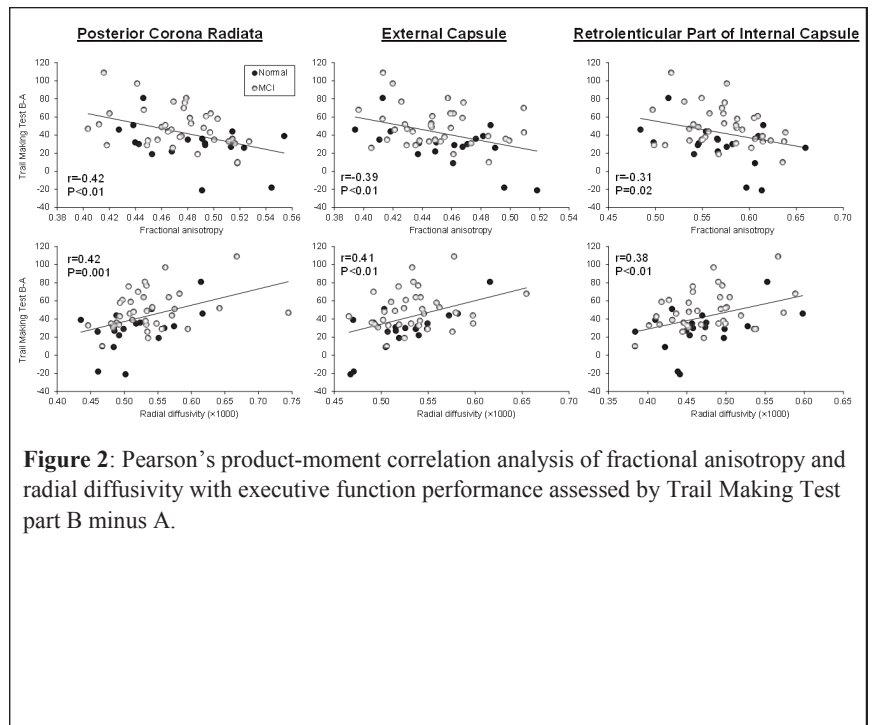


Figure 2: Pearson's product-moment correlation analysis of fractional anisotropy and radial diffusivity with executive function performance assessed by Trail Making Test part B minus A.

Saxagliptin Prevents Increased Coronary Arterial Stiffness and Advanced Glycation End Product Expression in a Miniature Swine Model of Heart Failure with Preserved Ejection Fraction

Bradley S. Fleenor¹, An Ouyang¹, Melissa S. Cobb², Emily Dehn², Jessica A. Hiemstra², Jan R. Ivey², and Craig A. Emter²

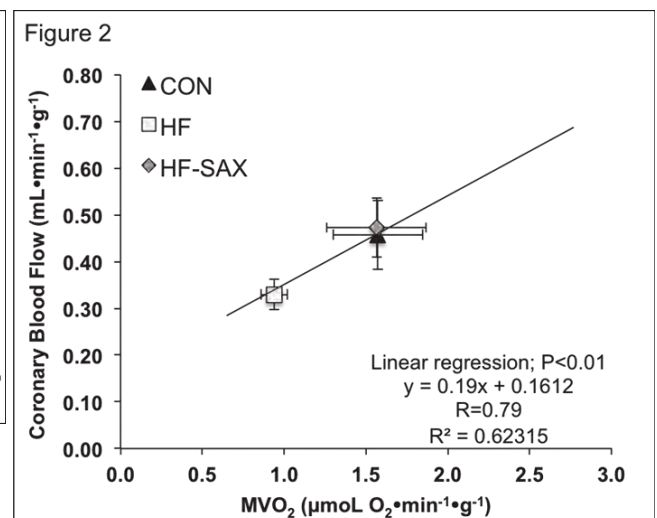
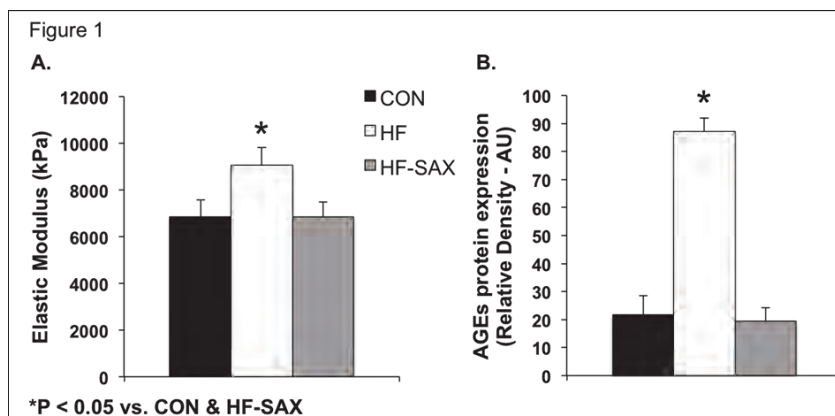
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Objective: Our lab recently reported coronary arterial dysfunction, a hallmark feature of heart failure (HF), and myocardial oxygen supply/demand imbalance in a mini-swine model of heart failure with preserved ejection fraction (HFpEF). Accumulation of advanced glycation end products (AGEs) may play a role in this process by increasing vascular mechanical stiffness. Dipeptidyl-peptidase 4 (DPP4) inhibitors have been shown to inhibit AGEs in diabetes, however, their impact on coronary fibrotic remodeling in HFpEF is unknown. We hypothesized chronic treatment with the DPP4 inhibitor saxagliptin would prevent enhanced mechanical stiffness and AGEs accumulation in coronaries from HFpEF swine.

Methods: Yucatan mini-swine (3-months old) were aortic-banded (AB) and divided into 3 groups: control (CON; n=6), HF-control (HF; n=7), and HF saxagliptin-treated (HF-SAX; n=9). Coronary blood flow (CBF), myocardial oxygen consumption (MVO₂), ex vivo mechanical stiffness, AGEs protein, and mRNA expression of stiffness-related genes were assessed on the left circumflex (LCX) and right coronary artery (RCA) 6 months post-AB and 23-weeks post-saxagliptin treatment (started 1-week post-AB).

Results: A significant increase in the elastic modulus of the RCA and LCX in HF animals was associated with increased vascular medial AGEs protein expression compared to CON. Increased mechanical stiffness and AGEs expression was prevented in HF-SAX animals. Increased AGEs expression in the HF group occurred independent of changes in plasma glucose concentration. Parallel trends in the mRNA expression of several extracellular matrix components and regulatory biomarkers were observed in HF animals, including increased collagen I/III, TIMP-1, and decreased MMP-9. Increased mechanical stiffness in HF animals was associated with a leftward shift in the CBF:MVO₂ relationship that was prevented by saxagliptin.

Conclusion: Saxagliptin prevented increases in coronary mechanical stiffness and AGEs expression independent of glucose regulation, suggesting DPP4 inhibition may be a viable therapeutic option for limiting vascular fibrosis and related coronary arterial dysfunction during developing HFpEF.

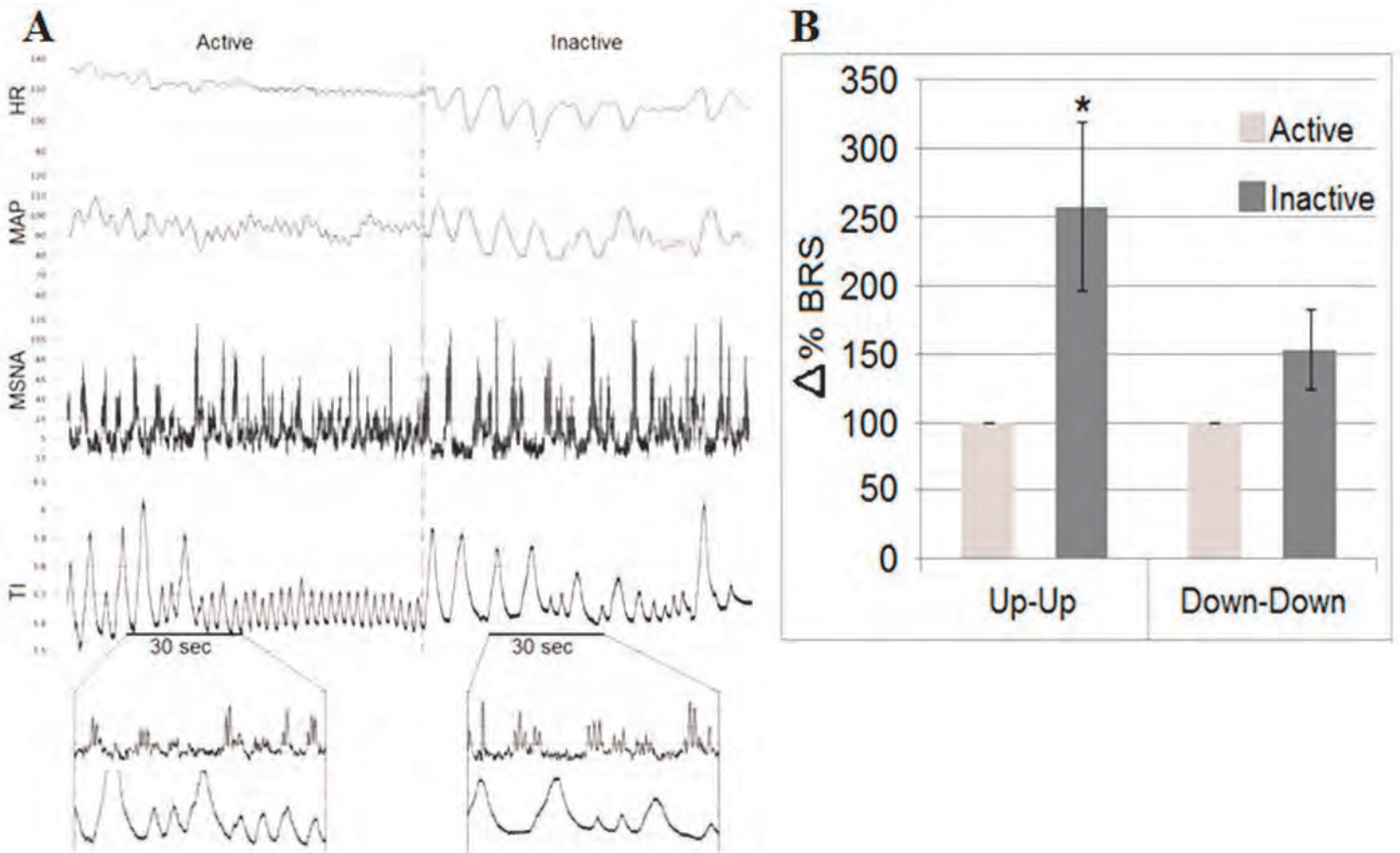


Cardio-Respiratory Interactions Immediately following Dynamic Leg Cycling: Influences of the Muscle Pump

Daniel W. White, Gilbert Morales, Victoria L. Kay, Wendy L. Eubank, Peter B. Raven

The University of North Texas Health Science Center at Fort Worth, Fort Worth, TX, USA

Changes in cardiorespiratory coupling during the moments immediately following prolonged exercise are not well understood and the mode of recovery during the transition to post-exercise may be important. Cardiorespiratory coupling influences the stresses put on the arterial system by oscillatory changes in cardiac output and systemic vascular resistance. We hypothesized that the cessation of muscle pump activity and the unloading of the cardiopulmonary baroreceptors during inactive recovery would allow for exacerbated oscillations in neutrally-mediated cardiovascular function and arterial control resulting in an unstable cardiorespiratory environment. To test this hypothesis, healthy subjects (n=13, 3 female) performed 40 minutes high intensity two-legged cycling exercise followed by active and inactive recovery. Electrocardiogram (HR), beat-to-beat blood pressure (BP), thoracic impedance (Z_0), respiratory frequency and muscle sympathetic nerve activity (MSNA) were continuously monitored throughout the protocol. Data analysis was performed in the minute prior to cessation of pedaling and the first minute of inactive recovery. Z_0 was significantly higher during inactive vs. active recovery (57.1 vs. 55.8 units, $P=0.02$; Fig A). Respiratory coupling to HR, BP and MSNA was confirmed by signal coherence analysis (0.98, 0.98 and 0.86, respectively). Spontaneous baroreflex sensitivity was significantly increased during inactive recovery for the Up-Up reflex (2.58 fold, $P<0.05$; Fig B) and tended to be increased for the Down-Down reflex (1.53 fold, $P=.10$; Fig B). We conclude that the magnitude of respiratory-induced oscillations in BP, HR, and MSNA during recovery from exercise is dependent on muscle pump induced changes in central blood volume. Greater cardiovascular sensitivity during inactive recovery may place a larger strain on the arterial system and may partially explain increased risk of sudden death following acute exercise.



Importance of Time Delay Estimation Methods for Aortic Pulse Wave Velocity Assessment with Phase-Contrast MRI

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Background: Pulse wave velocity (PWV) is a validated measure of arterial wall stiffness. Assessments of PWV are highly dependent on pulse transit time estimations between 2 points. No systematic assessments have been performed regarding the best method to assess pulse travel time using phase-contrast MRI.

Aim: To compare the relationship between MRI-derived PWV (distance/transit time) measured by different methods and: (1) Age; (2) Carotid-femoral PWV (CFPWV) assessed with arterial tonometry, the “gold standard” index of arterial stiffness.

Methods: We measured aortic flow using in plane phase contrast MRI in the “candy cane” aortic view among 261 adults. Transit time between the proximal ascending aorta and the distal thoracic descending aorta were assessed from flow velocity curves using various methods for pulse upstroke detection (table).

Results: Aortic PWV assessed based on the peak second derivative of flow demonstrated the best correlation with both age and tonometric CFPWV. The method based on 20% of the upstroke amplitude provided results comparable to the peak second derivative. On the other hand, the cross-correlation method (which is currently the most commonly used) demonstrated weak relationships and often resulted in non-physiologic PWV values (up to >200 m/sec) due to non-parallel up-slopes resulting in falsely short delays between cross-correlated upstrokes. Other methods provided intermediate correlation coefficients with age and CFPWV.

Conclusions: The method to compute the onset of the flow pulsatile upstroke using phase-contrast MRI markedly impacts the assessment of PWV. The peak of the 2nd derivative is the most robust method for PWV estimations. The use of the cross-correlation method, which is most frequently used at present, should be abandoned.

	Age	CF PWV
Method	R value (P value)	R value (P value)
2 nd derivative	0.43 (<0.0001)	0.48 (<0.0001)
Cross-correlation	0.12 (0.11)	0.41 (<0.0001)
DPDT	0.29 (<0.0001)	0.44 (<0.0001)
20% PH	0.42 (<0.0001)	0.46 (<0.0001)
10%	0.22 (0.001)	0.38 (<0.0001)
40%	0.34 (<.0001)	0.46 (<0.0001)
Intersecting tangents	0.35 (<0.0001)	0.42 (<0.0001)

Relationship of Common Carotid Artery Perivascular Adipose Tissue, Arterial Stiffness, and Intima-Medial Thickness, in Adult Humans

H. L. Choj, J. S. Au and M. J. MacDonald

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Objective: Most arteries in humans are directly surrounded by adipose tissue and it has been hypothesized that an excess of perivascular adipose tissue (PVAT) is involved in the pathogenesis of atherosclerosis and arterial stiffening. There is a lack of research examining the relationships between PVAT with other measures of arterial health (i.e., stiffness and wall thickness). The purpose of the current study was to examine relationships between the carotid PVAT measured through extra-medial thickness (EMT) ultrasonography and other measures of vascular health.

Methods: Central arterial stiffness by pulse wave velocity was obtained with applanation tonometry at the common carotid and femoral arteries, and common carotid artery intima-media thickness (IMT), compliance, distensibility and stiffness index were obtained with simultaneous sonographic imaging and applanation tonometry. Resting measures of heart rate and supine brachial blood pressure were also obtained. Carotid artery EMT and IMT measurements were sonographically imaged in the longitudinal section. Carotid EMT was denoted as the distance between the jugular intima-lumen interface to the carotid media-adventitia interface. Custom semi-automated edge detection software was used for image and data analysis.

Results: Data was collected from 20 healthy young adults (mean age 24.2 ± 13.8 yrs, 5 females). Carotid EMT was significantly correlated to brachial mean arterial pressure ($r = 0.52$, $n = 18$, $p < 0.01$), central pulse wave velocity ($r = 0.45$, $n = 20$, $p < 0.02$), IMT ($r = 0.55$, $n = 20$, $p < 0.01$), and carotid stiffness index ($r = 0.53$, $n = 20$, $p < 0.01$).

Conclusion: These preliminary findings indicate that an increased carotid PVAT may be associated with increases in both regional carotid and central arterial stiffness. Carotid EMT ultrasonography provides an additional tool that correlates significantly with the existing vascular health measures in this cohort. Further studies are needed to determine whether EMT will provide relevant additional information that can assist in the prediction of cardiovascular outcomes and the evaluation of risk reduction interventions.

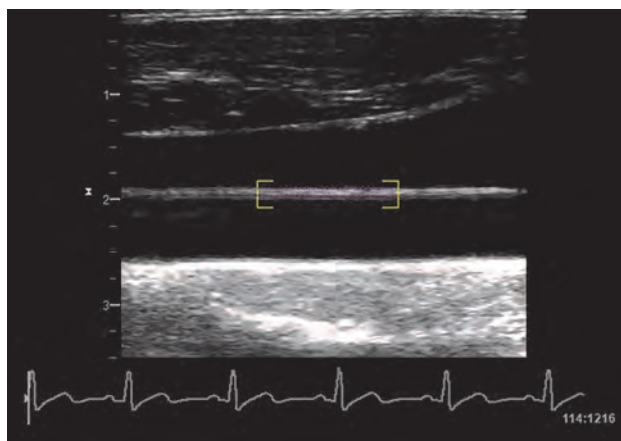


Figure 1. Custom edge-detection software uses a region of interest (yellow box) and quantifies the common carotid artery extra-medial thickness measurement, indicated by the red dotted lines

Table 1. Pearson correlation of extra-medial thickness and other arterial measures

Variable	Correlation	Sig. (1-tailed)	n
Systolic Blood Pressure	.366	.062	19
Diastolic Blood Pressure	-.036	.442	19
Mean Arterial Pressure	.515*	.014	18
Body Mass Index	.376	.051	20
Central Pulse Wave Velocity	.449*	.023	20
Intima-Medial Thickness	.548**	.006	20
Carotid Compliance	-.199	.200	20
Carotid Distensibility	-.213	.183	20
Carotid Stiffness Index	.534*	.008	20

Longitudinal and Circumferential Strain of the Proximal Aorta

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Objectives: Proximal aortic stiffness increases with age and contributes to pathogenesis of wide pulse pressure and epidemic proportions of isolated systolic hypertension, which is difficult to control. Elucidation of factors that contribute to abnormal mechanical properties of the proximal aorta may facilitate development of more effective interventions. During systole there is substantial aortic long axis displacement and longitudinal strain, which we hypothesize causes overestimation of ascending aortic stiffness calculated from circumferential strain.

Methods: We performed magnetic resonance imaging in 375 participants (72 to 94 years of age, 204 women) in the Age, Gene/Environment Susceptibility-Reykjavik Study and measured circumferential and longitudinal strain along the aortic arch. Local pulse wave velocity (PWV) was calculated from circumferential strain and central pulse pressure using the Bramwell-Hill equation.

Results: Observed circumferential area strain was lower (geometric mean [95% confidence interval], 7.7 [7.3, 8.1] vs. 12.7 [12.2, 13.2] %, $P < 0.001$) and PWV was higher (11.0 [10.7, 11.3] vs. 8.5 [8.3, 8.8] m/s, $P < 0.001$) in the proximal ascending versus proximal descending thoracic aorta. In contrast, peak flow was similar at the two locations (39 [38, 40] vs. 39 [38, 40] cm/s, $P = 0.78$), which was inconsistent with observed differences in strain and PWV. When ascending aortic circumferential strain was corrected for longitudinal strain ($7.8 \pm 2.6\%$), PWV was comparable in the ascending and descending aorta (8.3 [8.2, 8.5] vs. 8.5 [8.3, 8.8] m/s, $P = 0.074$), consistent with comparable flow velocities.

Conclusion: Longitudinal strain represents a substantial and previously ignored component of proximal aortic volume storage that should be considered in order to avoid misclassification of ascending aortic stiffness.

Effects of Acute Induced Inflammation on Pressure Waveforms: Does Age Matter?

Bunsawat, K¹, Lane, AD², Kappus, RM¹, Ranadive SM³, Yan, H⁴, Wee, Sang-Ouk¹, Phillips, S¹, Baynard, T¹, Woods, J⁴, Motl, R⁴, and Fernhall B¹.

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The Augmentation index (AIx) is a strong independent predictor of atherosclerosis. Aging is characterized by increased AIx and low grade inflammation. However, the effect of induced systemic inflammation on AIx is unclear.

Purpose: To investigate the effect of acute induced inflammation on wave reflection using wave separation analysis (WSA) in young (YA) vs. old adults (OA) pre-vaccination and 24-hr and 48-hr post vaccination.

Methods: Subjects were 22 YA (female=14; age 25±4 yrs; BMI 23.3±3.0 kg/m²) and 26 OA (female=17; age 63±6 yrs; BMI 29.6±6.3 kg/m²). AIx was assessed using applanation tonometry and followed by wave separation analysis (SphygmoCor, AtCor Medical). CRP and IL-6 were measured using ELISA assays.

Results: Compared to YA, OA had higher baseline aortic pulse pressure (aPP), AIx, AIx@75, central pulse wave velocity (cPWV), reflected wave pressure (RPH), IL-6, and CRP (*P*<0.05). AIx, AIx@75, and cPWV did not change from baseline, but were higher in OA at all time points (*P*<0.05). aPP, Forward wave pressure (FPH) and RPH decreased from baseline in OA (*P*<0.05), but did not change in YA. IL-6 increased from baseline at post 24-hr in YA, but not in OA (*P*<0.05). **Conclusions:** Although acute induced inflammation did not change indices of central arterial stiffness in OA, WSA revealed that FPH and RPH decreased in OA, concomitant with an aPP reduction. It appears that induced inflammation has a greater effect on arterial function and aPP in OA possibly due to greater effects of inflammation on peripheral vasodilatation in this group.

Variables		Baseline	Post 24-hr	Post 48-h	Time	Age	Interaction
aPP (mmHg)	<u>YA</u>	30±6	32±6	33±6	0.730	<0.001	0.001
	<u>OA</u>	43±10 [#]	41±10 [#]	39±9 ^{#,*}			
AIx	<u>YA</u>	7.80±11.26	3.05±11.14	4.60±11.54	0.085	<0.001	0.185
	<u>OA</u>	34.52±10.45 [#]	34.40±13.09	32.56±8.33			
AIx@75	<u>YA</u>	-1.40±12.3	-4.35±11.13	-5.05±10.61	0.132	<0.001	0.434
	<u>OA</u>	28.24±9.89 [#]	28.56±10.09	26.68±7.37			
cPWV	<u>YA</u>	5.38±0.76	5.48±0.90	5.50±1.05	0.681	<0.001	0.885
	<u>OA</u>	7.61±1.76 [#]	8.04±1.97	7.69±1.33			
FPH (mmHg)	<u>YA</u>	27±5	29±5	29±5	0.682	1.812	0.010
	<u>OA</u>	28±5	25±4 ^{#,*}	25±5			
RPH (mmHg)	<u>YA</u>	13±4	13±4	14±3	0.002	<0.001	<0.001
	<u>OA</u>	22±6 [#]	19±6 ^{#,*}	18±5 ^{#,*}			
IL-6 (ng/mL)	<u>YA</u>	0.89±0.57	2.29±2.14 [*]	1.14±1.33	<0.001	0.001	0.001
	<u>OA</u>	2.18±1.47 [#]	2.60±1.85	2.23±1.46 [#]			
CRP (mg/L)	<u>YA</u>	1.03±1.01	1.28±0.95	1.62±1.19	<0.001	0.002	0.492
	<u>OA</u>	2.60±2.19 [#]	3.94±3.76	4.38±4.13			

Data are mean±SD. BMI, body mass index; VO_{2peak}, peak oxygen consumption; aPP, aortic pulse pressure; AIx, augmentation index; AIx@75, augmentation index corrected for heart rate 75 bpm; cPWV, central pulse wave velocity; FPH, forward pulse height; RPH, reflected pulse height; IL-6, interleukin-6; CRP, C-reactive protein. *significantly different than baseline (*P*<0.05). [#]significantly different than young adults (*P*<0.05).

Sex Differences in Stiffness Parameters following Maximal Exercise

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¹University of Illinois at Chicago, Chicago, IL, USA, ²Mayo Clinic, Rochester, MN, USA, ³East Carolina University, Greenville, NC, USA, ⁴University of Iowa, Iowa City, IA, USA, ⁵University of Illinois at Urbana Champaign, Urbana, IL, USA

Objectives: The sex differences found in cardiovascular disease risk and progression are well established. These discrepancies are potentially attributed to the cardioprotective effect of estrogen or sex specific differences in fitness. There may also be sex differences in the cardiovascular responses to exercise, which could underlie this disease risk. We investigated arterial stiffness parameters at rest and following maximal exercise in untrained males and females.

Methods: Eighty-three young (mean age=25 years), healthy males (n= 39) and females (n=44) underwent measures of vascular stiffness at rest and both 15 and 30 minutes (po15, po30) following maximal exercise. The exercise stimulus was an acute progressive maximal exercise bout on a cycle ergometer.

Results: Females had significantly lower pressures (carotid, aortic and brachial) at all time points compared to males, with no heart rate differences. Arterial compliance (AC) and Elastic Modulus (Ep) changed similarly between sexes, with a decreased compliance at po15, returning to baseline values at po30. Males had significantly elevated central stiffness (cPWV) at both rest and po15 compared to females, but significantly decreased at po30 to match values of the females. The significance in cPWV between sexes remained after controlling for aortic MAP.

Conclusions: Females have a less stiff resting arterial profile compared to males. However, with maximal exercise, males altered their arterial profile to eliminate any significant differences between females in stiffness indices. This suggests that a maximal bout of exercise is an appropriate stimulus for evaluating stress induced sex differences in arterial stiffness.

Table 1: Descriptive Statistics

	Total (n=83)	Males (n=39)	Females (n=44)
Age (yr)	25.3 ± 0.8	25.2 ± 1.5	24.9± 0.7
BMI (kg/m ²)	27.2 ± 0.8	26.7 ± 0.7	27.6 ± 1.3
Height (cm) *	170.2 ± 1.1	178.2 ± 0.9	163.2 ± 1.
Weight (kg) *	79.1 ± 2.4	84.9 ± 2.4	74.1 ± 4.0
VO2peak (ml/kg/min) *	33.1 ± 0.9	38.4 ± 1.3	28.3 ± 0.9

Table 2: Pressure and stiffness response before and following maximal exercise

	Males			Females		
	rest	Post15	Post30	rest	Post15	Post30
bMAP (mmHg)	90±1*	92±2*	89±1* #	85±1	84±2	84±1
aorMAP (mmHg)	87±1*	90±2*	88±1*	84±1	82±1	82±1
HR (bpm)	63±2	86±2 \$	79±2 \$#	65±1	83±2 \$	78±2 \$#
cPWV (m/s)	6.12±0.17*	6.21±0.15*\$	5.84±0.17\$	5.50±0.16	5.34±0.14	5.56±0.15
Ep (kPa)	72.51±3.42*	81.09±4.52	71.51±3.93	61.33±3.12	71.41±4.13\$	66.14±3.49
AC (mm ² /kPa)	1.14±0.07*	0.97±0.07\$	1.12±0.06#	1.31±0.06	1.10±0.06\$	1.22±0.06#
B-stiffness	5.81±0.27	6.23±0.33	5.71±0.32	5.24±0.24	6.10±0.30\$	5.71±0.29

*p<0.05 between sexes
\$ sig diff from rest
#sig diff from po15

Correlations between Arterial Stiffness/Central Hemodynamics and Serum Cardiac Troponin T and Natriuretic Peptide Levels

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Objective: Elevated serum levels of cardiac troponin T (cTnT) and N-terminal fragment of B-type natriuretic peptide (NT-proBNP), and also increased arterial stiffness/abnormal central hemodynamics are well-known risk factors for future cardiovascular events. The present study was conducted to clarify which of the two - the serum level of cTnT or that of NT-proBNP - might be more closely associated with the arterial stiffness/central hemodynamics.

Methods and Results: In 2374 male employees of a company (46 ± 9 years old), the following parameters were measured: second peak of the radial systolic pressure waveform (SBP2), radial augmentation index (rAI), PP2 (SBP2 minus the diastolic blood pressure), brachial-ankle pulse wave velocity (baPWV), and serum levels of cTnT and NT-pro BNP. After adjustments for confounding variables, binary logistic regression analyses demonstrated that baPWV was associated with a significant odds ratio for serum NT-proBNP ≥ 125 pg/mL (1.690; 95% confidence interval = 1.136–2.514, $p = 0.002$) and rAI was associated with a significant odds ratio for serum NT-proBNP ≥ 55 pg/mL (1.205; 95% confidence interval = 1.012–1.435, $p = 0.036$). The baPWV, rAI, SP2 and PP2 were not associated with significant odds ratios for elevated serum cTnT levels (≥ 0.014 ng/mL and ≥ 0.010 ng/mL).

Conclusions: Increased arterial stiffness/abnormal central hemodynamics may be associated with elevated serum NT-proBNP levels, rather than with minimally elevated serum cTnT levels. This difference may be one of the plausible explanations for the independency of the predictive values of the two serum markers for future cardiovascular events.

Buffering of Carotid Artery Pressure and Flow Pulsatility during Cognitive Engagement in Healthy Adults

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The matching of vascular supply to neuronal metabolic demand during cognitive engagement is known as neurovascular coupling (NVC). Excessive hemodynamic pulsatility may have a detrimental effect on neural function and affect NVC. Arterial stiffness is a prominent determinant of pulsatility in the brain.^{1,2}

OBJECTIVES: We explored changes in arterial stiffness and cerebrovascular hemodynamic pulsatility during cognitive engagement in healthy adults.

METHODS: Twenty-seven adults (age 39 ± 3 yrs, BMI 24±1 kg/m²) underwent Doppler ultrasonography and applanation tonometry of the common carotid artery (CCA) to derive 1) CCA elastic modulus (Ep) and β-stiffness index; 2) CCA flow pulsatility index (PI); 3) CCA pulse pressure (PP), and 3) CCA augmentation index (AIx). Transcranial Doppler was used to assess cerebral PI at the middle cerebral artery (MCA). All measures were made simultaneously at rest and during a 4-minute Stroop task.

RESULTS: CCA PI was reduced (p<0.05) while MCA PI was unchanged (p>0.05) during Stroop. Brachial PP increased during Stroop (p<0.05) while CCA PP was unchanged (p>0.05). Similarly, CCA Ep (p>0.05) and β-stiffness (p>0.05) were unchanged. CCA AIx increased (p<0.05).

CONCLUSION: Carotid pressure pulsatility and cerebral flow pulsatility is unaltered while carotid flow pulsatility is reduced during cognitive engagement. Carotid stiffness does not change suggesting that factors other than the elastic properties of the vessel moderate cerebrovascular pulsatility during cognitive engagement.

TABLE 1. Hemodynamic and vascular parameters at rest and during Stroop task

Variable	Baseline	Stroop	p- value
Brachial Pulse Pressure, mmHg	43 ± 1	46 ± 1	0.002
Carotid Pulse Pressure, mmHg	36 ± 1	35 ± 1	0.324
Carotid β-Stiffness, aU	4.4 ± 0.4	4.2 ± 0.3	0.224
Carotid Ep, kPa	54.5 ± 5.5	53.8 ± 4.9	0.670
Carotid Pressure AIx, %	1 ± 4	13 ± 4	0.001
Carotid Distension AIx, %	4 ± 2	8 ± 2	0.001
Carotid Mean Diameter, mm	5.62 ± 0.13	5.74 ± 0.13	0.010
Carotid Pulsatility Index	1.75 ± 0.06	1.57 ± 0.06	0.016
Cerebral Pulsatility Index	0.75 ± 0.02	0.75 ± 0.01	0.841

REFERENCES

- Mitchell GF, van Buchem MA, Sigurdsson S, Gotlib JD, Jonsdottir MK, Kjartansson O, Garcia M, Aspelund T, Harris TB, Gudnason V, Launer LJ. Arterial stiffness, pressure and flow pulsatility and brain structure and function: The age, gene/environment susceptibility--reykjavik study. *Brain*. 2011;134:3398-3407
- Tarumi T, Ayaz Khan M, Liu J, Tseng BM, Parker R, Riley J, Tinajero C, Zhang R. Cerebral hemodynamics in normal aging: Central artery stiffness, wave reflection, and pressure pulsatility. *Journal of cerebral blood flow and metabolism*. 2014

Effects of Systemic Niacin Infusion on Sympathetic Activity, Arterial Stiffness and Aortic Wave Reflection: A Pilot Study

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Objective: Free fatty acids (FFA) may increase sympathetic activity and arterial stiffness. Niacin decreases FFA, however, little is known regarding the direct effects of niacin on sympathetic activity and arterial stiffness. We tested the hypothesis that niacin would decrease arterial stiffness, central aortic blood pressures, indices of aortic wave reflection, and muscle sympathetic nerve activity (MSNA).

Methods: High-fidelity radial arterial pressure waveforms and carotid-femoral pulse wave velocity (c-f PWV) were measured noninvasively by applanation tonometry before and during intravenous infusion of niacin (2.8 mg/min) at t=60, 90, 120 and 150 minutes in 5 healthy adults (2M/3F; aged 29±9 years). FFA (HPLC), MSNA (microneurography), arterial blood pressure (brachial arterial catheter) and heart rate (HR, ECG) were measured before and during niacin.

Results: While niacin produced a 75% reduction in FFA, contrary to our hypothesis, MSNA increased by 28-56% over all time points. After 60 minutes of niacin infusion, augmentation index (Alx) corrected for HR (Alx@75bpm) increased compared to baseline (Table 1; P<0.05). Repeated measures ANOVA also revealed trends for a main effect of niacin over time for Alx (P=0.12), augmented pressure (AP; P=0.18), and c-f PWV (P=0.13) (Table 1). When only comparing changes between baseline and t=60 (via paired t-test), both Alx and AP were both significantly increased (P<0.05).

Conclusions: Our preliminary results in a small group of subjects suggest that although IV niacin dramatically reduces FFA, it causes increases in MSNA and aortic wave reflection (Alx@75bpm). Inclusion of more subjects is needed to statistically confirm the strong trends for increased indices of wave reflection and arterial stiffness with niacin. Additionally, further studies are warranted to determine if chronic oral niacin therapy exerts similar effects.

Table 1. Hemodynamic and vascular measurements before and during niacin

	Baseline	60min	90min	120min	150min
HR (bpm)	73±6	71±5	69±7	71±8	76±9
BSP (mmHg)	122±4	128±5	126±7	126±6	126±6
BDP (mmHg)	76±2	79±3	79±3	77±3	78±3
BPP (mmHg)	47±2	49±3	48±4	48±4	48±4
ASP (mmHg)	105±4	115±6	112±8	110±6	110±6
ADP (mmHg)	77±3	80±4	80±3	79±3	79±3
APP (mmHg)	28±1	34±3	32±5	31±4	30±5
PPA (%)	165±6	146±8	154±10	159±9	165±10
Alx (%)	6.9±2.1	18.6±4.7	14.5±5.2	12.3±4.4	8.6±5.6
Alx@75bpm (%)	5.0±3.3	15.8±4.8*	10.9±3.4	9.8±2.7	8.6±2.5
AP (mmHg)	1.9±0.6	6.9±2.0	5.6±2.7	4.6±2.2	3.7±2.6
c-f PWV (cm/s)	7.1±0.4	7.8±0.8	7.8±1.0	7.3±0.6	7.2±0.5

Data are mean±SE; N=5; *P<0.05; BSP, brachial systolic pressure; BDP, brachial diastolic pressure; BPP, brachial pulse pressure; ASP, aortic systolic pressure; ADP, aortic diastolic pressure; APP, aortic pulse pressure; PPA, pulse pressure amplification

Racial Differences in Circulating csRAGE and Alternatively Spliced esRAGE in Healthy Adolescents: Relation with Aortic Stiffness

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Background: Binding of ligands to the receptor for advanced glycation end products (RAGE) triggers pro-inflammatory/oxidant signaling in the vascular wall. Increased circulating soluble forms of RAGE (sRAGE) are associated with decreased vascular risk and may be protective by acting as a decoy to prevent ligand binding to full-length RAGE. Sheddases, such as matrix metalloproteinase-9 (MMP 9) proteolytically cleave cell surface receptors including RAGE, forming cleaved soluble RAGE (csRAGE). However, sRAGE also includes endogenous secretory RAGE (esRAGE), an isoform of RAGE without receptor function derived from alternative splicing of RAGE pre-mRNA. sRAGE is lower in African-American (AA) compared with Caucasian adults and is hypothesized to contribute to elevated arterial stiffening and vascular risk in AAs. Indeed, we have previously demonstrated that sRAGE (1567±68.9 vs. 955±101.1 pg/mL, p<0.001) but not MMP9 is higher in Caucasian compared with AA adolescents and associated with lower carotid-femoral pulse wave velocity (CFPWV) (5.3±0.2 vs. 5.9±0.2 m/sec, p<0.05).

Objectives: We hypothesized that increased sRAGE in Caucasian versus AA adolescents is from increased circulating esRAGE through alternative splicing of RAGE pre-mRNA.

Methods and Results: Circulating esRAGE (ELISA) was significantly higher (369±24.8 vs. 242±26.5 pg/mL, P<0.01) in Caucasian (n=24, age 16.5±0.3 yrs; BMI 22.9±0.8 kg/m²) vs. AA (n=15, age 16.8±0.3 yrs; BMI 24.5±1.0 kg/m²) adolescents (P>0.05). esRAGE was correlated with sRAGE (r=0.708, P<0.001), but esRAGE:sRAGE ratio did not differ between race (0.24±0.01 vs. 0.33±0.09, p>0.05). Preliminary data in pooled Caucasian (n=3) human umbilical vein endothelial cells (HUVECs) demonstrates greater esRAGE mRNA (qRT-PCR) than AA HUVECs, but similar full-length RAGE mRNA.

Conclusion: These preliminary data suggest that higher sRAGE in Caucasian compared with AA adolescents is likely not from higher esRAGE but a combination of cleavage from non-MMP9 sheddases and alternative splicing of RAGE.

Effects of Acute Dietary Nitrate Supplementation on Aortic Wave Reflection in Young Adults

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Objective: Evidence suggests that dietary nitrate supplementation (i.e. beetroot juice) decreases measures of peripheral blood pressure. However, the effects of acute dietary nitrates on central aortic pressures are unclear. Thus, the objective of this study was to investigate the effects of beetroot juice consumption on central aortic pressures and indices of aortic wave reflection.

Methods: 13 healthy, normotensive, non-smoking, untrained young adults (25±1year) consumed 500ml of beetroot juice (BR). High-fidelity radial arterial pressure waveforms using applanation tonometry and venous blood samples were taken at baseline, 60, 90, 120, 150 and 180 minutes post BR consumption (Study 1). Indices of aortic wave reflection (Augmentation Index; Alx and Alx normalized for heart rate; Alx@75bpm) were analyzed using the generated central aortic blood pressure waveforms (SphygmoCor). To control for the potential confound of fluid ingestion on blood pressure, 7 of the subjects came back for an additional study visit which consisted of drinking 500ml of water (Study 2; control trial). Applanation tonometry measurements were performed at the same time points as Study 1.

Results: Study 1: Central systolic pressures were reduced after 90 min following BR (~3-4mmHg; $P<0.05$). Additionally, Alx and Alx@75bpm were reduced at all-time points following BR ($P< 0.05$; Figure 1). Study 2: Compared to the control trial, Alx was lower at all-time points following BR ($P<0.05$). However, Alx@75bpm was only reduced relative to the control condition at 150 and 180 min post consumption ($P<0.05$; Figure 2).

Conclusion: Our data provide evidence that in addition to the beneficial effects on peripheral blood pressures, acute dietary nitrate supplementation (via beetroot juice) also decreases central aortic pressures and wave reflection in young healthy adults. These effects on central aortic hemodynamics appear to be greatest 2.5-3 hours after BR consumption and are likely mediated by an increase in NO bioavailability via nitrate-nitrite-NO pathways.

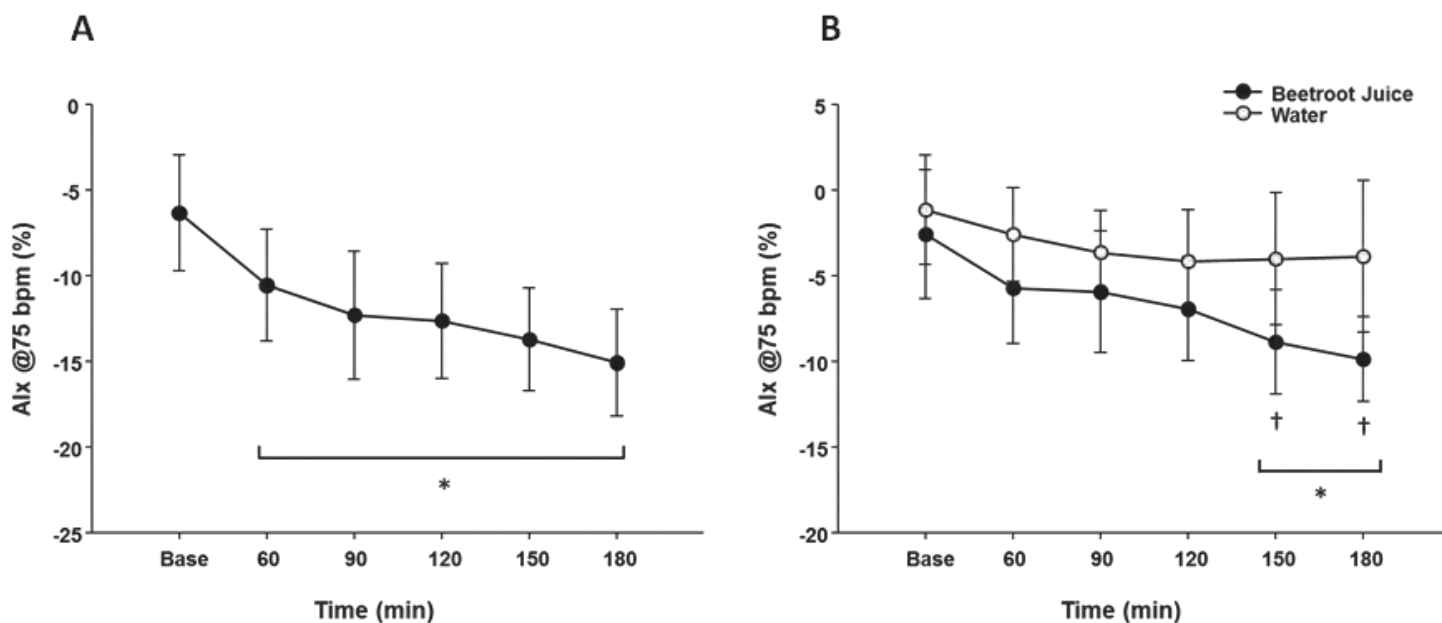


Figure 1. Beetroot juice (n=13) lowered Alx@75bpm over three hours (A; Study 1). When compared to water (control trial; n=7), BR decreased Alx@75bpm at 150 and 180 minutes post consumption (B; Study 2). * $P<0.05$ vs Baseline. † $P <0.05$ vs control.

Spirolactone as Add-On Therapy to Chlorthalidone Improves Endothelial Function, Arterial Stiffness and Insulin Resistance in European and African American Patients with Essential Hypertension – A Double-Blind Placebo-Controlled Randomized Study

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Diuretics have been shown to have a neutral effect on cardiovascular (CV) biomarkers like arterial stiffness and endothelial function despite their blood pressure (BP) lowering effect. Thiazide diuretics generally have harmful effects on glucose metabolism, however, the effect of mineralocorticoid receptor antagonists on insulin resistance in essential hypertension (eHTN) is only partially elucidated. We hypothesized that chlorthalidone (CHT) in combination with spironolactone (SPL) results in better arterial compliance than CHT therapy alone through additional improvement of glucose metabolism parameters.

Methods: This double-blind placebo-controlled randomized single center study aimed to identify SPL add-on therapy to CHT treatment alone on CV risk markers such as BP, 24-h ambulatory blood pressure monitoring (24-H ABPM), aortic BP (aBP), augmentation index (Aix), pulse wave velocity (cfPWV), flow-mediated dilation (FMD), fasting glucose, plasma insulin levels and insulin sensitivity (by homeostasis model assessment: HOMA-IR). A total of 34 patients (21.7% male, 40% white) were randomized to either CHT 25 mg + Placebo or CHT 25 mg + SPL 25 mg once daily. At baseline and after 3 months office BP, 24-H ABPM, markers of arterial stiffness, FMD, fasting glucose, plasma insulin levels and HOMA-IR.

Results: The study showed statistically significant improvements after three months in patients treated with CHT+SPL in clinic BP, 24-hour ABPM, FMD, markers of arterial stiffness, and glucose metabolism. In detail, clinic SBP (131.5±14.6 to 119.1±14.3 mmHg (P = 0.034), aortic SBP (122±13 vs 113±13.7 mm Hg, p = 0.048), 24-H ABPM SBP (151.5±15.1 to 131.7 ±10.4 mm Hg, p=0.0049, 24-H ABPM DBP 83.2±6.1 to 74 ±9.3 mm Hg, p=0.032, 24-H ABPM. Fasting plasma glucose, plasma insulin levels decreased and insulin sensitivity (by homeostasis model assessment: HOMA-IR) improved with SPL as compared to CHT alone (p<0.001), Aix (28±9 versus 25.4± 6.9 %) and cfPWV (9±2 vs 7.5±1.8 m/s) in the CHT+SPL group. Endothelial function improved significantly in the CHT+SPL group as compared to the control group (5.5 ± 1.7 to 8.8 ± 2.7 (p = 0.004)).

Conclusion: These results suggest that SPL as add-on therapy to CHT improves BP, markers of arterial compliance, and glucose metabolism in patients with eHTN, while CHT only therapy may have unfavorable effects. Treatment with SPL additional to CHT may represent a novel approach to improve unfavorable metabolic disturbances and CV risk markers.

A Multi-Modality 4D System for Analysis of the Aortic Morphology and Function from MR or CT

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Objective: Develop an integrated system for multi-modality 4D (3D+time) aortic data analysis including data construction, interactive pre-segmentation, accurate multi-surface segmentation and refinement, and quantitative index measurement. Provide a graphical user interface (GUI) with intuitive data visualization and workflow control. Test the capabilities of the system on MR and CT data.

Methods: 4D image with isotropic 3D voxels is constructed from DICOM images of a study. Candy-cane and LVOT MR data are fused together to benefit from their combined information. Lumen pre-segmentation is achieved by a few mouse clicks with instant feedback. Lumen (and outer wall for CT) surfaces are segmented in 3D by optimal graph search with embedded geometric constraints that guarantees to be global optimum. The result is refined using approximate clues instead of tediously redrawing individual contours. Quantitative indices – cross-sectional area, eccentricity and distensibility, centerline curvature and motion, wall thickness and calcification volume – are computed from complete 4D aortic surfaces. Due to its modularized design, each component can be independently fine-tuned for performance or extended to handle new modality or imaging protocol. The developed system provides simultaneous visualization of image, volume and surface data. The segmentation and quantitative analysis are guided by GUI with clear instructions and examples.

Results: Preliminary evaluation of segmentation accuracy on 20 dataset (10 MR, 10 CT) showed good absolute surface positioning errors (MR: 1.5±1.4mm, CT: 0.4±0.6mm). The user only needs to specify two aortic end points and several points inside the lumen on one 3D image. The computational time is approximately 20 seconds for 2.5GB 10-phase CT data or 500MB 20-phase MR data.

Conclusion: We develop a multi-modality 4D aorta analysis system with user-friendly interface and powerful segmentation and refinement tools. Various novel quantitative indices are computed from the complete 4D aortic surfaces, thus enabling comprehensive analysis of aortic physiology and morphology.

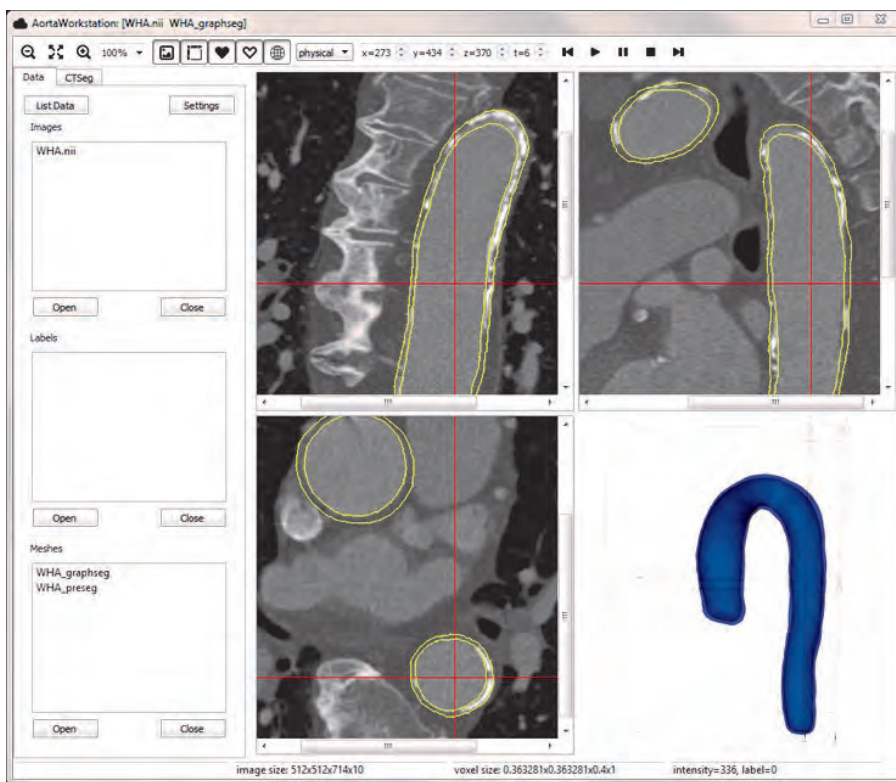


Figure 1: Example of data visualization: image data is shown on three orthogonal slices, segmented surface is shown by 3D rendering and its intersections with image slices (yellow contours).

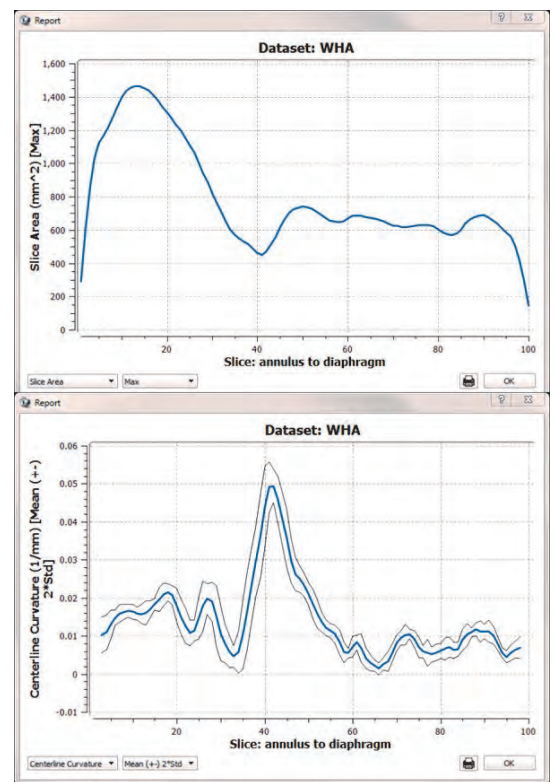


Figure 2: Examples of quantitative indices derived from a cardiac cycle. Top: maximal cross-sectional areas, bottom: range (mean and 2*standard deviation) of centerline curvature.

Sex Differences in the Development of Abnormal Endothelium-Dependent Vasodilation in Aorta from Type 2 Diabetic Rats: Possible Role of Nitric Oxide

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Little is known about the interaction between diabetes and sex in vasculature. This study was designed to investigate whether there were sex differences in rat aortic endothelium-dependent vasodilation (EDV) in Zucker diabetic fatty (ZDF) rats, and the potential role of nitric oxide (NO). EDV to acetylcholine (ACh) was measured in aortic rings pre-contracted with phenylephrine (PE). Contractile responses to PE were generated before and after treatment with L-NAME (200 μ M), a NO synthase (NOS) inhibitor. In addition, the levels of endothelial NOS (eNOS) and NADPH oxidase (NOS, a potent source of superoxide) mRNA expression were determined using real-time RT-PCR. Type 2 diabetes significantly impaired EDV in aortic rings from female ZDF rats, however, potentiated the relaxation in males. Diabetes decreased the contractile responses to PE in aortic rings from rats, regardless of sex. Moreover, diabetes enhanced the extent of PE potentiation after blocking eNOS with L-NAME in females. Accordingly, the levels of eNOS mRNA expression were substantially enhanced in aorta of female ZDF rats compared to those in lean animals. In addition, Nox1 and Nox4 mRNA expression were substantially enhanced in aorta of female ZDF rats. These data suggest that the predisposition of the female aorta to injury in type 2 diabetes may be, in part, due to the alteration of NO production (supported by NIH/NIDCR).

Racial Differences of eNOS Expression Respond to C-reactive Protein

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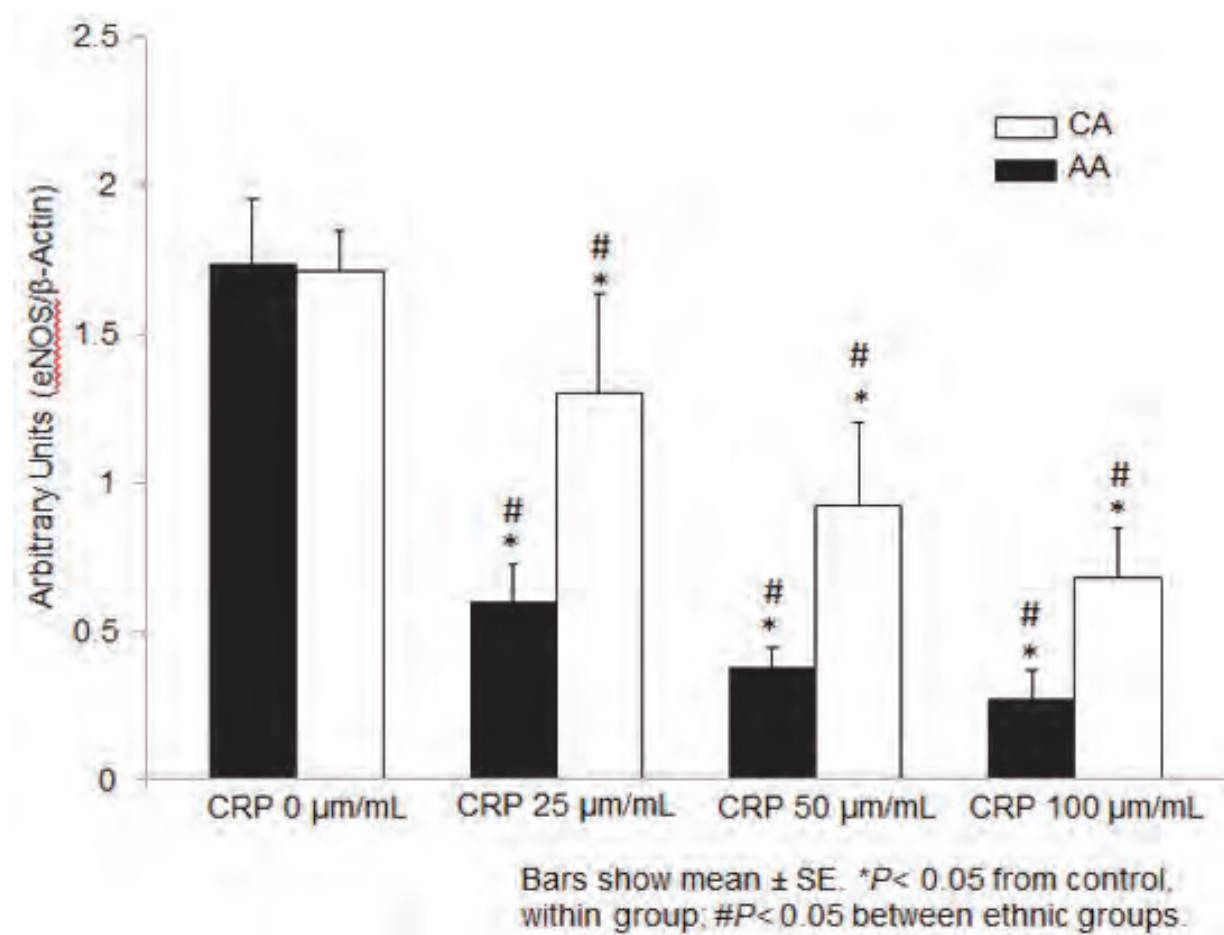
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Background: African Americans (AA) have higher rates of cardiovascular diseases (CVD) compared to Caucasians (CA). Endothelial dysfunction is a common feature of CVD risk factors. Previous studies suggest racial differences in endothelial function exist at the physiological level. C-reactive protein (CRP), a risk marker for CVD, causes a reduction in eNOS expression and bioactivity in endothelial cells (ECs). AA individuals have significant higher concentrations of CRP than Caucasian (CA) individuals. The aim of this study was to investigate the racial differences of endothelial function under CRP stimulation at the cellular level.

Methods: Eight human umbilical vein endothelial cells (HUVECs) lines from African American (AA) and Caucasian (CA) donors with gender split evenly were cultured and incubated with CRP for 24-hrs. Doses of CRP were 0, 25, 50 and 100 µg/mL. Western blot was conducted to measure the expression of eNOS after CRP incubation. ImageJ densitometric analysis of eNOS bands expressed in relation to β-actin.

Results: As Figure 1 shows, at control condition, there was no difference in the eNOS protein expression between AA and CA HUVECs. The incubation of CRP significantly reduced the expression levels of eNOS on both AA and CA HUVECs in a dose-dependent manner. The reductions of eNOS protein expression in AA HUVECs at all three different concentrations were significantly greater than those in CA HUVECs.

Conclusion: AA HUVECs respond differently to CRP compared to CA HUVECs. CRP incubation causes greater reduction of eNOS expression on AA than CA HUVECs. The results suggest a possible mechanism for the racial differences in endothelial dysfunction.



Arterial Hemodynamics in Overweight Young Adult Males Following Maximal Exercise

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Objective: Overweight (OV), defined by body mass index (BMI), is related to increased cardiovascular risk and greater aortic stiffening. In contrast, enhanced cardiorespiratory fitness (CRF) is associated with reduced cardiovascular risk, and lower aortic stiffness. It is unknown whether CRF is related to aortic stiffness in young OV adult males. We hypothesized CRF would be inversely associated with aortic stiffness, and the post-exercise hemodynamic response would be impaired in OV males.

Methods: Thirty-four apparently healthy, young adult males (22.12 ± 0.09 years) were categorized based on BMI as healthy weight (H, ≤ 24.9 kg/m²), or OV (24.9-29.9 kg/m²). Resting measures of arterial stiffness (carotid-femoral pulse wave velocity, cfPWV), heart rate (HR), blood pressure (BP), pulse pressure (PP), mean arterial pressure (MAP), percent body fat (BF%), waist (WC) and hip circumference (HC), and waist-to-hip ratio (W:H) were obtained. Peak oxygen consumption (VO_{2peak}), a measure of CRF, was assessed with a maximal exercise treadmill test (EX). cfPWV and BP were obtained at 2, 5, 10, 20, 30, 45 and 60 minutes following EX.

Results: Compared with H at rest, OV had greater cfPWV, BMI, BF%, systolic BP (SBP), PP, MAP, WC, HC, and W:H ($p < 0.05$, all). VO_{2peak} was greater in H compared with OV ($p < 0.05$). A positive association was observed between resting cfPWV and SBP, whereas cfPWV was inversely related to VO_{2peak} ($p < 0.05$, both). Compared with H, post EX MAP was increased in OV at 10, 20, 30, 45 and 60 minutes ($p < 0.05$). A main effect of weight was observed for cfPWV, SBP and DBP, and a main effect of time for PP, SBP and DBP ($p < 0.05$, all).

Conclusion: Increased resting aortic stiffness in young OV adult males is, in part, attributable to lower levels of CRF and increased SBP. In addition, post EX arterial hemodynamics is impaired in young adult OV males.

Figure 1. Peak Volume of Oxygen Consumption (VO₂) vs. carotid-Femoral Pulse Wave Velocity (cfPWV) (n=34).

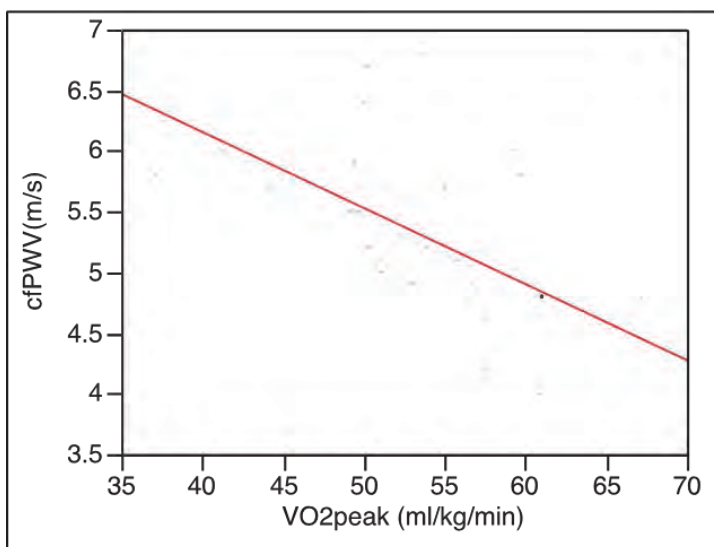
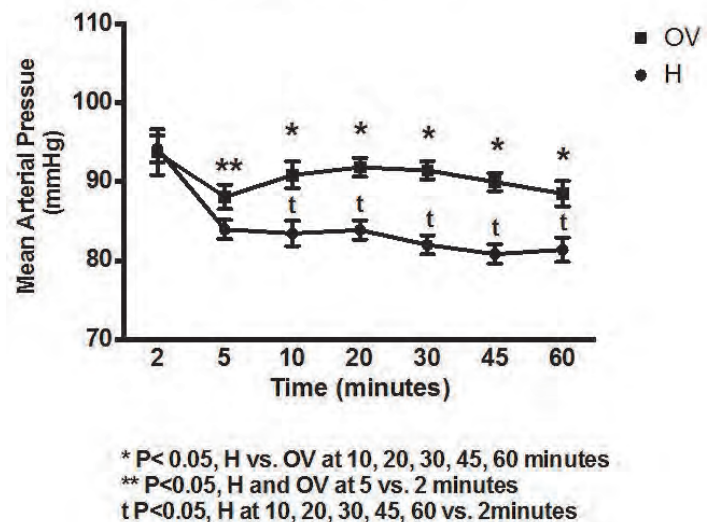


Figure 2. Post EX MAP



Relationship between Carotid Artery Stiffness and Altered Cerebrovascular Hemodynamics in South Asian Indian Older Adults

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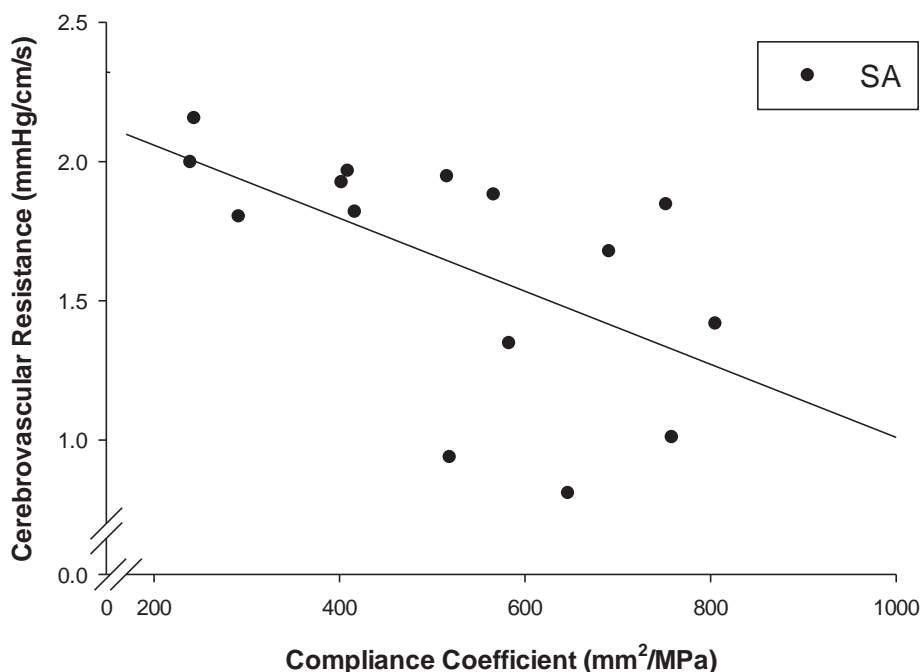
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OBJECTIVES: To investigate whether differences exist in common carotid artery (CCA) stiffness between South Asian (SA) and white Caucasian (CA) older adults, and its association with cerebrovascular hemodynamic properties.

METHODS: Carotid artery stiffness indicators, including pulse pressure (PP), distensibility coefficient (DC), and compliance coefficient (CC), were measured by applanation tonometry and ultrasound imaging. Continuous blood pressure (MAP), heart rate, and middle cerebral artery blood flow velocity (MFV) using non-invasive transcranial Doppler ultrasound, were monitored in 44 age- and gender-matched SA and CA community-dwelling older adults free of cardio- and cerebrovascular diseases (22 CAs/SAs: 11 M/F in each group, aged 64-82 years). Cerebrovascular resistance index (CVRi) and pulsatility index (PI) were also calculated for evaluation of cerebrovascular hemodynamics.

RESULTS: Carotid artery stiffness was higher in SA compared to CA group, as evidenced by lower arterial compliance (CC=601±282 vs. 789±323 mm²/MPa, respectively, p=0.048), and greater PP (59±18 vs. 46±10 mmHg, respectively, p=0.005). A significant interaction effect between ethnic group and arterial compliance on PP was observed (r²=0.562, p<0.001), indicating that less compliant arteries resulted in higher PP amplitudes in SA compared to CA group. Furthermore, a moderate negative relationship between arterial compliance and CVRi was found only in the SA group (r=-0.574, p=0.025). Correspondingly, CVRi was strongly associated with lower MFV (r=-0.925, p<0.001).

CONCLUSIONS: SA group presented greater stiffness and less compliant arteries compared to CA group independent of age and gender. SA older adults appear to have impaired dampening capacity of central arteries to the changes in arterial pressure, thereby increasing the risk of hemodynamic pulsatility transmission into the brain. Consequently, an increase in CVRi might be a compensatory mechanism to protect the cerebral microcirculation, or reflect prior damage, resulting in lower CBF. These findings may aid in understanding the increased risk of cardio- and cerebrovascular diseases in people of SA origin.



The Temporal Relationship between Metabolically Healthy Obesity and Carotid Atherosclerosis in Men

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There is conflicting evidence regarding the relationship between metabolically healthy obesity and the burden of carotid atherosclerosis, but whether metabolically healthy obesity is related to the progression of atherosclerosis remains unclear.

Purpose: We investigated the cross-sectional and follow-up associations between metabolically healthy obesity and carotid atherosclerosis.

Methods: Cardiometabolic risk factors and carotid artery intima-media thickness (CIMT) in 556 men, mean aged 51yrs (36-76 yrs), were measured at baseline and one year later. All participants were free of hypertension and type 2 diabetes at baseline. Participants were divided into four groups based on cross-classifications of body mass index (BMI) and metabolic health status using the ATP-III criteria: metabolically healthy normal weight (MHNW, less than one metabolic abnormality with BMI <25 kg/m²), metabolically unhealthy normal weight (MUNW, more than one metabolic abnormality with BMI <25 kg/m²), metabolically healthy obesity (MHO, less than one metabolic abnormality with BMI ≥25 kg/m²), metabolically unhealthy obesity (MUO, more than one metabolic abnormality with BMI ≥25 kg/m²). Carotid atherosclerosis was defined as >75 percentiles of CIMT. The changes in CIMT were calculated as the difference between the first and second examinations (median interval 367days).

Results: At baseline, mean CIMT was not significantly different between the MHNW and the MHO (0.58±0.12mm vs. 0.62±0.13mm, *P*=0.13), but was different between the MHNW and the MUO (0.64±0.13mm, *P*=0.01) after adjusting for age. The prevalence of carotid atherosclerosis tended to be higher in the MHO as compared to the MHNW after adjusting for age, heart rate, CRP, and VO_{2peak}, but this was not statistically significant (Odds Ratio (OR) 1.80 95% Confidence Interval (CI) 0.93-3.52). There was an increase in the OR for carotid atherosclerosis in the MUO (OR 2.08 95% 1.16-3.73). After one year, the progression of mean CIMT was not significantly different between the MHO and the MHNW after adjusting for covariates (Δ 0.03±0.11mm vs. Δ 0.05±0.10mm, *P*=0.52). Furthermore, the MHO at baseline was not significantly associated with the prevalence of carotid atherosclerosis at the second examination (OR 0.85 95% 0.39-1.87) when compared with MHNW.

Conclusions: These results demonstrate that the burden of carotid atherosclerosis was not increased in the MHO when compared with the MHNW in both cross-sectional and longitudinal associations.

Reduced Cardiac Baroreflex Sensitivity Is Associated with Greater Aortic Stiffness in Middle-Aged/Older Humans: Beneficial Effect of Habitual Aerobic Exercise

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Introduction: Sedentary aging is characterized by reduced cardiac baroreflex sensitivity (BRS) and increased aortic stiffness, both independent predictors of higher cardiovascular disease (CVD) risk in middle-aged/older (MA/O) adults. However, MA/O adults who perform habitual endurance exercise demonstrate lower CVD risk perhaps in part from reduced aortic stiffness and enhanced cardiac BRS.

Objectives: We hypothesized that reduced BRS (sequence technique derived from intra-brachial artery BP waveforms) is associated with greater aortic stiffness (aortic pulse wave velocity, aPWV) among sedentary and endurance-trained MA/O adults, and that endurance exercise training initiated in previously sedentary MA/O adults enhances BRS and reduces aPWV.

Methods and Results: In a cross-sectional study, MA/O sedentary (MA/O-S, n=24, age 62 ± 4 yrs, VO_{2max} 26 ± 1 ml/kg/min) adults demonstrated reduced BRS (11.7 ± 1.5 vs 40.7 ± 8.6 ms/mmHg, $P < 0.05$) and greater aortic stiffness (aPWV 9.7 ± 0.8 vs. 6.4 ± 0.8 m/sec, $P < 0.05$) compared with young sedentary (YS, n=6, age 22 ± 2 yrs; VO_{2max} 39 ± 2 ml/kg/min) adults. MA/O endurance-trained (MA/O-T, n=15, age 61 ± 2 yrs, VO_{2max} 46 ± 1 ml/kg/min, $P < 0.05$) adults had greater BRS (24.3 ± 4.0 ms/mmHg) and smaller aPWV (8.0 ± 0.3 m/sec, $P < 0.05$) than MA/O-S. In the entire cohort after adjustment for age and mean blood pressure, aPWV was inversely correlated with BRS ($r = -0.55$, $P < 0.05$). In a subset of MA/O-S adults (n=18), 8 weeks of aerobic exercise training (n=12, 6-7 days/week, 40-45 min/day, 60-80% HRmax) improved BRS (11.7 ± 2.1 vs. 16.1 ± 2.7 ms/mmHg, $P < 0.05$) but not aPWV (9.8 ± 0.8 vs. 9.2 ± 0.9 m/sec, $P = 0.08$), while there was no change in sedentary time-controls (n=6, $P > 0.05$).

Conclusions: Habitual aerobic exercise attenuates the age-related reduction in cardiac BRS and greater aortic stiffness in humans. However, short-term aerobic exercise training initiated in MA/O-S adults improves BRS but not aortic stiffness.

A New Arterial Stiffness Index Permitting Isobaric Comparisons

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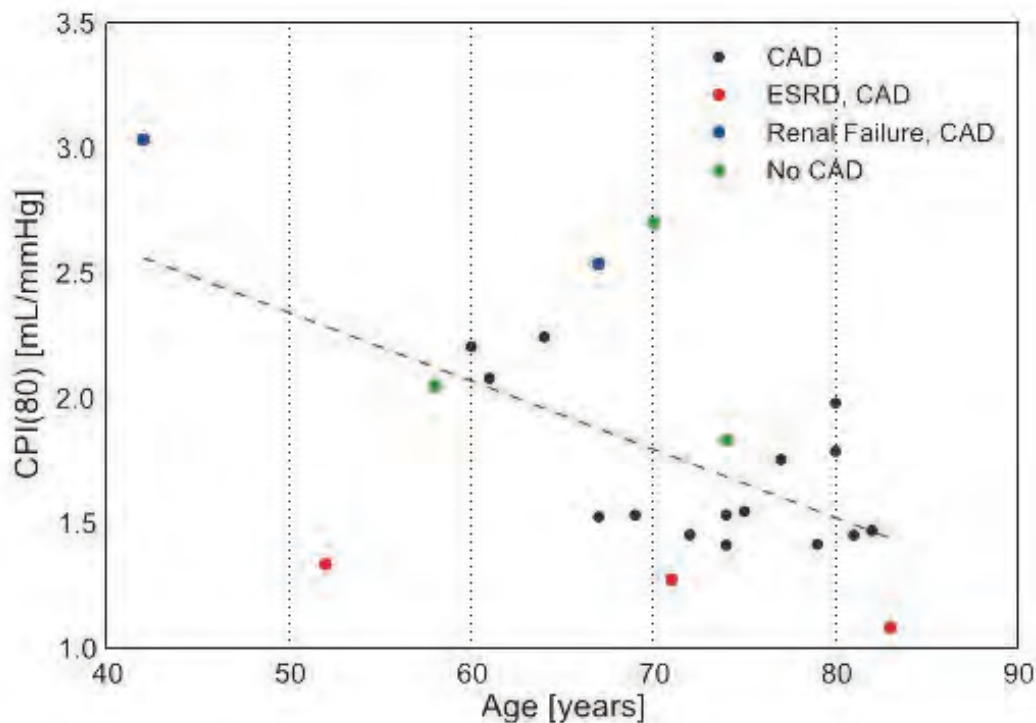
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Objectives: Arterial stiffness is pressure-dependent and comparisons among individuals and between groups should be made under isobaric conditions. Statistical methods are typically employed to adjust stiffness indices for pressure-dependence. In this ongoing study, we employ our new stiffness index, CPI, which allows for explicit evaluation at a reference pressure and stroke volume, to investigate its change with age and disease.

Methods: We studied twenty-three patients (n=23: 9 men and 14 women; mean age 70 years) that underwent diagnostic cardiac catheterization. Aortic pressure waveforms were used to evaluate CPI at a reference pressure of 80 mmHg and stroke volume of 100 mL. A closed-form expression of pressure-dependent compliance index, or CPI, was derived and computed for each subject. Linear regression was used to assess the trend of CPI with age.

Results: CPI values ranged from 1.08 to 3.03 mL/mmHg. A negative correlation was found between CPI and age ($r=-0.57$, $p<0.01$). End-stage renal disease patients had the lowest values within their respective decade of age. Patients without coronary artery disease had the higher values within their decade.

Conclusions: CPI is an index of pressure-dependent arterial compliance. Its decrease with age, further exaggerated by presence of disease, is consistent with studies using other stiffness indices. The allowance for explicit evaluation at a common pressure relieves the need for statistical adjustments for pressure-dependence and permits a more individualized measure of arterial stiffness. Moreover, this allows separation of active and passive changes in arterial stiffness when cardiac properties or blood pressure levels are altered. Continuing studies will provide better sampling of age and disease states.



Ultrasound Biomicroscopic Study of Arteries in Detection of Doxorubicin-induced Disorders

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Ultrasound biomicroscopy (UBM) has been a valuable, non-invasive technique in monitoring cardiac function such as echocardiography. However, UBM is not commonly used in vascular research, especially in small animals. In addition, the use of doxorubicin (DOX), an anti-cancer drug, in treatment for malignancies is limited because of its cardiotoxicity. Whether DOX causes vascular disorders is unknown. Objectives: this study aimed to use UBM to monitor function of major arteries in response to DOX treatment. Methods: Mice were injected intrapleurally with a single dose of DOX (20 mg/kg body weight) or an equivalent volume of saline. The kinetics of blood flow through ascending aorta (AAo), pulmonary artery trunk (PAT), and left coronary artery (LCA) were monitored with Doppler UBM before and after DOX treatment using Vevo®2100 and VisualSonics® software. Results: While abnormal cardiac function was usually observed 3 days after DOX treatment, mean velocity and mean pressure gradient of time-integral AAo blood flow were reduced by 30% and 49%, respectively (n=6). The blood flow of LCA was reduced about 40% (n=5) accompanied by an increased resistive index. The reduction in peak velocity of LCA blood flow during systole was greater than that during diastole. In contrast, the peak velocity of blood flow in PAT was reduced by 10% (n=7), which worsened by 22% with a 40% decrease of mean pressure gradient at 7 days after DOX treatment. Meanwhile, no significant change in these arteries was observed in control group. The reduction in AAo blood flow could result from DOX-induced cardiotoxicity, while reduction of LCA blood flow could cause cardiac dysfunction. The change in PAT could be due to the effect of increased oxidative stress by DOX. Conclusion: UBM could effectively detect hemodynamic changes in major arteries induced by DOX, and thus enhance its application in preclinical research and drug discovery.

Significant Basal and Stimulated Variations in Inflammatory Gene Expression Profiles in African American and Caucasian HUVECS

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Biomarkers related to hypertensive disease onset and progression are differentially implicated in African Americans (AA) and Caucasians (Cau) and investigation of these biomarkers is needed to elucidate their significance. Racial disparity studies are carried out solely in vivo making it difficult to focus on the cause(s) of endothelial dysfunction (EnDy) leading to vascular complications. Therefore, building on data from our laboratory that reveals a mechanism of EnDy in AA human umbilical vascular endothelial cells (HUVECs) (increased ROS), we report basal differences and effects of activating HUVECs on relative gene expression ($2^{\Delta\Delta CT}$) of important immune mediators (IL-1 β , VCAM-1, ICAM-1, eNOS, and MMP-2).

In an n=2-4 (both AA & Cau) cell lines in passage 6, we show that in control and after 4 hr stimulation with TNF- α (50ng/ml) that basal MMP-2 gene expression, a strong predictor of severe cardiovascular events in AA, is different in AA ECs compared to Cau. IL-1 β basal expression is higher in AA and significantly increases ($F_{1,12}=10.76;p=.007$) after stimulation, being higher in AA. Both AA and Cau ECs show reductions in eNOS expression after TNF- α and there is a trend in AA ECs for eNOS to be lower after stimulation ($p=0.06$). Further, basal expression of cell adhesion molecules (ICAM-1 & VCAM-1) are significantly greater ($p<.05$) in AA ECs while after stimulation VCAM-1 was significantly exaggerated in AA (race x treatment interaction: $F_{1,12}=6.05;p=.030$).

Increases in IL-1 β and CAMs in AA ECs indicate they are operating at a higher basal immunological active status. As ROS is known to be indirectly involved with expression of inflammatory genes, it is probable the effect exaggerated ROS has on MMP-2 activation, and its detrimental downstream effects, may play a role in activating immune pathways. Experiments are being performed to assess MMP-2 intracellular activities on cytosolic peptides.

Aortic Hemodynamics following Discontinuation of Menopausal Hormone Therapy in Postmenopausal Women

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Background and Objective: Arterial stiffness and aortic hemodynamics are important determinants of cardiovascular disease risk. Menopausal hormone therapy (MHT) reduces progression of cardiovascular disease in postmenopausal women due to its effects on the endothelium and smooth muscle of the central and peripheral vasculature. However, it remains unclear whether these effects are sustained after MHT cessation. We hypothesized that MHT administered early during the menopausal transition (less than three years from menopause) would not produce a sustained protective effect on aortic hemodynamics in women following discontinuation of MHT.

Methods: We studied fifty-seven women, as part of the Mayo Clinic Specialized Center of Research on Sex Differences, who were randomized into either oral conjugated equine estrogen (oCEE, n=15), transdermal 17 β estradiol (tE2, n=20), or placebo (n=22) for four years. After a three year washout period, aortic hemodynamics were measured using radial arterial applanation tonometry.

Results: Age, body mass index and mean arterial pressure were similar among the women. Augmentation index (AIx) was similar among groups (32.6 \pm 2.3%, 33.9 \pm 1.9%, 31.5 \pm 1.9%; oCEE vs. tE2 vs. placebo, respectively, p>0.05) and did not change when normalized for heart rate at 75 bpm (27.6 \pm 2.3%, 28.2 \pm 1.6%, 25.7 \pm 1.8%; oCEE vs. tE2 vs. placebo, respectively, p>0.05). There were no differences in augmented pressure (12.6 \pm 1.6, 13.6 \pm 1.2, 12.0 \pm 0.9 mmHg; oCEE vs. tE2 vs. placebo, respectively, p>0.05) or left ventricular wasted energy (2843 \pm 170, 3208 \pm 360, 2559 \pm 205 dyne \cdot cm² \cdot sec; oCEE vs. tE2 vs. placebo, respectively, p>0.05) among the three groups.

Conclusion: These data suggest that any changes in aortic hemodynamics during MHT use are not sustained following MHT discontinuation.

Racial Differences in Vascular Function

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Objective:

Racial disparities are evident in regards to cardiovascular health and prevalence. Currently, there have not yet been any studies investigating the differences in markers of vascular function between Hispanics (HS), Caucasians (CA), and African Americans (AA). This study sought to assess the differences in vascular function at the endothelial cell level between these racial groups.

Methods:

Three human umbilical vein endothelial cell (HUVEC) lines from different donors with HS, CC, and AA backgrounds were used. All cells were grown until confluent before cell medium and cell lysate was harvested. The cell medium was collected for the measurement of Interleukin 6 (IL-6) in an ELISA assay kit. The harvested cell lysate was used for western blotting for the measurement of Endothelial Nitric Oxide Synthase (eNOS), Phosphorylated Endothelial Nitric Oxide Synthase (p-eNOS), and Endothelin Converting Enzyme (ECE).

Results:

The expression of eNOS in both the CC and HS cell lines was significantly lower when compared to the AA cell lines ($p \leq 0.001$). p-eNOS expression was significantly higher in the HS cell lines compared to both the AA and the CA cell lines ($p \leq 0.001$). The p-eNOS to eNOS ratio was significantly lower in both the AA ($p \leq 0.03$) and CA ($p \leq 0.001$) cell lines compared to the HS cell lines. ECE expression was significantly higher in the HS cell lines compared to the AA cell lines ($p \leq 0.001$). IL-6 levels were significantly higher in the CA and HS cell lines compared to the AA cell lines ($p \leq 0.001$).

Conclusions:

Differences in endothelial cell biology that could affect function were evident among cell lines of different racial origin.

Higher Aortic Stiffness and Carotid Systolic and Pulse Pressure are Selectively Associated with Lower White Matter Integrity in the Genu and Frontal Cortex in Older Healthy Adults

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Introduction: Previous studies have demonstrated an association between higher aortic stiffness and central pulse pressure (PP) with lower brain white matter structural integrity (WMI) and neuropsychological functioning in older adults. However, it is unknown if aortic stiffness and central PP are associated with lower WMI in select brain regions or if they relate to cognitive abilities that decline with age such as processing speed.

Objectives: We hypothesized that greater aortic stiffness and carotid PP would be associated with lower regional WMI and slower processing speed.

Methods and Results: In younger (n=12, age 23.2 ± 2.3 yrs) and older (n=7, 67.7 ± 2.7 yrs) healthy adults, aortic stiffness (carotid-femoral pulse wave velocity, cfPWV) and carotid blood pressure (BP) were determined non-invasively using applanation tonometry and brachial cuff BP (Cardiovascular Engineering, Inc.). Fractional anisotropy (FA) (3T MRI, Siemens) assessed from diffusion imaging measured WMI. The association between vascular variables and FA was determined using voxel-wise and region-of-interest (ROI) analyses. Letter and pattern comparison assessed processing speed.

Results: In the entire cohort, cfPWV (adjusted for age, mean BP) and carotid and brachial PP (adjusted for age) were not correlated with WMI in any brain regions using voxel-wise or ROI. Among older adults using ROI, cfPWV (adjusted for mean BP) was correlated with genu corpus callosum (r=-0.90, p<0.05) and frontal (r= -0.77, p<0.05) FA values and corroborated in voxel-wise analyses. Carotid, but not brachial systolic BP or PP, was negatively correlated with genu and superior frontal gyrus and medial prefrontal cortex FA values (p<0.05) using voxel-wise analysis. cfPWV, but not FA in the genu or frontal ROIs, was correlated with processing speed (p<0.05) in older adults.

Conclusion: Preliminary results suggest that greater aortic stiffness is selectively associated with lower WMI in the genu and frontal cortex, and slower processing speed in older adults.

Dependency of Arterial Stiffness Indicators on Acute Blood Volume Changes

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Increased arterial stiffness is associated with greater risk for cardiovascular disease. It is unknown if indicators of stiffness are dependent on acute changes in cardiovascular conditions (such as altered central blood volume).

Objectives: To examine if arterial stiffness indicators change with acute reductions in stroke volume (SV) within normal physiological variability.

Methods: Seven young healthy volunteers (4M, 3F) were recruited to participate in this study. To acutely alter blood volume, subjects were sealed from their waist down into a lower body negative pressure (LBNP) box and a vacuum was used to create a pressure gradient of 30mmHg. Heart rate (HR) was continuously monitored and SV was obtained with Doppler ultrasound. Aortic and femoral artery velocity profiles were obtained with Doppler ultrasound to determine central pulse wave transit time (cPWTT). cPWTT was calculated by subtracting the time between the peak of the R-wave and the foot of the aortic velocity profile from the time between the peak of the R-wave and the foot of the femoral velocity profile. Common carotid distensibility (cDa) was determined with simultaneous tonometry to determine pulse pressure (PPcar) and ultrasound imaging to determine diastolic and systolic diameters ($cDa = \text{systolic area} - \text{diastolic area} / \text{PPcar} - \text{carotid diastolic area}$).

Results: The increase in HR from baseline to LBNP was not significant while SV was significantly lower at LBNP ($45 \pm 13 \text{ mL/beat}$) compared to baseline ($69 \pm 11 \text{ mL/beat}$; $p=0.002$). PPcar was lower at LBNP ($43 \pm 6 \text{ mmHg}$) compared to baseline ($48 \pm 5 \text{ mmHg}$; $p=0.007$). While cDa was significantly decreased (Baseline = $0.00732 \pm 0.00186 \text{ mmHg}^{-1}$ vs. LBNP = $0.00592 \pm 0.00219 \text{ mmHg}^{-1}$; $p=0.033$), cPWTT tended to get faster with LBNP (baseline = $95 \pm 17 \text{ sec}$ vs. LBNP = $87 \pm 13 \text{ sec}$; $p=0.089$).

Conclusions: The arterial stiffness indicators, cDa and cPWTT, might be affected by acute changes in central blood volume and cardiac SV within normal physiological variations.

Sex Differences in Hemodynamic Responses following Acute Inflammation: Wave Separation Analysis

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ABSTRACT: Acute inflammation temporarily increases risk of cardiovascular events and alters hemodynamics. However, it is unknown whether acute inflammation differentially affects blood pressure and pulse wave characteristics, including forward or reflected pressure waves, in males versus females.

OBJECTIVES: The purpose of this study was to investigate the potential sex differences in the response to acute inflammation in blood pressure and pulse wave characteristics, measured with wave separation analysis

METHODS: 63 adults (29 males, 34 females) participated in the study. Participants received an influenza vaccine to induce acute inflammation. Central blood pressure and pulse waves were measured using tonometry and separated into forward and reflected waves, at baseline, 24hr post, and 48 hr post-vaccination. 2 x 3 repeated measure Analysis of Variance (ANOVA) was performed to investigate sex differences in acute inflammation.

RESULTS: (See table) There were significant sex differences in brachial SBP, brachial DBP, aortic DBP and aortic MAP with higher values in males. (p<0.05) However, there were no statistically significant sex differences in wave separation variables or aortic SBP during acute inflammation, but acute inflammation decrease brachial DBP, aortic SBP, and aortic MAP in all subjects combined, and reflected pulse pressure approached a decline in the entire cohort (p=0.06).

CONCLUSIONS: The results suggest that blood pressure, forward and reflected pulse wave pressure exhibited similar responses in males and females during acute inflammation.

	Brachial DBP(mmHg)†			Aortic DBP(mmHg)†			Aortic MAP(mmHg)†			Forward wave pressure(mmHg)			Reflected wave pressure(mmHg)		
	Baseline	24 hr Post	48 hr post	Baseline	24 hr Post	48 hr post	Baseline	24 hr Post	48 hr post	Baseline	24 hr Post	48 hr post	Baseline	24 hr Post	48 hr post
Male	69±9	67±9	69±9	70±9	68±9	69±9	87±10	84±9	85±10	29±5	29±5	28±6	19±7	17±7	18±6
Female	66±8*	63±7	64±7	66±8*	64±7	64±7	82±11*	79±8	79±9	27±5	27±5	26±5	17±7	15±5	15±4

* Different from other time point, p<0.05

† Sex difference. Significant at p<0.05

Left Ventricular End-Systolic Elastance (Ecavi) Estimated with CAVI

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Objective: Left ventricular end-systolic elastance (Ecavi) was estimated using the parameters measured for calculating cardio-ankle vascular index (CAVI).

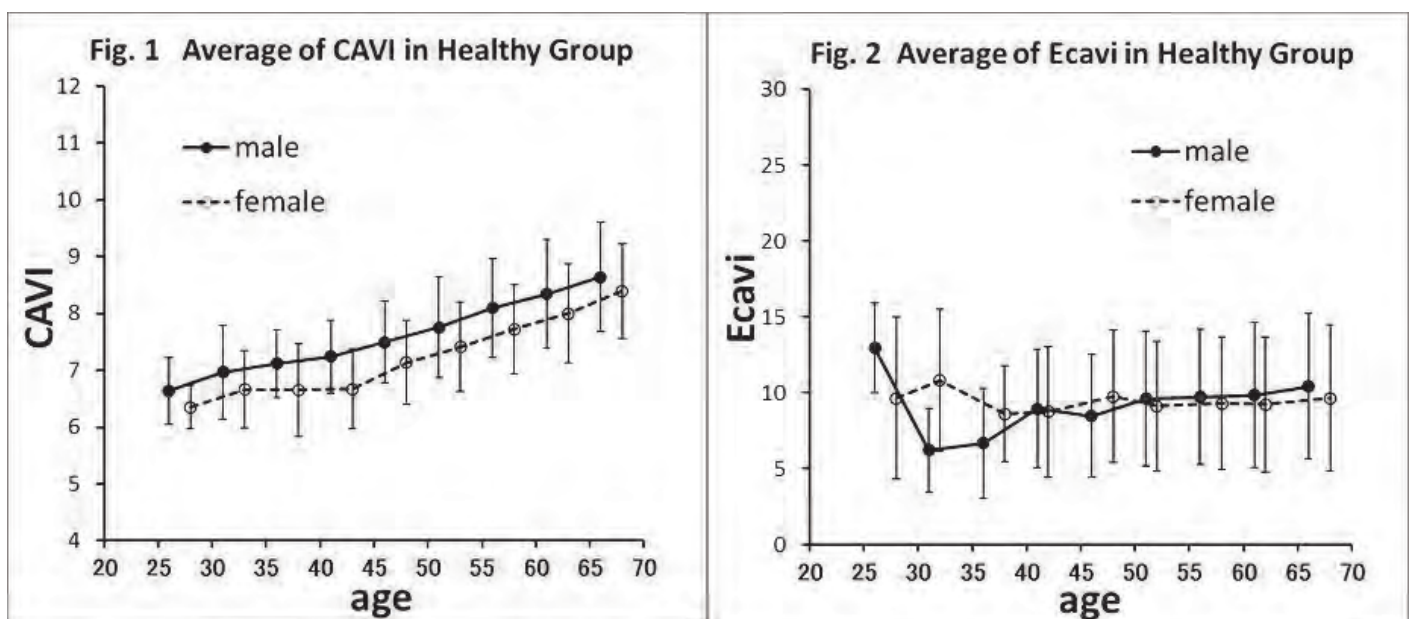
Methods: Participants comprised 4,954 healthy individuals (2,679 males, 2,275 females) who visited the health examination center at Fukui-ken Saiseikai Hospital between July 2007 and November 2013. Left ventricular-arterial coupling (Ees/Ea) was obtained from end-systolic arterial pressure (Pes), end-diastolic arterial pressure (Pd), pre-ejection period (PEP) and ejection time (ET), all of which were obtained as parameters measured on a vascular screening system (VaSera VS- 1500N; Fukuda Denshi, Tokyo, Japan) based on the non-invasive method described by Hayashi et al.⁽¹⁾. Mean arterial pressure (Pm) was assumed to be equal to Pes for the calculation of Ees/Ea⁽²⁾ in this study. Ees/Ea was assumed as the balance of stiffness between the end-systolic left ventricle and aorta. Left ventricular end-systolic elastance estimated with CAVI was defined as $CAVI \times Ees/Ea$.

Results: The population showed the same results as the healthy group recruited in the user’s manual of the vascular screening system (Fig. 1); namely, normal range of CAVI was between 6.3 and 8.7, CAVI was higher in males than in females, and CAVI was slightly increased in the high aged group. Mean and standard deviation of Ecavi were 9.3 and 4.5, respectively, in all age groups, and in both males and females (Fig. 2).

Conclusion: The original left ventricular end-systolic elastance (Ees) could be estimated as Ecavi, representing $CAVI \times Ees/Ea$, using a non-invasive vascular screening system.

References:

- 1) Hayashi K. et al., Anesthesiology, 2000;92:1769-76.
- 2) Takaku A. et al., Proc of 11th Annual Meeting Tokai-Hokuriku Branch JSA, 2013;11:Q01-1.



The Implications of Poor Sleep Quality on Arterial Health in Persons with Multiple Sclerosis

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Objective: Multiple sclerosis (MS) is a chronic, autoimmune disease that is associated with increased risk of cardiovascular disease (CVD) when compared to the general population. Approximately 47% of patients with MS have reported poor sleep quality. Evidence supports an association between poor sleep and increased CVD risk. Augmentation index (AIx) is a marker of arterial health. The purpose was to examine the association between sleep quality and arterial health in patients with MS.

Methods: Thirty two patients with MS (Age: Mean \pm SD = 47.6 \pm 10.6 yrs) and 32 matched controls (47.6 \pm 11.3 yrs) were administered the Pittsburgh Sleep Quality Index (PSQI) to assess self-reported sleep quality. Subjects having a global score >5 were classified as "poor sleepers." Applanation tonometry was performed on the radial artery to obtain arterial pressure waveforms.

Results: Twenty MS subjects and 7 control subjects were classified as "poor sleepers." Statistical analysis confirmed that "poor sleep" was associated with higher AIx (16.2 \pm 2.3 vs 23.7 \pm 2.9, $p < 0.05$) regardless of having MS. Among those with MS, AIx was significantly higher in the subjects who reported poor sleep quality when compared with those who reported good sleep quality (15.7 \pm 3.8 vs 27.1 \pm 3.0, $p < 0.05$).

Conclusions: Poor sleep quality has a negative effect on arterial health overall and in those with MS. Additionally, those with MS who report poor sleep quality have an amplified negative arterial outcome compared to patients with MS with good sleep quality and healthy controls.

Higher Central Augmentation Pressure/Index Is Associated with Tension-Type Headache but Not Migraine in Middle-Aged/Older Obese Humans

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Objectives: Obesity is associated with a five-fold increased risk of developing chronic daily headache, especially chronic migraine. Migraine attacks are more frequent and more severe among obese migraineurs and they improve with weight loss; however, the underlying mechanisms are unknown. Given that elevated aortic stiffness and central pulse pressure are associated with cerebral microvascular dysfunction/damage, we hypothesized that obese middle-aged/older adults with history of migraine would demonstrate higher aortic stiffness, central blood pressure (BP) and augmentation index (AI) /pressure (AP) compared with those without a history of migraine.

Methods: Middle-aged/older obese adults who were stratified (via detailed survey and physical exam by a neurologist) by presence of migraine (n=39; age 54 ± 8 yrs, BMI 38 ± 6 kg/m², 67% female), tension-type headache (n=25; age 57 ± 6 yrs, BMI 37 ± 4 kg/m², 72% female) or no headache of any type (n=29; age 54 ± 7 yrs, BMI 37 ± 5, 37 ± 5 kg/m², 48% female) had aortic stiffness (carotid-femoral pulse wave velocity, CFPWV), brachial and central BP, and central AI and AP assessed by applanation tonometry (SphygmoCor).

Results: Obese adults with tension-type headache, but not migraine (P=0.29), demonstrated higher AI (25.4 ± 9.6 vs. 17.8 ± 6.9%, P=0.02) and AP (11.7 ± 9.6 vs. 6.8 ± 6.9 mmHg, P=0.01) compared with no headache controls, but no difference in CFPWV between the 3 groups (P=0.47). After adjusting for age, mean BP, female sex, weight, height, and antihypertensive medication, higher AP (b=2.95, p=0.04) and AI (b=4.41, P=0.07) remained associated with greater frequency of tension-type headache.

Conclusions: Higher central AI and AP, but not aortic stiffness, is associated with tension-type headache but not migraine in obese middle-aged/older adults. Whether excessive penetration of pulsatile pressure into cerebral microcirculation contributes to the development of tension-type or migraine headache in obesity requires further study.

Changes in Cerebrovascular Pulsatility during Aerobic Exercise Are Unrelated to Brachial-Ankle Pulse Wave Velocity in Chronic Stroke

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Arterial stiffness contributes to increased cerebral hemodynamic pulsatility and independently predicts negative outcomes post-stroke. Exercise can contribute towards recovery after stroke, yet it is unclear whether arterial stiffness influences acute cerebrovascular responses to exercise. One study in healthy young men showed high-intensity resistance exercise increased stiffness and pressure pulsatility up to 30 minutes post-exercise without affecting cerebral hemodynamics (1). The influence during acute aerobic exercise, however, is unknown.

Objectives: To investigate the association of arterial stiffness with changes in pulse pressure (PP) and middle cerebral artery pulsatility index (PI) during aerobic exercise in chronic stroke adults. We hypothesized that resting brachial-ankle pulse wave velocity (baPWV) would be associated with greater exercise-related increases in PP and PI.

Methods: Participants were recruited 3 to 12 months post-stroke. BaPWV was quantified using applanation tonometry. A symptom-limited cardiopulmonary assessment determined peak aerobic fitness ($\dot{V}O_{2peak}$). In a subsequent session, participants cycled on a recumbent ergometer for 20 minutes at 60% heart rate reserve. Cerebral blood flow velocity was measured using transcranial ultrasound. Arterial blood pressure was measured using finger-cuff photoplethysmography.

Results: Preliminary results from 9 men and 2 women are reported (age: 68 ± 9 years; $\dot{V}O_{2peak}$: 19 ± 5 mL/kg/min; baPWV: 12.0 ± 2.0 m/s). At rest, baPWV was not correlated with PP or PI ($p > 0.6$). During exercise, PP and PI increased $22 \pm 11\%$ and $44 \pm 21\%$, respectively ($p \leq 0.001$). A non-significant association was noted between Δ PI and Δ PP ($r = 0.68$, $p = 0.096$). Resting baPWV was unrelated to Δ PP ($r = 0.42$, $p = 0.228$) or Δ PI ($r = -0.04$, $p = 0.932$).

Conclusions: BaPWV, an index of stiffness influenced by central and peripheral vasculature, was unrelated to blood pressure or cerebrovascular pulsatility in this small cohort. Change in cerebral blood flow pulsatility during moderate intensity exercise appears to be independent of systemic arterial stiffness, although a larger sample is still necessary.

References:

1. Lefferts WK *et al.* (2014) *Front. Physiol.* 5: 101.

Creation of a Fixed Central Arterial-Venous Anastomosis on Arterial Stiffness and Central Haemodynamics: A Treatment for Hypertension Targeting the Physical Properties of the Arterial Vasculature

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Introduction: Current device based treatments for resistant hypertension target selective modification of the somatic, sympathetic, or parasympathetic nervous systems. The influence of the respective nervous systems on vascular stiffness and haemodynamics is unclear, and there is little data on the effect of current devices nor pharmacotherapy on arterial stiffness often associated with resistant hypertension.

A novel device technology (ROX Coupler, San Clemente, CA) has been developed that causes an immediate, significant and sustained reduction of blood pressure by exploiting the mechanical effects of creation of a low resistance, high compliance venous segment to the central arterial tree. The Coupler creates a 4 mm diameter AV anastomosis between the iliac artery and vein.

To date no data exist on the effect of AV fistula placement on central haemodynamics and arterial stiffness. We present data on central pressure, and aortic pulse wave velocity (aPWV) from a 63yr old woman before and 4 months after AV fistula formation using the ROX Coupler device.

Methods: Peripheral blood pressure, central haemodynamics and carotid femoral pulse wave velocity (c-f PWV) were assessed (SphygmoCor AtCor Medical) before and 4 months after insertion of the ROX Coupler. Results are tabulated in (Table 1).

Results:

	PRE AV Fistula	POST AV fistula
Peripheral SBP mmHg	184	172
Central SBP mmHg	172	158
Peripheral DBP mmHg	102	84
Central DBP mmHg	102	84
Aix %	34%	27%
HR b/m	66	68
C-f PWV m/s	15.2	13.7
Peripheral MAP mmHg	130	113
Peripheral PP mmHg	82	88
Central PP mmHg	70	74

aPWV decreased by 1.5 m/s from 15.2 to 13.7 m/s and MAP decreased by 17mmHg. Given that a 10mmHg reduction in MAP would produce an approximate reduction in aPWV of 0.5 m/s it would appear that the reduction in aPWV was in part blood pressure independent.

Conclusions: Insertion of the ROX Coupler was shown to produce a large reduction in aPWV which may not all be blood pressure dependent. These findings suggest that a mechanical solution to reduced arterial compliance may result in safe and effective lowering blood pressure, and address a mechanism of persistent hypertension unapproached by current therapy. Haemodynamic measurements in larger numbers of patients undergoing ROX Coupler insertion will be necessary to confirm this physiology and better appreciate its potential role in the prevention and treatment of the cardiovascular complications of hypertension.

Carotid Strain Does Not Explain Sex Differences in Blood Pressure

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Objective: Women have a lower incidence of cardiovascular morbidity and mortality prior to menopause when compared to age-matched men. Specifically, on the vascular level, carotid arterial stiffness increases with age in both sexes, but with greater changes in older postmenopausal women. Arterial stiffness is a well-established predictor of future risk of CVD, and 2-dimensional ultrasound imaging of vascular deformation (Strain) using speckle tracking directly characterizes the elastic properties of the carotid arterial wall. The purpose of this study was to determine if sex differences exist for strain in the common carotid artery.

Methods: Twenty-eight healthy men and women (12/16; Range = 19-77 yrs) had 2-dimensional ultrasound images of the carotid artery taken. These images were obtained using an optimal circumferential view, and carotid strain (CS) and CS time to peak (TPK) were analyzed via speckle tracking software. Women were tested in the early follicular phase of menstrual cycle if they were premenopausal. Brachial (bSBP, bDBP, bMAP) and carotid (carSBP, carDBP, carMAP) pressure measurements were obtained in the supine position at rest using applanation tonometry.

Results: Females exhibited significantly lower resting blood pressure (bSBP, bDBP, bMAP, carMAP), radial displacement (RD) TPK, and CS TPK (p<0.05). Strain and strain-rate were not different between sexes, even after controlling for age.

Conclusion: Women had lower resting blood pressures and a greater CS and RD TPK parameters compared to males. However, there were no sex differences in CS measurements. Therefore, elastic properties of the carotid artery do not account for the pressure difference demonstrated between sexes.

Variables	Males (n=12)	Females (n=16)
Age (yrs)	46 ± 21	46 ± 19
BMI (kg/m ²)	27.2 ± 4.3	25.3 ± 4.3
bSBP (mmHg) *	125 ± 12	111 ± 14
bDBP (mmHg) *	72 ± 7	66 ± 8
bMAP (mmHg) *	90 ± 8	81 ± 9
carSBP (mmHg)	117 ± 14	105 ± 19
carDBP (mmHg) *	73 ± 7	67 ± 8
carMAP (mmHg) *	92 ± 9	83 ± 10
Beta Stiffness Index	7.3 ± 3.3	6.8 ± 3.7
CS (PK%)	5.24 ± 3.22	5.58 ± 3.78
CS Time to Peak (ms) *	314 ± 36	356 ± 61
CS Rate (PK 1/s)	0.43 ± .25	0.42 ± .28
CS Rate TPK (ms)	170 ± 18	181 ± 25
Radial Displacement (PK mm)	0.19 ± .10	0.18 ± 0.10
Radial Displac. TPK (ms) *	313 ± 35	358 ± 61
Radial Velocity (cm/s)	0.17 ± 0.08	0.15 ± 0.09
Radial Velocity TPK (ms)	170 ± 18	181 ± 24

All Data are mean ± SD, * Gender Difference, p<0.05

Sex-Specific Differences in Cardiovascular Parameters in Spinal Cord Injured Individuals

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Introduction: Females represent 20% of the spinal cord injury (SCI) population, yet sex-specific differences in cardiovascular parameters have not been examined. Given that SCI is associated with an increased risk of cardiovascular disease, establishing whether sex-specific differences in cardiovascular health exist is essential.

Objective: To examine sex-specific differences in cardiovascular parameters between females and males with a traumatic, chronic (>1 year), motor-complete (American Spinal Injury Association Impairment Scale A-B) SCI.

Methods: Eleven females (43 ± 7 years; C4-T5; 20 ± 8 years post-injury) and 11 age and lesion-level matched males (43 ± 7 years; C4-T5; 19 ± 9 years post-injury) participated in the study. Applanation tonometry was used to calculate aortic pulse wave velocity (aPWV) from arterial pressure waves collected at the carotid and femoral arterial sites. Discrete measurements of brachial artery systolic (SBP) and diastolic (DBP) blood pressure and heart rate (HR) were collected for 10 minutes during supine rest, and for 15 minutes following a passive sit-up test. The change (Δ) in SBP and DBP from supine to seated was calculated, and the incidence of orthostatic hypotension (ΔSBP ≥ -20 mmHg or ΔDBP ≥ -10 mmHg) was determined.

Results: Height (1.80 ± 0.06 vs. 1.69 ± 0.07, p=0.001) and mass (75.1 ± 13.6 vs. 60.8 ± 7.4, p=0.008) were higher in males compared to females, respectively. There were no between-group differences in aPWV, supine or seated hemodynamics, or ΔSBP and ΔDBP (see Table 1). In both females and males, the incidence of OH was 36%. When height and weight were included as covariates, there were still no between-group differences in aPWV.

Conclusion: Findings from this pilot study suggest there are no sex-specific differences in cardiovascular parameters between females and males with SCI. However, further investigations are warranted.

Table 1. Cardiovascular parameters

Variable	Females (n=11)	Males (n=11)	p value
aPWV (m/s)	7.5 ± 0.8	7.6 ± 1.1	0.688
Supine SBP (mmHg)	114 ± 13	116 ± 14	0.761
Supine DBP (mmHg)	67 ± 8	68 ± 10	0.804
Supine HR (bpm)	57 ± 7	60 ± 7	0.344
Seated SBP (mmHg)	110 ± 15	122 ± 20	0.131
Seated DBP (mmHg)	64 ± 8	69 ± 12	0.279
Seated HR (bpm)	63 ± 7	69 ± 13	0.223
ΔSBP (mmHg)	-14 ± 17	-6 ± 15	0.301
ΔDBP (mmHg)	-8 ± 9	-8 ± 12	0.921

Data are means ± SD.

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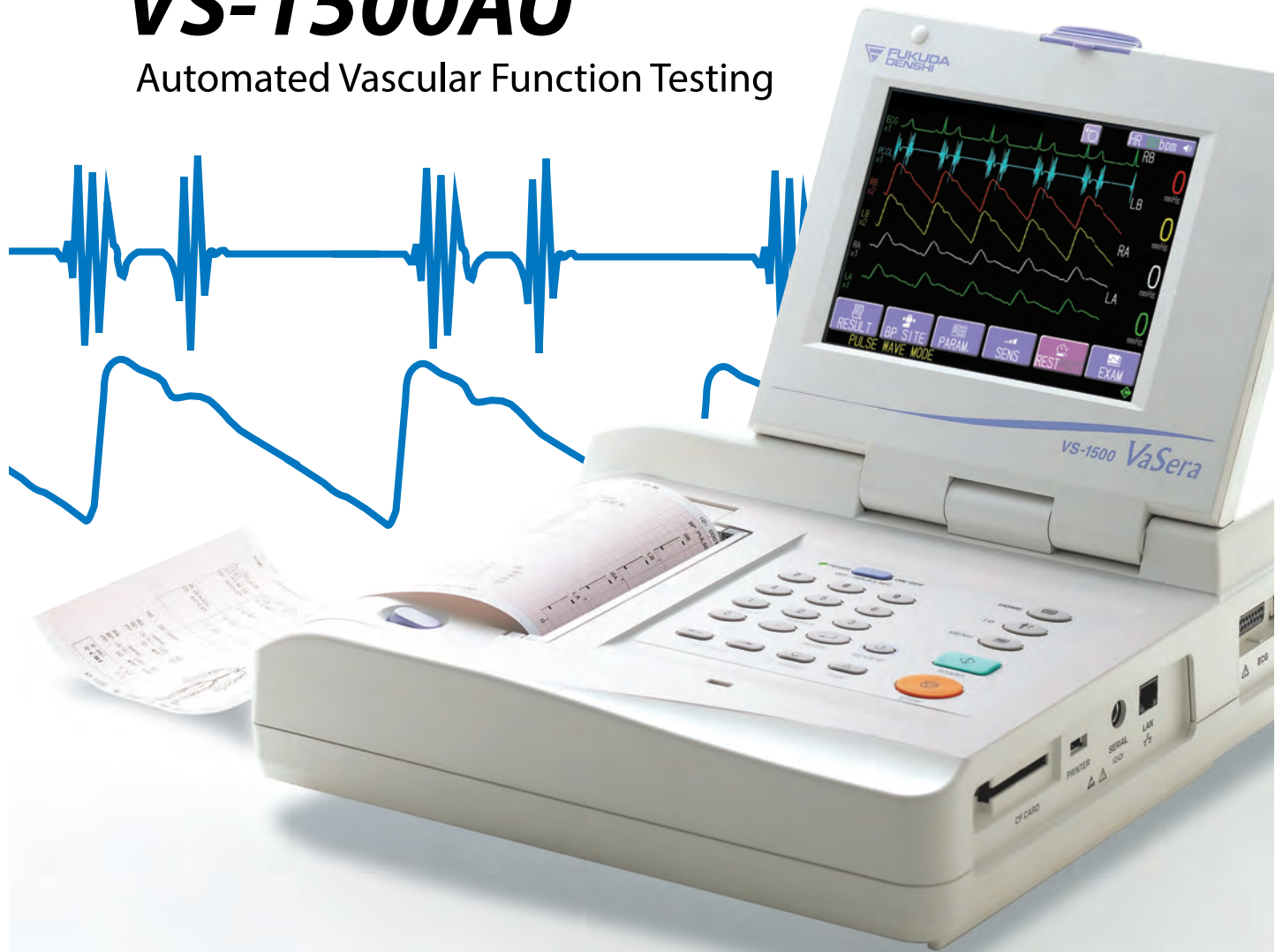
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