European Group for the Study of Insulin Resistance

EGIR Annual Meeting
23-24 April, 2015

School of Medicine, University Paris Descartes

12 rue de l'Ecole de Médecine

75006 Paris

Chairman: Professor Fabrice Bonnet

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Programme

Thursday 23th April

10h30-11h	Coffee
10h50	Welcome to Paris from the EGIR President, John Petrie, and Fabrice Bonnet
11h00-11h45:	Session 1: ***with the support of Janssen*** Pr Etienne Larger (Paris): *Alterations of the exocrine pancreas in diabetes*
11h45-12h30:	Abstracts session 1 Chair: John Petrie
12h15-14h00:	Lunch
14h15-15h:	Dr Michael Hansen (USA): *Identification of novel biomarkers of beta-cell function*
15h-16h:30	RISC investigators meeting and future collaborative studies EGIR Annual General Meeting
16h30:	Coffee break
17h-18h:	Pr Karine Clement (Paris) *Microbiota and bariatric surgery*
19h30-20h30:	Visit and cocktail at Jewellers "Mellerio"
20h45	Dinner at Procope

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Friday 24th April

9h00-9h45:	Pr Jean-François Gautier (Paris) : *Long-term consequences of foetal exposure to maternal diabetes*
9h45-10h45:	Abstracts sessions 2 Chair: Andrea Natali
10h45-11h15:	Coffee break
11h15-12h:	Pr Guy Rutter (London): *Beta cell connectivity in pancreatic islets*
12h15: 14h	Lunch
14h15-15h:	Pr Martine Laville (Lyon): *Lessons from experimental overfeeding*
15h-16h00	Abstract session 3 Chair: Martine Laville
16h30	End of the meeting.

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INVITED LECTURERS

Prof. Etienne Larger, Dept of Diabetology, University Paris Descartes, Paris, France

Dr Michael Hansen, Janssen, USA

Prof. Karine Clement, Institute of Cardiometabolism and Nutrition, University Paris VI, Paris

Prof. Jean-François Gautier, Dept of Diabetology, University Paris VII, Paris

Prof. Guy Rutter, Imperial College, London, UK

Prof. Martine Laville, Dept of Nutrition, University Lyon 1, Lyon, France

SPONSORS

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		Name	Country
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3	Blair	Helen	UK
4	Bonner	Caroline	France
5	Bonnet	Fabrice	France
6	Clement	Karine	France
7	Gautier	Jean-François	France
8	Golay	Alain	Switzerland
9	Griffith	Jones Jones	Portugal
10	Hansen	Michael	USA
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24	Rutter	Guy	UK
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26	Saponaro	Chiara	Italy
27	Segrestin	Bérénice	France
28	Simeon	Soline	France
29	Stafie	Céline	Romania
30	Triantafyllou	Areti	Greece

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ABSTRACT SESSIONS

Abstract session 1 - Thursday 23April; 11:45-12:30

Chair: John Petrie

The association between sleep duration and insulin sensitivity	Rutters et al
Insulin resistance and subcellular distribution of intramyocellular lipids	Amati, F.
Elevated heart rate predicts beta cell function in non-diabetic individuals	Bonnet et al

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The association between sleep duration and insulin sensitivity: the EGIR-RISC study

Rutters F PhD[1,2], Besson H PhD[3], Balkau B[4,5] and Dekker JM , [1,2] on behalf of the EGIR-RISC Study group[*]

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Background and Aims: In the past 10 years, over three-dozen studies reported a relationship between short sleep and disturbed glucose metabolism. Studies with insulin sensitivity assessed according to the gold standard hyperinsulinemic–euglycemic clamp are however still missing. We therefore evaluated the cross-sectional association of sleep duration and insulin sensitivity in the European Relationship between Insulin Sensitivity and Cardiovascular Disease (EGIR-RISC) study.

Methods: We used data from the baseline measurements of the European, multi-centre EGIR-RISC study, which included 1500 clinically healthy men and women. Sleep and physical activity were measured objectively using a single-axis accelerometer, which was worn for at least 3 days and up to 8 days. Insulin sensitivity was measured by hyperinsulinemic-euglycemic clamp (M/I). Other markers of glucose homeostasis included levels of fasting plasma glucose and insulin, 2-h plasma glucose and insulin.

Results: In our current analysis, we included 797 participants (57% female, age 44±8 years). A weak U-shaped association between hours of sleep and M/I was observed: after adjustment for age and sex, M/I was 10.7 (-4.4- 25.9), 3.6 (-10.2-17.4), -0.8 (-15.9-14.3) and 4.7 (-14.3-23.9) $\mu molmin^{-1}kgffm^{-1}nM^{-1}$ higher for the 6-7 hour group, 7-8 hour group, 8-9 and the >9 hour group, respectively, compared to the < 6h group. Additionally, we observed a J-shaped association for basal glucose: after adjustment for age and sex, glucose levels were 0.13 (0.02-0.24), 0.12 (0.02-0.22), 0.16 (0.05-0.27) and 0.19 (0.05-0.33) mmol/l higher for the 6-7 hour group, 7-8 hour group, 8-9 and the >9 hour group, respectively, compared to the < 6h group. Similar J-shaped associations were observed for basal insulin levels and 2-h glucose and insulin levels.

Conclusions: Short and long sleep duration are weakly associated with insulin sensitivity and markers of glucose homeostasis in a healthy population.

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Insulin resistance and subcellular distribution of intramyocellular lipids

Amati, Francesca[1]

[1]University of Lausanne, Switzerland

Background and Aims: Accumulation of lipids inside of skeletal muscle is associated with increased insulin resistance. Subcellular compartments encompass the intramyofibrillar (IMF) and the subsarcolemmal (SSL) regions. The aim of this study was to explore lipid droplets and mitochondria distributions and see how they relate to insulin sensitivity and markers of body adiposity.

Methods: Nested in a pre/post intervention design, 12 insulin resistant volunteers (IR, 6 females and 6 males) underwent a 4 months endurance exercise intervention. 12 age- and gender-matched insulin sensitive (IS) subjects were used as controls for all outcomes at baseline. Insulin sensitivity was measured by an euglycemic hyperinsulinemic clamp. Muscle biopsies of the vastus lateralis were used to assess lipid droplets volume density (LVD) and mitochondria volume density (MVD), both quantified by stereology on electron microscopy micrographs. Body composition was measured by DXA and MRI.

Results: IS and IR subjects had equal amounts of LVD in IMF (p=0.69) and SSL (p=0.06). IS subjects had greater MVD in IMF (p=0.002) and SSL (p=0.0003). SSL LVD was associated negatively with insulin sensitivity (R2=0.26 p=0.01) but not IMF LVD. MVD in the IMF and SSL positively correlated with insulin sensitivity (R2=0.31 p=0.004 and R2=0.5 p=0.0001). SSL LVD was associated with BMI, percent body fat, and visceral adipose tissue (R2=0.23 p=0.02, R2=0.22 p=0.02, and R2=0.25 p=0.01). After intervention, SSL LVD decreased (p=0.03) and IMF LVD increased (p=0.04). MVD increased in IMF and SSL (both p=0.001).

Conclusion: Lipids in the SSL region and not IMF seem to be more associated with insulin resistance and markers of adiposity associated with metabolic disease. SSL lipids decreased after an exercise intervention pointing to the possibility that IMF lipids may serve as a substrate during exercise while SSL lipids may explain the harmful aspects of ectopic lipids.

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Elevated heart rate predicts beta cell function in non-diabetic individuals: the RISC cohort

Bonnet F[1,2] , Empana JP [3] , Natali A [4] , Monti L[5] , Golay A [6], Lalic K[7] , Dekker JM [8] , Mari A[9] , Balkau B[2] for the RISC Study Group

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Background and Aims*:* Elevated heart rate has been associated with insulin resistance and incident type 2 diabetes but its relationship with β-cell function is not known. Our aim was to investigate whether baseline heart rate is associated with β-cell function and hyperglycaemia.

Methods : We used the prospective RISC cohort with 1005 non-diabetic individuals who had an oral glucose tolerance test (OGTT) at baseline and after 3 years. Impaired glucose regulation was defined as a fasting plasma glucose ≥6.1 mmol/l or a 2-hour plasma glucose ≥7.8 mmol/l. Insulin sensitivity was assessed by the OGIS index and insulin secretion and β-cell glucose sensitivity at both baseline and 3 years.

Results: Baseline heart rate was positively related to both fasting (p<0.0001) and 2h glucose levels (p=0.02) at year 3 and predicted the presence of impaired glucose regulation at year 3 in a logistic regression model adjusting for insulin sensitivity at inclusion [OR per 10 beats/min: 1.31; 95% CI (1.07-1.61); p=0.01]. Baseline heart rate was associated with lower insulin sensitivity (β=-0.11; p<.0001), a decrease in both □-cell glucose sensitivity (β=-0.11; p=0.003) and basal insulin secretion rate (β=-0.11; p=0.002) at 3 years in an adjusted multivariable regression model. Baseline heart rate predicted the 3-year decrease in β-cell glucose sensitivity (β=-0.10; p=0.007) and basal insulin secretion (β=-0.12; p=0.007).

Conclusions*:* Heart rate predicts β-cell function and impaired glucose regulation at 3 years in non-diabetic individuals, independently of the level of insulin sensitivity. These findings suggest a possible effect of the sympathetic nervous system on β-cell dysfunction, which deserves further investigation.

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Abstract session 2 - Friday 24 April; 09:45-10:45

Chair: Andrea Natali

Association between insulin resistance and indices of micro- and macrovascular function in low cardiovascular risk individuals	Triantafyllou et al
The effect of PEX11β knockdown on peroxisome abundance and insulin secretion in MIN6 cells	Blair et al
Study of the association between renal function and insulin resistance in a healthy population	Simeon et al
Adverse impact of visceral fat on lipid and metabolic profile in fatty liver disease	Saponaro et al

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Association between insulin resistance and indices of micro- and macrovascular function in low cardiovascular risk individuals

Triantafyllou A[1], Anyfanti P[1], Zabulis X[2], Gkaliagkousi E[1], Mitrakou A [3], Douma S[1]

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[2]Institute of Computer Science, Foundation for Research and Technology – Hellas
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Background and Aims: Disorders of the metabolic profile, including insulin resistance, have been associated with atherosclerosis, hypertension and target organ damage. The aim of the present study was to investigate whether an association exists between insulin resistance and accumulation of micro- and macro-vascular damage in multiple target organs, in a sample of hypertensive patients and healthy individuals.

Methods: Newly-diagnosed patients with essential hypertension, indicated by medical history and clinical examination, free from other comorbidities and under no antihypertensive or other medication, as well as healthy normotensive volunteers, were included in the study. Aortic stiffness was used as an index of macrovascular status, estimated by measurement of Pulse Wave Velocity (PWV) and Augmentation Index (AIx), using the Sphygmocor device. For the evaluation of the small vessels, all participants underwent bilateral, non-mydriatic digital fundus photography (estimation of retinal vascular diameters), 24hour urine collection (detection of microalbuminuria) and nailfold capillaroscopy (evaluation of capillary rarefaction). To achieve retinal vessel as well as capillary density measurements and analysis, semi-automated computer software was developed through the collaboration of our Hypertension Unit and the Institute of Computer Science, Foundation for Research and Technology–Hellas (FORTH). Insulin resistance was calculated with the index HOMA-IR.

Results: In total, 214 subjects with a mean age of 43.9±11.8 years were included in the study, 162 hypertensives and 52 normotensives. Insulin resistance was increased in subjects with macrovascular damage compared to individuals with normal macrocirculation [1.38 (0.94-3.27) vs 1.97 (1.24-3.36), $p<0.001$]. Regarding microvascular alterations, increased insulin resistance (HOMA-IR) was observed in subjects with microalbuminuria [1.89 (1.41-3.55) vs 1.70 (1.06-2.66), $p=0.035$] and capillary rarefaction [2.34 (1.23-4.15) vs 1.69 (1.11-2.36), $p=0.001$], compared to participants without respective damage. Insulin resistance was associated with accumulation of multiple micro- and macrovascular organ damage ($p<0.001$) even after adjustment for other factors (beta 0.237), $p=0.013$).

Conclusion: These findings support that an aggravated micro- and macrovascular profile is accompanied by metabolic disorders, even in a population of early-stage hypertensive and normotensive individuals, long before the clinical complications of elevated blood pressure levels are overt.

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The effect of PEX11β knockdown on peroxisome abundance and insulin secretion in MIN6 cells.

Blair HR, Brown AE, Gunn D, Walker M

Diabetes Research Group, Institute of Cellular Medicine, Medical School, Newcastle University. Framlington Place, Newcastle Upon Tyne

Background and Aims: Lipotoxicity results from the accumulation of fats within non-adipose tissue, and is one of the causes of β-cell dysfunction in type 2 diabetes. In 2009 it was proposed that lipotoxicity in insulin producing cells may be mediated through hydrogen peroxide generated by peroxisomes, organelles which are primarily responsible for the initial oxidation of very long chain fatty acids. *Pex11*β encodes a protein involved in the division and proliferation of peroxisomes. The aim was to explore the impact of altered *Pex11*β expression on peroxisome abundance and insulin secretion in cultured pancreatic β-cells.

Methods: Cultured MIN6 cells were transfected with siRNA's specific for *Pex11*β or a scrambled control, and following a 24hr or 48hr recovery period were incubated in the presence or absence of 250μM palmitate for a further 48hrs. Gene expression was determined using real time PCR. PMP-70 protein expression was used as a marker of peroxisomes, and quantified by western blotting. Cells were challenged with either basal (3mM) or stimulating (25mM) glucose levels before measuring insulin release by ELISA.

Results: Transfection of MIN6 cells resulted in >80% reduction in *Pex11*β expression compared to the scrambled control at 72hrs ($P<0.001$) and 96hrs ($P<0.001$). At 96hrs a 35% reduction in PMP-70 protein levels ($P<0.01$) was also seen. At 25mM glucose, incubation with 250μM palmitate decreased insulin secretion by more than 50% compared with the BSA control (2.54±0.34 and 7.07±1.56 ng insulin/μg protein; $P<0.05$). In the *Pex11*β knockdowns, the reduction in glucose stimulated insulin secretion (GSIS) caused by incubation with 250μM palmitate was no longer significant.

Conclusion: Palmitate incubation decreased insulin secretion at 25mM glucose in control cells. *Pex11*β knockdown resulted in a decrease in PMP-70 protein, a marker of peroxisome abundance. Unexpectedly, *Pex11*β knockdown led to the partial recovery of the inhibitory effect of palmitate on insulin secretion.

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Study of the association between renal function and insulin resistance in a healthy population – the RISC study

Simeon S, Massy ZA, Stengel B, Balkau B and The RISC Study Group.

INSERM U1018, CESP: EpReC, Renal and cardiovascular Epidemiology, UVSQ-UPS, Villejuif, France

Background and Aims: Studies have shown that insulin resistance is greater in people with chronic renal disease. We hypothesized that in healthy people without chronic renal disease, the level of the glomerular filtration rate would be associated positively with insulin sensitivity.

Methods: Between 2003 and 2006, the RISC study included volunteers in 19 clinical centres, in 14 European countries. Non-inclusion criteria included acute and chronic kidney disease, diabetes, hypertension, dyslipidaemia, cardiovascular disease, a treatment for any of the above or for obesity and pregnancy. Insulin sensitivity was measured by the reference method, the hyperinsulinemic euglycemic clamp; insulin sensitivity was also estimated by the HOMA index, the index of insulinosensitivity (ISI) of Matsuda and the OGIS index, using data from the oral glucose tolerance test. Renal function was estimated by the glomerular filtration rate (eGFR) using the CKD-EPI equation; eGFR was studied in three classes: ≥ 105 ml/min, 90-104.9 ml/min and 60-89.9 ml/min. Socio-demographic, anthropometric, clinic and biologic factors were collected. The association between insulin resistance and renal function was studied cross-sectionally using linear regression models, stratified on sex.

Results: 514 women and 391 men were eligible to be included in our study as they had an evaluation of both the eGFR rate and a hyperinsulinemic euglycemic clamp. In women, insulin sensitivity was associated with renal function: those with an eGRF ≥ 105 ml/min had a lower insulin sensitivity than the two other eGFR groups; these two groups did not differ. For men, there was no statistically significant association. Further, there was no association between the HOMA or the ISI indices with eGFR, for either sex.

Conclusion: A lower insulin sensitivity in women with a trend towards glomerular hyperfiltration (eGFR ≥ 105 ml/min) was observed. However a minimal decrease in renal function (eGFR between 60 and 90 ml/min), in the absence of chronic renal disease, was not associated with a lower insulin sensitivity. The next part of our work will study the prospective relation between change in insulin sensitivity and renal function.

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Adverse impact of visceral fat on lipid and metabolic profile in fatty liver disease

Saponaro C[1], Gaggini M[1], Rosso C[2], Buzzigoli E[1], Carli F[1], Ciociaro D[1], Mezzabotta L[2], Vanni E[2], Saba F[2], Abate ML[2], Smedile A[2], Rizzetto M[2], Bugianesi E[2], Gastaldelli A[1].

[1]Cardiometabolic Risk Unit, Institute of Clinical Physiology, CNR, Pisa, Italy;
[2]Division of Gastroenterology and Hepatology and Lab. of Diabetology, Dept. of Medical Sciences, University of Turin, Turin, Italy.

Background and Aims: Abdominal/visceral (VF) adiposity is a major risk factor for metabolic syndrome and type 2 diabetes and could be implicated in onset and development of fatty liver (FL) disease. However, the relative role in the progression of liver damage and dysfunction is still unknown. Insulin resistance, lipotoxicity and inflammation are the main events that occur in FLD. The aim of this work was to evaluate the impact of visceral fat on histological liver damage, lipid profile and metabolic alterations in patients with proven NAFLD.

Methods: In 34 non diabetic subjects with biopsy proven non alcoholic FLD and 8 controls (CT)we measured visceral, subcutaneous and hepatic fat by MRI, plasma concentrations of triglycerides (TG), total cholesterol, free fatty acids (FFA), and GGT. Gas chromatography mass spectrometry was used to assess FFAs composition. From plasma FFA we calculated the de novo lipogenesis index (DNL= palmitic/linoleic acid) and unsaturated to saturated fat ratio (PUFA/SFA). By use of tracers we evaluated lipolysis and endogenous glucose production (EGP) and calculated adipose tissue insulin resistance (Adipo-IR= Lipolysis x Insulin) and hepatic insulin resistance (Hep-IR= EGP x Insulin). Histology was scored according to Kleiner.

Results: Of the 34 recruited patients 10 were without fibrosis (F0), 24 with fibrosis score 1 to 4 (F1-4). Fibrosis was associated with a worse metabolic profile, with increased both adipo-IR (8.3±4.3 vs 7.4±6.0 vs 3.6±1.4) and HOMA index (3.2±1.9 vs 2.6±1.2 vs 1.3±0.4) in F1-4 vs F0 vs CT (all $p<0.05$ for F1-4 vs CT). In addition patients with F1-4, compared to F0 and CT, had higher VF (2.9±1.1 vs 2.1±0.6 vs 0.7±0.4 kg, $p<0.03$). VF and hepatic fat correlated with Adipo-IR ($r=0.42$, $r=0.64$) and HOMA index ($r=0.42$, $r=0.52$) and with increased plasma levels of TG ($r=0.53$, $r=0.52$) and DNL ($r=0.46$, $r=0.52$) all $p<0.05$. Also alterations in FFA composition, in particular reduced PUFA/SFA ratio, were associated with higher VF ($r=-0.41$) and hepatic fat ($r=-0.57$ $p<0.005$).
Moreover, VF and hepatic fat correlated positively with MCP-1 ($r=0.52$, $r=0.55$) and oxLDL ($r=0.37$, $r=0.25$) and negatively with adiponectin ($r=-0.49$, $r=-0.53$), all $p<0.05$, documenting a pro-inflammatory profile.

Conclusions: In patients with NAFLD, hepatic fat is associated with metabolic derangements and IR, but Adipo-IR and visceral fat accumulation appear to provide a major contribution to liver damage. and is associated with an adverse lipid and inflammatory profile.

Abstract session 3 - Friday 24 April; 15:30-16:15

Chair: Martine Laville

More pronounced alteration of longitudinal displacement of the carotid artery wall in diabetic women than in diabetic men	Segrestin et al
Risk factors for oedema following initiation of thiazolidinedione therapy: a pharmacoepidemiological study	Vella et al
Hypertension in type 2 diabetes: influence of peripheral insulin resistance associate with adiposity	Lukic et al

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More pronounced alteration of longitudinal displacement of the carotid artery wall in diabetic women than in diabetic men

Segrestin B[1], Serusclat A[1], Zahnd G[2], Moulin G[1];

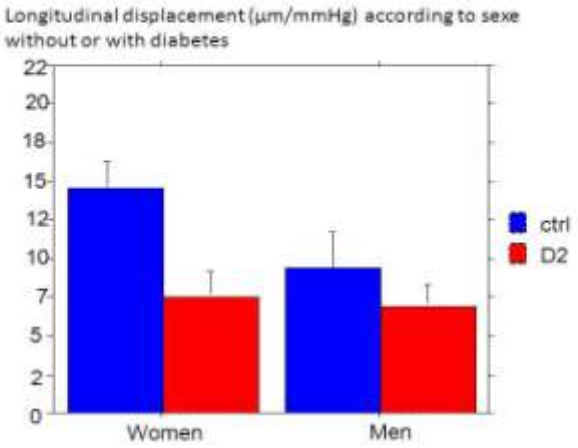
[1] Hopital Louis Pradel, Lyon, France, [2] Erasmus University, Rotterdam, Netherlands.

Background and Aims: Large artery stiffness is an important independent predictor of cardiovascular risk in type 2 diabetes. It accounts for changes in Systolic Blood Pressure, Pulse Pressure and Diastolic Blood Pressure. Parameters that approach artery tiffness such as Carotid-femoral Pulse Wave Velocity, Intima Media Thickness and Ankle to Arm Index are independently associated with the incidence of cardiovascular disease. Additionally, arterial stiffness can also be assessed by means of quantifying the motion of the wall during the cardiac cycle. Speckle tracking can measure the longitudinal movement of the common carotid artery which might be a relevant additional surrogate for the evaluation of cardiovascular risk in type 2 diabetes.

Materials and methods: 26 type 2 diabetic patients and 26 controls matched for age and sex, free of carotid atheromatous plaque were involved in this study. Systolic blood pressure was higher in type 2 diabetic patients 138mmHg(±16) vs 125mmHg(±12), p=0,003. LDL cholesterol was lower in type 2 diabetic patients 2,14mmol/l±1,2 vs 3,65mmol/L±0,8, p ≤0,0001, as 15 of them were taking statins. A speckle tracking estimation of the 2-D trajectory of the vessel wall was performed and applied to B- mode ultrasound sequences of the left common carotid artery.

Results: 13 men, 13 women were included in each group. The type 2 diabetic patients were 55,2(±9,3) years old, the controls 52,3 (±4) p=0,29. The BMI was 30,7kg/m2(±4,0) and 25,4kg/m2 (±5,1),for the diabetics and the controls respectively(p=0,0001). Type 2 diabetic patients had diabetes for 16 years(±11,8). Eighteen type 2 diabetic patients were taking antihypertensive drugs. The longitudinal displacement indexed on the pulse pressure was significantly lower in diabetics than in the volunteer group, namely 7µm/mmHg(±3) versus 12µm/mmHg(±6) p=0,0005 . This variation was accounted by the difference of longitudinal displacement according to sex: 6 µm/mmHg(±3) in diabetic women and 15 µm/mmHg(±6) (p=0,043)in female volunteers. Whereas for men, it was of 7µm/mmHg(±3) in diabetic men and 9µm/mmHg(±6) in male volunteers. Intima media thickness was significantly greater in diabetics (0,79mm(±0,18)) than in the controls (0,67mm(±0,14)), p=0,01. Pulse wave velocity was significantly faster for diabetics, that is 15,4cm/s(±8,3) versus 8,2cm/s(±1,7),p=0.004. The longitudinal displacement was independent of HbA1c, Pulse Wave Velocity, Intima Media Thickness.

Conclusion: Longitudinal displacement in diabetic women is much more altered than in men. This study using speckle tracking as a new tool to explore the arterial wall gives new insights about the more pronounced increase of cardiovascular risk of diabetic women.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Women
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D2

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Risk factors for oedema following initiation of thiazolidinedione therapy: a pharmacoepidemiological study

Vella S,[1] Donnelly L,[1] Lang CC,[1] Donnan PT,[1] Pearson ER,[1] Petrie JR[2]

[1]University of Dundee, UK; [2]University of Glasgow, UK

Background and Aims: Use of thiazolidinediones (TZDs) in type 2 diabetes has been hampered by concerns which include the risk of oedema. We therefore investigated risk factors for oedema in the population of Tayside, Scotland using time to index loop diuretic prescription as a pharmacoepidemiological surrogate.

Methods: Using one year follow up data from 2097 Tayside patients with type 2 diabetes commenced on TZD therapy and 2785 patients commenced on metformin-sulphonylurea (MFSU) therapy we entered index TZD prescription (vs MFSU), age, diabetes duration, female gender and baseline clinical variables (macrovascular disease, systolic blood pressure [SBP], body mass index [BMI], haematocrit [%], serum creatinine, serum albumin, alanine aminotransferase [ALT]) in a multivariate Cox regression model. Time-dependent variables were constructed for all covariates by adding an interaction term ($\log_e$ time [days]) to index loop diuretic prescription.

Results: Age, haematocrit, BMI, ALT, SBP and macrovascular disease (in decreasing order of importance), and their respective interactions with time, made significant contributions to the model. Hazard ratios for index loop diuretic prescription decreased over time for baseline macrovascular disease, ALT and low serum albumin but not for age, BMI, SBP and haematocrit which were relatively stable. Importantly, index TZD therapy was not a significant predictor of oedema.

Conclusions: Risk factors for oedema unrelated to choice of glucose-lowering agent are important in type 2 diabetes: our findings suggest patient characteristics that may be associated with increased risk. Time-dependent risk variation for oedema is a novel finding which should be examined in other cohorts.

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Hypertension in type 2 diabetes: influence of peripheral insulin resistance associate with adiposity

Lukic L, Lalic NM, Jotic A, Rajkovic N, Lalic k, Milicic T, Seferovic JP, Macesic M, Stanarcic Gajovic J.

Clinic for Endocrinology, Diabetes and Metabolic Diseases, Clinical Center of Serbia, Belgrade, Serbia

Background and Aims: It has been shown that adiposity amd insulin resistance (IR) are related and each make independent and different contributions to the development of hypertension in type 2 diabetes (T2D). We analyzed the levels of (1) IR, (2) abdominal obesity and (3) body composition in: overweight T2D with hypertension (group A, n=30, 30≤BMI≥25kg/m2), overweight T2D without hypertension (group B, n=15, 30≤BMI≥25kg/m2), nonobese T2D with hypertension (group C, n=15, BMI<25kg/m2), nonobese T2D without hypertension (group D, n=15, BMI<25kg/m2) and nonobese nondiabetics without hypertension (group E, n=15, BMI<25kg/m2).

Materials and methods: Insulin sensitivity were measured with two complementary methods: (a) homeostasis model assessment of IR (HOMA-IR) from fasting plasma glucose and insulin levels (b) a 75 g oral glucose tolerance test using oral glucose insulin sensitivity (OGIS) index. Fasting plasma insulin (PI) levels were measured by RIA method. Waist circumference (WC) was measured at the level of umbilicus (cm). Body composition was determined using (TANITA, TBF 300) scale. Hypertension was defined as systolic BP ≥140 and diastolic BP ≥ 90mmHg measured by sphygmomanometer, or by established use of antihypertensives.

Results: We have found higher PI levels in group A (A:25.03+/-10.8; B:22.23+/-8.24; C:18.54+/-4.67 D:17.89+/-7.17; E:11.12+/-2.69 mIU/ml, A vs B; B vs C; B vs D p = NS; A vs C $p < 0.05$; A vs D $p < 0.01$), together with the lowest OGIS as measurement of peripheral insulin resistance (A:287±71.40; B:336.22±39.29; C:291.29±83.44 D:343.67±68.02; E:496.80±63.35 A vs B $p < 0.05$; A vs C; B vs C; B vs D p = NS; A vs D $p < 0.01$; C vs D $p < 0.05$) and higher HOMA-IR, reflecting hepatic insulin sensitivity (A:8.43+/-4.69; B:6.52+/-3.04; C:5.83±1.42; D:5.57±2.33; E:2.36+/-0.71 A vs B, B vs C, B vs D, C vs D p = NS; A vs C $p < 0.05$; A vs D $p < 0.05$). WC significantly correlate with PI r=0.467, p<0.01 and HOMA-IR r=0.460, p<0.01, while peripheral insulin resistance correlates only with Fat Mass r=-0.330 p<0.05 and Fat% r=-0.243 p<0.05. However, only peripheral IR correlates with the presence of hypertension (OGIS: r=-0.334; p<0.01) among diabetics.

Conclusion: Our results have demonstrated that peripheral insulin resistance associated with adiposity significantly impact the presence of hypertension in overweight T2D patients.