Discussed Posters

SESSION 1:
Body fat distribution: basic epidemiological and intervention studies

309
GLUCOSE INTOLERANCE CONTRIBUTES TO CARDIAC REMODELLING BUT NOT ATHEROSCLEROTIC DEVELOPMENT IN A MOUSE MODEL OF DYSLIPIDEMIA AND TYPE 2 DIABETES

M.-A. Laplante[1], **K. Le Quang[1], A. Charbonneau[1], X.P. Fang[2], P. Pelletier[1], C. Dion[1], R. Kohen[1], M.-J. Dubois[1], Y. Deshaies[1], M. Laakso[3], S. Ylä-Herttuala[3], J. Couet[1], M. Arseneault[1], G. Sweeney[2], A. Marette[1]**
[1]Institut Universitaire de Cardiologie et de Pneumologie de Québec (Hôpital Laval), Quebec, QC, [2]York University, Toronto, ON, Canada, [3]Department of Medicine, University of Kuopio, Kuopio, Finland

Objective: To investigate the impact of dyslipidemia and type 2 diabetes (T2D) on cardiovascular complications.

Methods: We have characterized wild-type C57Bl/6J (WT) and murine models of dyslipidemia and diabetes. Mice with an LDL receptor deletion and expressing only apolipoprotein B100 (LDLr$^{-/-}$/ApoB$^{100/100}$) were used. These were crossbred with mice overexpressing insulin growth factor II in pancreatic β-cells (LDLr$^{-/-}$/ApoB^{100}x IGF-II) to promote β-cell dysfunction and T2D. We determined glucose homeostasis, atherosclerosis and aortic vascular function, while cardiac function and remodelling were evaluated before and after myocardial infarction (MI, 30 min coronary artery ligation, 24h reperfusion).

Results: LDLr$^{-/-}$/ApoB$^{100/100}$xIGF-II mice exhibited increased fasting glycemia and glucose intolerance compared with LDLr$^{-/-}$/ApoB$^{100/100}$, while hyperinsulinemic-euglycemic clamps showed similar insulin resistance indicating that defective β-cell function underlie the development of T2D in the IGF-II model. Heart and liver pAkt(Ser473) signalling was similarly blunted in these two groups compared with WT animals. Relative to WT mice ($p< 0.05$), LDLr$^{-/-}$/ApoB$^{100/100}$xIGF-II animals had a higher ratio of ventricular weight/tibia length with a post-MI decrease in ejection fraction measured by echocardiography and a post-MI increase in the expression of hypertrophy and fibrosis markers β-MHC, BNP and procollagen 1a. These parameters were not significantly different between WT and LDLr$^{-/-}$/ApoB$^{100/100}$ mice. However, neither atherosclerotic plaque size nor vascular function of aortic rings were found to be altered in LDLr$^{-/-}$/ApoB$^{100/100}$ xIGF-II mice compared to LDLr$^{-/-}$/ApoB$^{100/100}$and WT controls.

Conclusions: Our results suggest that T2D contributes to cardiac remodelling and post-MI cardiac dysfunction but has little impact on atherosclerosis and vascular dysfunction in LDLr$^{-/-}$/ApoB$^{100/100}$ x IGF-II mice.

638
PERTURBATIONS IN INSULIN SIGNALING AND LIPID HOMESTASIS AD THE LEVEL OF THE SMALL INTESTINE OF OBESE PATIENTS

A. Veilleux[1], É. Grenier[1], A. Carpentier[2], D. Richard[3], É. Levy[1,4]

[1]Departement of Nutrition, Université de Montréal, Research Center CHU Sainte-Justine, Montréal, [2]Endocrinology Unit, Université de Sherbrooke Hospital Centre, Université de Sherbrooke, Sherbrooke, [3]Institut Universitaire de Cardiologie et de Pneumologie de Québec, Laval University, Québec, [4]J.A. de Sève, Research Chair in Nutrition, Université de Montréal, Montréal, QC, Canada

Introduction: Insulin resistance is commonly associated with atherogenic dyslipidemia. Mounting evidence indicates the active implication of the small intestine in this disorder.

Objective: To establish whether alterations in small intestine insulin sensitivity, accompanied with oxidative stress and inflammation, modify lipid and lipoprotein homeostasis in obese insulin resistant subjects compared to obese insulin sensitive subjects.

Methods: Markers of insulin sensitivity, oxidative stress and inflammation, as well as the production rates of lipids, apolipoproteins (apo) and lipoproteins were measured in small intestine sections obtained from obese subjects undergoing bariatric surgery.

Results: In intestinal explants of obese insulin-resistant subjects, we observed:

(a) a defect in insulin signaling as pointed out by a decreased phosphorylation of insulin receptor, insulin receptor substrate-1 and Akt as well as an increased phosphorylation of p38 MAPK;

(b) a higher level of lipid peroxidation markers which suggests the occurrence of oxidative stress;

© raised tissue concentrations of TNF-α and IL-6, supporting a local inflammatory state;

(d) increased protein level of fatty acid-binding proteins and microsomal triglyceride transfer protein, and finally

(e) elevated lipids and apo B-48 synthesis along with increased triglyceride-rich lipoprotein production.

Accordingly, high expression levels of transcription factors (SHREBP and LXR) were noticed in obese insulin-resistant subjects compared to obese insulin-sensitive individuals.

Conclusion: The small intestine could be classified as an insulin-sensitive organ. Its deregulation, caused by oxidative stress and inflammation, may lead to the amplification of lipid and lipoprotein synthesis, which could therefore contribute to atherogenic dyslipidemia observed in metabolic syndrome and type 2 diabetes.

182
ASSOCIATIONS OF SLEEP DURATION WITH ABDOMINAL ADIPOSITY, INSULIN RESISTANCE AND HBA1C IN NON-DIABETICS

M.T. Haren[1,2,3], G. Misan[2,3], J.F. Grant[4], J.D. Buckley[5], P.R.C. Howe[5], J. Newbury[2], A.W. Taylor[4], R.A. McDermott[1]

[1]Sansom Institute for Health Research, University of South Australia, Adelaide, [2]Spencer Gulf Rural Health School, [3]Centre for Rural Health and Community Development, University of South Australia, Whyalla, [4]Discipline of Medicine, University of Adelaide, [5]Nutrition Physiology Research Centre, Universiity of South Australia, Adelaide, SA, Australia

Background and aims: Evidence suggests that short sleep (SS) may cause weight gain, alter glucose metabolism and increase the risk of prediabetes. We examined the association of (normal sleep (NS) and long sleep (LS), relative to short sleep with abdominal adiposity, insulin resistance (IR) and HbA1c in non-diabetics.

Methods: A random population sample of adults from Whyalla, South Australia were recruited between February 2008 and July 2009 (n=722, 32.4% response rate). Abdominal adiposity (AbFat%) was measured by dual-energy x-ray absorptiometry (DXA). Average daily sleep duration was self-reported; SS was defined as < 7h/day, NS 7-9h/day and LS ≥9h/day. HbA1c was measured by HPLC and IR was calculated from fasting plasma glucose and serum insulin using the Homeostasis Model Assessment 2 (HOMA2). Linear regression was used to reduce confounding which included age, depression scores, alcohol consumption, caffeine and soft drink consumption, smoking, sleep disordered breathing, mastery and happiness.

Results: Seven-hundred participants completed DXA. Of these, 200 (28.6%) were classified as SS, 380 (54.3%) as NS, and 116 as LS. Data for sleep

duration was missing in four participants. NS was associated with average effects of -2.7% (95%CI -4.8, -0.5%) for AbFat%, -0.34 (95%CI -0.54, -0.15) for IR and -0.12% (95%CI -0.20, -0.04) for HbA1c. Associations with LS were non-significant for AbFat% and IR, and were similar to those of NS for HbA1c.

Conclusions: Relative to SS, NS but not LS was associated with improved outcomes suggesting sleep extension in non-diabetic short-sleepers may have the potential to prevent metabolically detrimental gains in abdominal adiposity.

129

THE ASSOCIATION BETWEEN ABDOMINAL ADIPOSE TISSUE DEPOTS AND INSULIN RESISTANCE IN FOUR ETHNIC GROUPS

D. Gasevic, S. Kohli, S.A. Lear

Simon Fraser University, Vancouver, BC, Canada

Objectives: To explore the association of IR with superficial subcutaneous (SSAT), deep subcutaneous (DSAT) and VAT in Aboriginal, Chinese, European, and South Asians.

Methods: Participants (n=784) were assessed for socio-demographics, fasting blood glucose and insulin, height, weight, total lean mass, SSAT, DSAT, and VAT. Partial correlations (age and sex adjusted) explored the association between abdominal adipose tissue depots and IR (Homeostasis model assessment (HOMA-IR)). Logistic regression explored the association between one standard deviation (SD) increment in SSAT, DSAT, and VAT and IR (HOMA-IR ≥75%) after controlling for age, sex, smoking, alcohol consumption, total lean mass, and body mass index. To facilitate comparisons between the abdominal depots, these were standardized (ethnic-specific) to a mean of zero and SD of one.

Results: VAT showed strongest and SSAT weakest positive correlation with IR ($p < 0.001$ for all depots). After controlling for confounders, one SD increase in SSAT was associated with decreased risk of IR (OR:0.257; 95%CI:0.081-0.817) among Aboriginals. On the other hand, one SD increase in DSAT was associated with an increased risk of IR in Europeans (OR:2.240; 95%CI:1.043-4.812). Furthermore, for one SD increase in VAT, the odds of being IR increased among Aboriginals (OR:2.023; 95%CI:1.138-3.596), Europeans (OR:3.784; 95%CI:1.753-8.171), and in South Asians (OR:2.192; 95%CI:1.343-3.578). In Chinese the results did not reach statistical significance (OR:1.641; 95%CI:0.982-2.742).

Conclusions: VAT increases risk of IR two to four fold among Aboriginals, Europeans, and South Asians. Deep SAT increases risk of IR among Europeans, while SSAT showed to play a protective role for Aboriginals.

486

VISCERAL/SUBCUTANEOUS ABDOMINAL ADIPOSITY AND LIVER FAT CONTENT DISTRIBUTION IN NORMAL GLUCOSE TOLERANCE, IMPAIRED FASTING GLUCOSE AND/OR IMPAIRED GLUCOSE TOLERANCE

A.-L. Borel[1,2], J.-A. Nazare[2], J. Smith[2], S.M. Haffner[3], B. Balkau[4], R. Ross[5], C. Massien[6], N. Alméras[2], J.-P. Després[2]

[1]Endocrinology, HP2 INSERM Laboratory INSERM U1042, Endocrinology Department, University Hospital of Grenoble, Grenoble, France, [2]Cardiology, Centre de Recherche de l'Institut Universitaire de Cardiologie et de Pneumologie de Québec, Québec, QC, Canada, [3]Baylor College of Medicine, Houston, TX, USA, [4]INSERM, CESP Centre for Research in Epidemiology and Population Health, U1018, Epidemiology of Diabetes, Obesity and Chronic Kidney Disease over the Lifecourse; University Paris Sud 11, UMRS 1018, Paris, France, [5]Queen's University, Kingston, ON, Canada, [6]Sanofi-Aventis, Paris, France

Objectives: To examine the specific distribution of visceral and subcutaneous adiposity and also liver fat content in normal glucose tolerance (NGT), impaired fasting glucose (IFG), impaired glucose tolerance (IGT) or combined conditions (IFG+IGT).

Methods: 2249 patients (50.6% women, 54.5% non-Caucasian) without diabetes from 29 countries were recruited in an observational study. Abdominal fat distribution was measured by computed tomography. Liver fat was estimated using the CT-liver mean attenuation.

Results: Compared to NGT patients, increased visceral adiposity levels were found in IFG, IGT and IFG+IGT without any difference between them; liver fat, however, progressively increased across these conditions. One SD increase in visceral adiposity was associated with an increased risk of having IFG [Men: OR 1.40 (1.15-1.72), women: OR 1.59 (1.27-1.99)], IGT [Men: OR 1.57 (1.14-2.18), women: OR 1.28 (0.96-1.71)] or IFG+IGT [Men: OR 1.62 (1.26-2.11), women: OR 1.77 (1.34-2.37)]. A one SD increase in liver fat was associated with IGT [Men: OR 1.44 (1.12-1.85), women: OR 1.76 (1.38-2.25)] and IFG+IGT [Men: OR 1.40 (1.14-1.72), women: OR 1.69 (1.33-2.17)]. Subcutaneous adiposity showed no relationship with glucose/insulin homeostasis conditions. Within each glucose/insulin homeostasis condition, patients having the highest levels of visceral adiposity and liver fat also demonstrated the lowest insulin sensitivity, as measured by the HOMA-RI.

Conclusions: Liver fat is only associated with increased odds of having IGT and not IFG, whereas visceral adiposity is associated with both. This suggests that liver fat reflects the multi-organ ectopic fat deposition that is associated with IGT, whereas increased hepatic insulin resistance characterizes IFG.

83

EFFECTS OF A LIFESTYLE-INDUCED WEIGHT LOSS ON CARDIOMETABOLIC RISK OF METABOLICALLY NORMAL, YET OBESE INDIVIDUALS

R.H.-L. Liu[1], S. Wharton[2], J.L. Kuk[1]

[1]Kinesiology and Health Sciences, York University, Toronto, [2]Wharton Medical Clinic, Hamilton, ON, Canada

Aim: To determine if a clinically significant weight loss (WL) of 5% or 10% would have a differential effect on metabolic factors in metabolically normal, yet obese (MNOB) versus metabolically abnormal obese (MAOB) individuals attending the Wharton Medical Clinic.

Methods: Patients included 404 adults (Age: 53.5 ± 12.3years, BMI: 40.8 ± 7.8kg/m^2) who were treated for at least 3 months. Subjects were defined as MNOB if at least four of the five low-risk clinical cut-offs were satisfied for glucose, triglyceride (TG), blood pressure [Systolic-BP(SBP) | Diastolic-BP(DBP)], HDL-cholesterol and LDL-cholesterol, otherwise these patients were classified as MAOB.

Results: In MNOB and MAOB, improvements in risk factors were more commonly observed with a clinically significant WL in comparison to those who did not lose weight, ($p< 0.05$). MAOB patients who did not achieve a 5 or 10%WL still significantly improved blood pressure and cholesterol by attending the clinic ($p< 0.05$), yet their improvement in TG and SBP were not as great as MAOB who lost weight. The likelihood of having a metabolically normal profile at follow-up increased 2.4-fold with a 5%WL and 5.6-fold with a 10%WL, relative to those who did not lose weight, ($p< 0.05$).

Conclusions: A clinically significant WL is beneficial to the cardiometabolic risk profile of MNOB and MAOB individuals. However, a 5%WL is not necessarily required to improve the metabolic profile of MAOB. Thus, positive lifestyle modifications associated with attempting to lose weight may be associated with improvements in metabolic health, even in the absence of weight loss.

620

TARGETING WAIST AND CARDIORESPIRATORY FITNESS TO REDUCE CARDIOMETABOLIC RISK AT THE WORKPLACE: RESULTS FROM THE GRAND DéFI ENTREPRISE

M. Vallières[1], P. Poirier[1,2], C. Rhéaume[1], J.-P. Després[1,3], N. Alméras[1]

[1]Institut Universitaire de Cardiologie et de Pneumologie de Québec, [2]Faculté de Pharmacie, Université Laval, [3]Département de Médecine Sociale et Préventive, Université Laval, Québec, QC, Canada

Introduction: Our poor lifestyle habits leading to the current epidemic of metabolic syndrome have changed the mosaic of modifiable risk factors for cardiovascular disease. While most abdominally obese individuals fail to adopt healthy behaviours over the long term, few cardiometabolic health programs are offered in the workplace.

Methods: About 600 employees from four companies were involved in a pilot project of the "Grand Défi Entreprise" (Great Corporate Challenge), which involved a 3-month friendly in-house competition among employees to improve their lifestyle habits. For that purpose, a comprehensive health assessment provided by a mobile risk assessment unit before and after the 3-month challenge was performed.

Results: After the 3-month contest, waist circumference (WC) was significantly reduced (-4.4±3.9 cm, $p< 0.0001$). Cardiorespiratory fitness (CRF) was improved as indicated by a significantly reduced heart rate assessed at a standardized submaximal workload on a treadmill (3.5mph at 2% slope) ($p< 0.0001$). The sample was then classified into four groups on the basis of WC loss and CRF improvement. Results show that individuals who both decreased their WC and increased their CRF improved the most their cardiometabolic (HDL-C=+0.04±0.18 mmol/L; TG=-0.42±0.18 mmol/L; $p< 0.0001$) as well as their hemodynamic profiles at rest and during a submaximal exercise (mean arterial pressure changes; -5.1±7.1 mmHg; -6.1±9.6 mmHg; $p< 0.0001$, respectively). Individuals who only increased CRF did not improve their cardiometabolic profile.

Conclusion: Results from this pilot intervention study conducted at the workplace provide evidence that targeting both WC and CRF is relevant to reduce cardiometabolic risk of workforce.

608

TARGETING CARDIORESPIRATORY FITNESS TO IMPROVE CARDIOMETABOLIC RISK PROFILE IN PATIENTS WITH ESTABLISHED CORONARY ARTERY DISEASE: A PILOT STUDY

V. Lévesque[1,2], P. Poirier[1,3], A. Marette[1], P. Mathieu[1], J.-P. Després[1,2], É. Larose[1]

[1]IUCPQ, Université Laval, [2]Division Kinésiologie, [3]Pharmacie, Université Laval, Québec, QC, Canada

Introduction: Cardiorespiratory fitness(CRF) is recognized as a major predictor of cardiovascular disease and is also associated with cardiovascular health.

Objective: The present pilot study tested the relevance of targeting CRF to improve the cardiometabolic risk profile of patients with established coronary artery disease (CAD) who had a coronary artery bypass graft surgery followed by a 1-year lifestyle modification program.

Methods: Anthropometric measurements, assessment of lipid profile, abdominal magnetic resonance imaging, OGTT and a maximal treadmill test were performed 6-weeks following surgery and after the lifestyle intervention (n=33).

Results: In response to the lifestyle modification program, patients showed a significant increase in CRF as reflected by an increase in VO_2max(Δ=+4.6mlO_2/kg/min,$p< 0.0001$) and by a reduced HR assessed at a standardized submaximal workload(1.7mph,5%slope)(Δ=-9bpm,$p< 0.0001$). Patients also showed decreases in their BMI(Δ=-0.9 kg/m^2,$p< 0.01$), waist circumference(Δ=-4.5cm,$p< 0.01$), visceral(VAT) (Δ=-26.5ml/5mm,$p< 0.05$) and subcutaneous(SAT) adipose tissue volumes(Δ=-28.5ml/5mm, $p< 0.01$). They also significantly reduced their glucose area under the curve(AUC)(Δ=-0.14pmolx10^{-3}/L,$p< 0.0001$), 2h-plasma glucose(Δ=-1.23mmol/L,$p< 0.01$) and insulin levels(Δ=-46.00mmol/L,$p< 0.05$), TG(Δ=-0.15mmol/L,$p< 0.01$) and increased their HDL-C(Δ=+0.20mmol/L, $p< 0.0001$). Changes in VO_2max were significantly correlated with changes in BMI, waist circumference, SAT, HDL-C, 2h-plasma glucose, 2h-plasma insulin, and glucose/insulin AUC. In a multivariate model that included changes in VAT and CRF, the response of CRF was the most important predictor of changes in 2h-plasma glucose(r^2=056,$p< 0.0001$) and insulin levels(r^2=0.36,$p< 0.01$), glucose-AUC(r^2=0.32,$p< 0.01$), insulin-AUC(r^2=0.52,$p< 0.01$) and HDL-C(r^2=0.20,$p< 0.05$).

Conclusion: Improvement of CRF appears to be an important target to improve cardiometabolic risk profile in patients with established CAD.

SESSION 2:
Adipose tissue and cardiometabolic risk through the lifespan

317
TRANSCRIPTIONAL CONTROL OF ADIPOGENESIS BY OCAB

S. Miard[1], S. Carter[1], C. Roy-Bellavance[1], L. Boivin[1], É. Rondeau[1], M. Simard[2], D. Marsolais[1], F. Picard[1]

[1]IUCPQ, Université Laval, quebec, [2]Hotel-Dieu de Québec, Quebec, QC, Canada

Objectives: Using a differential screening by large scale genomics, our team recently discovered that Ocab levels are robustly reduced in WAT upon ageing and obesity. The objective of this study was to determine the role of Ocab in energy metabolism.

Methods: Using the Ocab knockout mouse model, visceral adipose tissue was quantified and glucose and insulin tolerance tests were performed. Circulating proinflammatory cytokines were quantified by milliplex assay. Mouse embryonic fibroblasts (MEFs) were isolated to compare their adipogenic potential, lipolysis was tested using primary adipocytes and adipogenesis was compared between 3T3L1 cells overexpressing Ocab and controls. Molecular mechanism was identified using, co-immunoprecipitation, luciferase assay and GST pull down.

Results: Analyses showed that compared to their wild type counterparts (WT) Ocab-/ - animals had more visceral adipose tissue, were more resistant to insulin and had higher levels of circulating proinflammatory cytokines. These findings are supported by ex vivo analyses, which demonstrated that Ocab -/ - MEFs were more easily differentiated into adipocytes and that isolated adipocytes have impaired response to insulin, whereas overexpression of Ocab in 3T3-L1 suppresses adipogenesis. Mechanistically, the binding of Ocab to its transcription factor Oct-1 results in the sequestration of RXRalpha. The latter is unable to bind with its partner PPAR$_{\gamma}$, which causes a reduction of adipogenic gene transcription.

Conclusion: This study reveals for the first time the role of OCAB in lipid metabolism.The results suggest that OcaB could be an interesting pharmacological target for treating fat accumulation observed during aging.

Study funded by CIHR.

729
ABDOMINAL FAT TISSUE EXPRESSES CYTOKINES AND PRO-COAGULANT GENES UPON INFLAMMATORY STRESS IN AN AGE-DEPENDENT FASHION

M.E. Starr[1], T.G. Wood[2], A. Stromberg[3], B.M. Evers[1], **H. Saito[1]**

[1]Surgery, University of Kentucky, Lexington, KY, [2]Biochemistry and Molecular Biology, University of Texas Medical Branch, Galveston, TX, [3]Statistics, University of Kentucky, Lexington, KY, USA

Objectives: To identify genes which are strongly expressed in abdominal fat tissue upon inflammatory stress.

Methods:

(1) Gene expression profile was obtained by microarray analysis of 45,000 gene probes (Affymetrix) using purified RNA samples from the epididymal fat pads of young and aged mice with or without inflammatory stress caused by bacterial endotoxin.

(2) Expression of selected genes of interest was further confirmed by qRT-PCR analysis and compared in fat and other tissues.

(3) Adipocytes and stromal cells were separated to localize gene expression.

Results: Among 30,043 genes that are expressed in the adipose tissue, nearly half (13,352) showed altered expression (> 2-fold change) by inflammatory stress. Among these, 1,418 showed age-associated changes (>1.5 fold change) in gene expression. A large number of genes for inflammatory cytokines (including IL-1α, IL-1β, and IL-6) and pro-thrombotic factors (including tissue factor, thrombospondin-1, plasminogen activator inhibitor-1 and -2) were found to be strongly expressed in the adipose tissue. Expression of many of these genes was increased by inflammatory stress, further augmented by aging, and more abundant in adipose tissue compared to liver and kidney. Additionally, expression of these genes in the fat was localized mainly to stromal cells rather than adipocytes.

Conclusions: Abdominal adipose tissue is a major source of various inflammatory cytokines and pro-coagulant factors. Expression of these genes is up-regulated by inflammatory stress and further augmented by aging, indicating that adipose tissue plays a major role in age-associated vulnerability to such inflammation-mediated diseases as sepsis, systemic inflammation, and disseminated intravascular coagulation.

122
ALANINE TRANSAMINASE AND WAIST TO HIP RATIO PREDICT REGRESSION TO NORMOGLYCEMIA AND AUC$_{\text{GLUCOSE 0-120 MIN}}$ IN ADULT PATIENTS WITH PREDIABETES

N. Yakubovich[1], S.S. Anand[1,2], P. Raina[2], E. Pullenayegum[2], H.C. Gerstein[1,2]

[1]Medicine, [2]Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada

Methods: We performed analyses on 1,209 people with prediabetes in the placebo-placebo group of the DREAM trial to evaluate ALT and waist to hip ratio (WHR) as predictors of AUC$_{\text{glucose0-120min}}$ and regression of prediabetes to normoglycemia.

Results: The effects of ALT and WHR on regression to normoglycemia 2 years later were found to be interdependent (P=0.01 for interaction). Adjusted odds ratios ORs (95% CI) of regression to normoglycemia per 10 U/L higher ALT were 0.79 (0.66-0.94), 0.90 (0.80-1.02), and 1.03 (0.90-1.18) when WHR was at the mean minus 1 standard deviation (SD), at the mean, and at the mean+1SD, respectively. Adjusted ORs of regression to normoglycemia per 0.1 unit higher WHR were 0.75 (0.60-0.95), 0.91 (0.76-1.08), and 1.09 (0.89-1.35) when ALT was at the mean-1SD, at the mean, and at the mean+1SD, respectively.

Similarly, the effects of ALT and WHR on AUC$_{\text{glucose0-120min}}$ were interdependent (P=0.056 for interaction). A 10 U/L lower ALT was associated with an adjusted AUC$_{\text{glucose0-120min}}$ decrease of 19.5 (5.3-33.7), 11.0 (1.4-20.6), and 2.5 (-9.2 to 14.1) min*mmol/L when WHR was at the mean-1SD, at the mean, and at the mean+1SD, respectively. A 0.1 unit lower WHR was associated with an adjusted AUC$_{\text{glucose0-120min}}$ decrease of 30.3 (10.2-50.3), 18.3 (3.8-32.9), and 6.4 (-11.5 to 24.3) when ALT was at the mean-1SD, at the mean, and at the mean+1SD, respectively.

Conclusions: Low ALT predicts regression of prediabetes to normoglycemia and a decrease in AUC$_{\text{glucose0-120min}}$ when WHR is relatively low. Low WHR predicts these outcomes when ALT is relatively low.

601
CLUSTERING OF THE METABOLIC SYNDROME ABNORMALITIES DIFFERS IN ADOLESCENT BOYS AND GIRLS

M. Melka[1], M. Abrahamowicz[2], G.T. Leonard[3], M. Perron[4], L. Richer[4], S. Veillette[4], D. Gaudet[5], T. Paus[3,6], T. Paus[6], **Z. Pausova**[1]

[1]The Hospital for Sick Children, Toronto, ON, [2]McGill University, [3]Montreal Neurological Institute, McGill University, Montreal, [4]Université du Québec à Chicoutimi, [5]Community Genomic Centre, Université de Montréal, Chicoutimi, QC, [6]Rotman Research Institute, Toronto, ON, Canada

Background: Metabolic Syndrome (MetS) is defined as a cluster of risk factors for cardiovascular disease and type-2 diabetes mellitus. The mechanisms of clustering of these risk factors in the same individual are not understood, but they may not stem from a single pathway and may not be the same in males and females.

Aim: To identify components of shared variance among the individual MetS abnormalities in adolescent boys and girls.

Participants and methods: A community-based sample of adolescent boys (n=286) and girls (n=312) was studied. Principal component analysis was conducted using blood pressure (BP) measured beat-by-beat during an hour-long protocol, serum concentrations of triglycerides (TG), HDL-cholesterol and glucose (Glu) assessed from a fasting blood sample, and visceral fat (VF) measured with magnetic resonance imaging.

Results: The analysis identified 2 main independent components of shared variance in boys and girls. Component 1 was similar in the two sexes; it captured ~30% of the variance and was loaded positively by VF, TG and Glu and negatively by HDL-cholesterol. Component 2, in contrast, was quite different between the sexes; in boys, it explained ~20% of variance and was loaded positively by BP, VF and HDL-cholesterol, whereas in girls, although it also explained ~20% of variance, it was loaded positively by BP and TG and negatively by Glu.

Conclusions: Several independent pathways may contribute to the development of MetS and some of them may differ between males and females. These findings indicate the need for sex-specific prevention and treatment strategies of MetS.

235
PUBLIC OPEN SPACES AND FOOD ENVIRONMENT ARE ASSOCIATED WITH THE DEVELOPMENT OF CARDIO-METABOLIC RISK FACTORS

C. Paquet[1,2], N. Howard[1], N. Coffee[1], G. Hugo[3], A.W. Taylor[4], R. Adams[4], M. Daniel[1,5]

[1]Sansom Institute for Health Research, University of South Australia, Adelaide, SA, Australia, [2]Research Centre of the Douglas Mental Health University Institute, Montreal, QC, Canada, [3]Discipline of Geography, Environment and Population, [4]Discipline of Medicine, The University of Adelaide, Adelaide, SA, [5]Department of Medicine, St Vincent's Hospital, The University of Melbourne, Melbourne, VIC, Australia

Objectives: To investigate whether residential environment characteristics related to food and public open spaces (POS) are associated with the incidence of cardio-metabolic risk factors.

Methods: Adult cohort participants (n=3205) provided clinical data in 2000-2003 and 2005-2006. Cardio-metabolic risk factors included: pre-diabetes/diabetes (HbA_{1c} ≥5.7% or FPG ≥5.6mmol/L or diagnosed diabetes); hypertension (diastolic/systolic BP ≥85/130mmHg); dyslipidemia (tryglicerides ≥1.7 mmol/L or HDL < 1.03(males)/< 1.29(females) or on lipid-modifying medication); and abdominal obesity (≥94cm(males)/≥80cm(females)). The food environment was expressed for a 1000m road distance from each participants' residence as the ratio of fast-food restaurants and unhealthful food stores to healthful food stores. POS characteristics were expressed as the number, median size, greenness and type (proportion with sporting facilities) of POS within 1000m of participants' residence. Poisson modelling with robust variance estimation was used to calculate the Relative Risks (RR) of developing each risk factor. Models accounted for participants' gender, age, education, income, residential area deprivation and spatial clustering.

Results: Proportions of participants who developed these risk factors over an average of 3.5 years were: 24.5% for prediabetes/diabetes, 19.5% for dyslipidemia, 26.2% for abdominal obesity, and 24.6% for hypertension. Incident prediabetes/diabetes was inversely associated with living in proximity to larger POS (RR(per SD): 0.76, 95%CI: 0.69, 0.84). Incident abdominal obesity was positively associated with the unhealthful food environment index (RR(per SD): 1.11, 95%CI: 1.03, 1.20). No significant associations were found with incident hypertension or dyslipidemia.

Conclusion: The results provide new evidence, beyond cross-sectional associations, for the role of the built environment in shaping cardio-metabolic health.

80
NOVEL AND ESTABLISHED ANTHROPOMETRIC MEASURES AND THEIR PREDICTION OF INCIDENT ISCHEMIC CARDIOVASCULAR DISEASE IN 60-YEAR OLD MEN AND WOMEN

A. Carlsson[1], U. Riserus[2], J. Ärnlöv[2], M.-L. Hellensius[3], U. de Faire[3]

[1]Karolinska Institutet, Stockholm, [2]Uppsala University, Uppsala, [3]Karolinska Institutet, Solna, Sweden

Background: The Emerging Risk Factors Collaboration studied BMI, WC and WHR in 58 cohorts and showed no added risk prediction beyond established risk factors of cardiovascular disease (CVD). Yet, other anthropometric measures may be better.

Aim: To study the association between anthropometric measures and incident CVD.

Methods and results: A population-based study of 1751 men and 1990 women, aged 60-years and free from cardiovascular disease, with 375 incident cases of CVD, during 11-years of follow-up was used. Fasting blood samples were drawn and weight, height, waist circumference (WC), hip circumference and sagittal abdominal diameter (SAD) was measured at baseline. Body mass index (BMI), Waist-Hip-Ratio (WHR) and Waist-Hip-Height-Ratio (WHR divided by height, WHHR) was calculated. Hazard Ratios (HR) with 95% (confidence intervals) were calculated using multivariable Cox regression. Model discrimination (C-statistics) and likelihood ratio tests calculations were performed.

All anthropometrical measures predicted CVD in unadjusted Cox regression models per standard deviation increment, where significant associations were found for WHHR, HR 1.41 (1.29-1.55), WHR, HR 1.39 (1.26-1.54) and SAD, HR 1.24 (1.17-1.32). WHHR was the strongest predictor beyond the established risk factors as evaluated by increase in C-statistics and results of likelihood ratio tests (p< 0.001). The multivariable-adjusted HR per standard deviation increment for WHHR was 1.20 (1.08-1.33 (p< 0.001)).

Conclusion: Only WHHR, WHR and SAD predicted CVD beyond established CVD-risk factors. WHHR, a new anthropometric measure reflecting body composition and central obesity, was the strongest predictor in both sexes before and after adjustments for established cardiovascular risk factors.

737

THE EFFECT OF MAXIMUM BODY WEIGHT IN LIFETIME ON THE DEVELOPMENT OF TYPE 2 DIABETES: MAXWEL STUDY

S. Lim[1,2], M.J. Kim[1], S.H. Choi[1], H.C. Jang[1], D.J. Wexler[3], J.B. Meigs[2]

[1]Internal Medicine, Seoul National University College of Medicine, Seongnam, Republic of Korea, [2]General Medicine, Harvard Medical School, [3]MGH Diabetes Unit, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Background: Obesity antedates the development of type 2 diabetes (T2D). However, the relationship between the magnitude and rate of weight gain to T2D development has not been investigated.

Methods: We studied 2127 consecutive Korean subjects aged ≥30 years newly diagnosed with diabetes by HbA1c ≥6.5%. Anthropometric and clinical parameters were measured at diagnosis. Data of body weight at age 20 years (Wt_{20y}) were obtained from participants' document. Participants recalled their maximum weight (Wt_{max}) prior to T2D diagnosis and age at maximum weight (Age_{max_wt}). The rate of weight gain ($Rate_{wt\_gain}$) was calculated from magnitude of weight gain ($Magnitude_{wt\_gain} = Wt_{max}-Wt_{20y}$) divided by Age_{max_wt} -20.

Results: The mean age at T2D diagnosis (Age_{T2D}) was 50.1 ± 10.5 years. The Wt_{20y} and Wt_{max} were 59.9 ± 10.5 kg and 72.9 ± 11.4 kg, respectively. The Age_{max_wt} was 41.5 ± 10.9 years and the $Rate_{wt\_gain}$ was 0.56 ± 0.50 kg/year. Earlier Age_{max_wt}, greater $Magnitude_{wt\_gain}$, and higher $Rate_{wt\_gain}$ were significantly associated with earlier Age_{T2D} after adjusting for age, sex, lifestyles, family history of diabetes, and Wt_{20y}. Male sex, BMI at age 20 years, current smoking, non-exercise, the earlier Age_{max_wt}, and the greater $Magnitude_{wt\_gain}$ but not $Rate_{wt\_gain}$ were significantly associated with HbA1c at diagnosis after adjusting for the same variables.

Conclusion: Rapid and substantial weight gain were associated with early development of T2D and poor glycemic status independently of body weight at age 20 years. This finding supports public health recommendations to reduce the risk of T2D by preventing weight gain from early adulthood. (NCT00816608)