Diabète(s)
et
Dénutrition(s)

Rigalleau 2017

Conflits d'intérêts

- **1996: prix de recherche en nutrition CIDEF* (50000 FF) pour le projet "Rôle des interactions lipides-glucides … »**
- **1999: prix de recherche en nutrition de l'Institut Appert (50000 FF) et subvention du conseil Régional d'Aquitaine (40000 FF) pour le projet "Effet des acides gras … »**
- **2011: Président comité de Titration essai GALAPAGOS (Sanofi-Aventis)**
- Bourses : Servier, Roche, Merck-Lipha
- Partenariats : Bayer, GSK, Novo, Lilly, Pfizer, Takeda, Scherring-Plough, MSD, Novartis

- * CIDEF: Comité Interprofessionnel de la Dinde en France

Plan

- Nutrition: Glucides, lipides
- Diabète
- DT1, DT2, DT3
- D compliqués
- Traitements

végétaux

- (Wikipédia)
  un **végétal** est un organisme appartenant à l'une des diverses lignées qui *végètent* : c'est-à-dire qui respirent, se nourrissent, croissent comme les plantes, selon l'étymologie du terme[1].
- Les végétaux n’ont pas de neurones et donc pas de système nerveux structuré.
- **Réserves énergétiques**
- Les précurseurs des réserves sont au départ toujours des glucides, puisqu'ils sont synthétisés dans les parenchymes chlorophylliens.

- **Glucides = 4kcal/g**

Animaux

- Par opposition à végétal, être vivant organisé, généralement capable de se déplacer et n'ayant ni chlorophylle ni paroi cellulaire cellulosique.

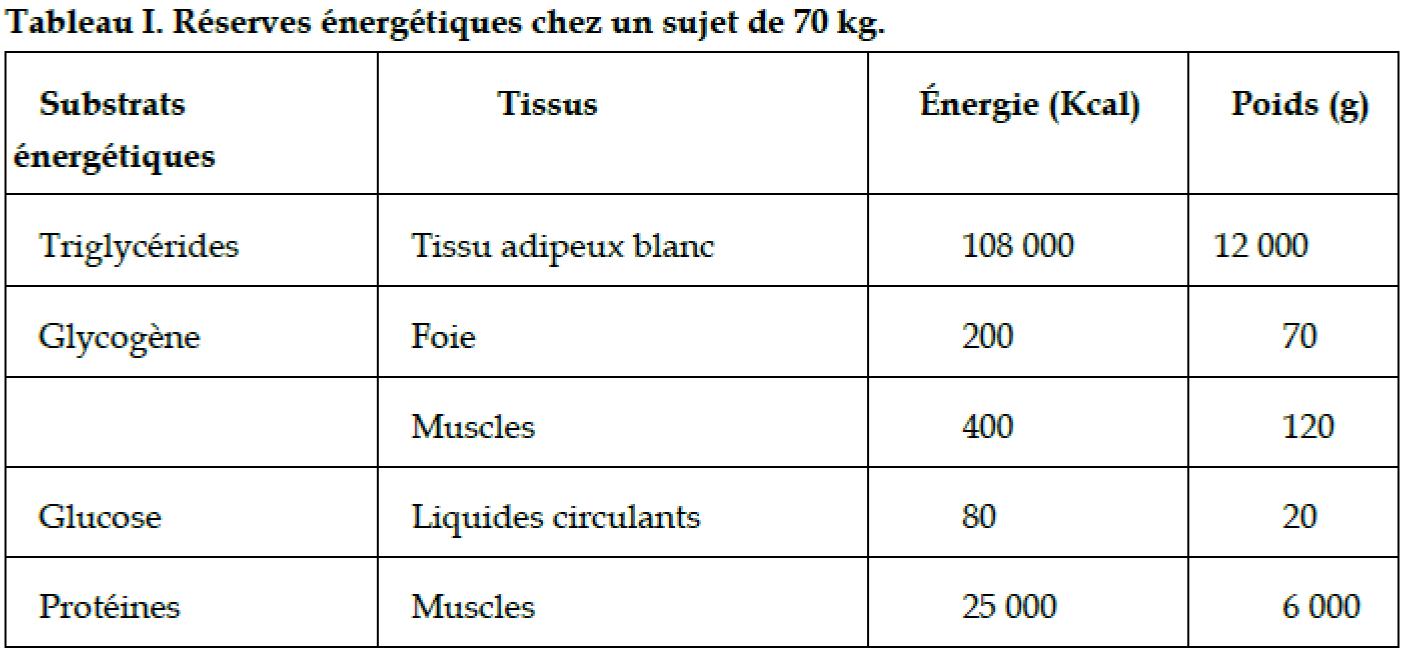
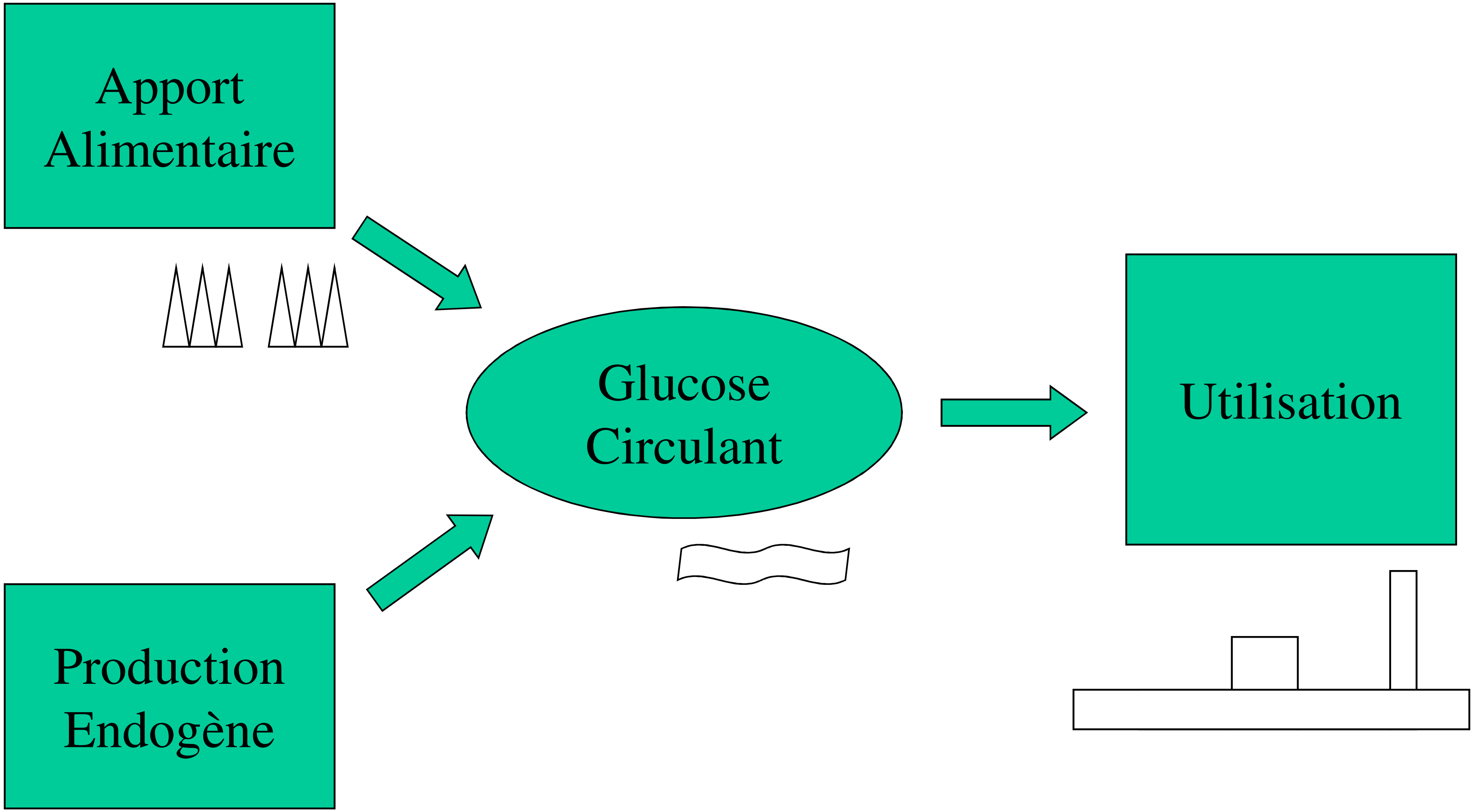


Tableau I. Réserves énergétiques chez un sujet de 70 kg.

Substrats énergétiques	**Tissus**	**Énergie (Kcal)**	**Poids (g)**
Triglycérides	Tissu adipeux blanc	108 000	12 000
Glycogène	Foie	200	70
	Muscles	400	120
Glucose	Liquides circulants	80	20
Protéines	Muscles	25 000	6 000

Lipides = 9 kcal/g



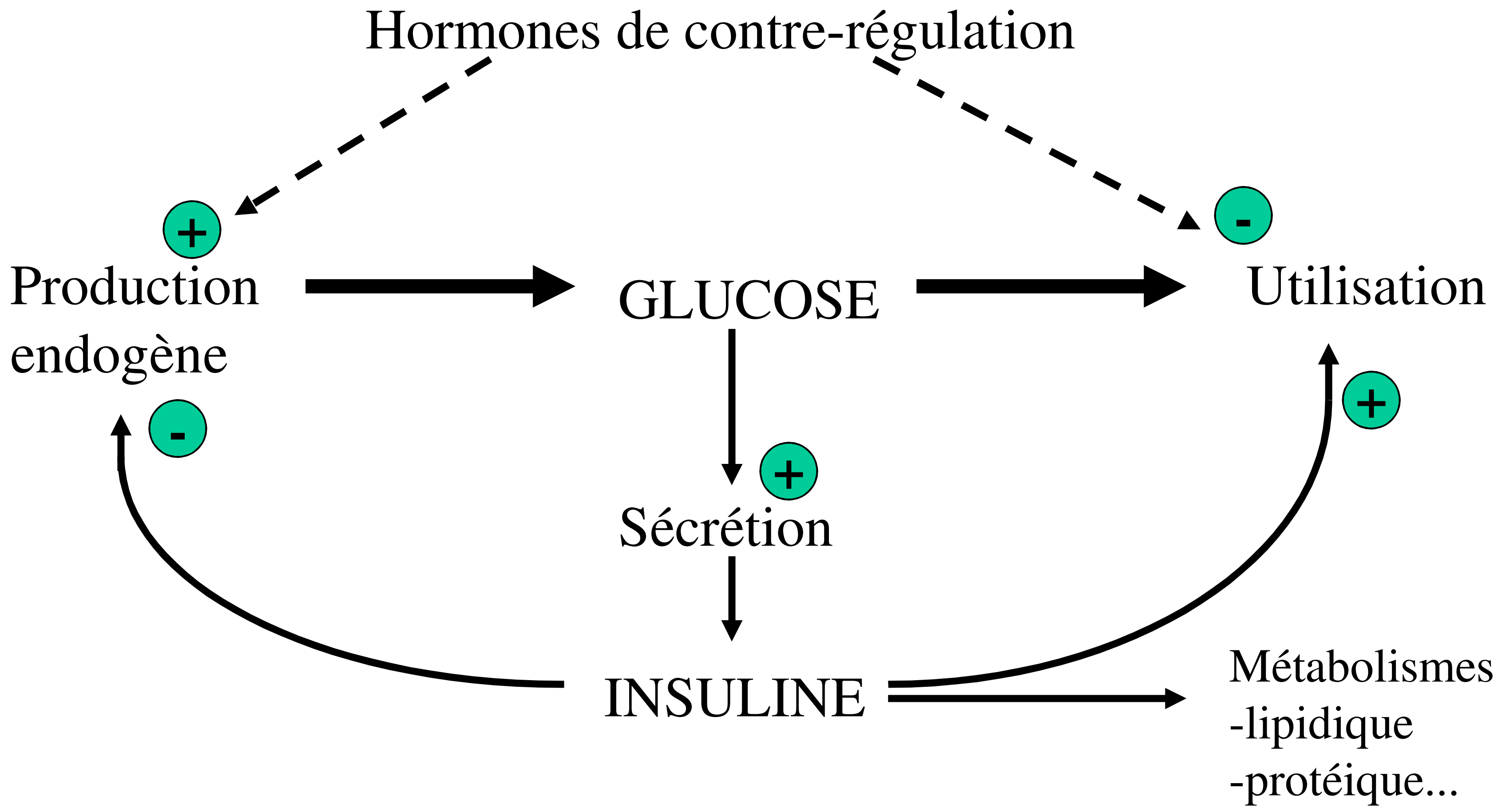
Apport Alimentaire

Production Endogène

Glucose Circulant

Utilisation

Base physiopathologique : régulation glycémique



Hormones de contre-régulation

+

-

Production endogène

GLUCOSE

Utilisation

-

+

+

Sécrétion

INSULINE

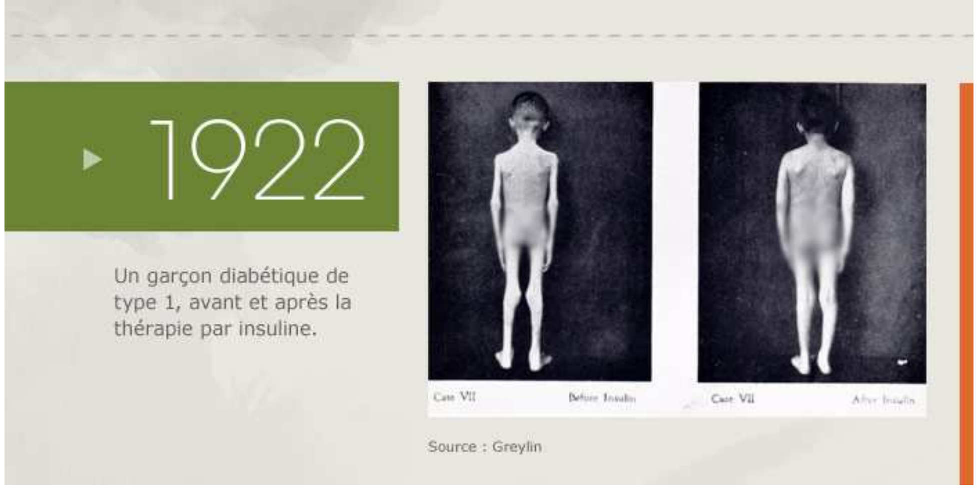
Métabolismes
-lipidique
-protéique...

Diabète : définitions

- OMS: « Hyperglycémie chronique avec complications. »

- DT2 (ADA -2017)
  - 90-95% des diabètes
  - « relative insulin deficiency, and peripheral insulin resistance »

Diabète de type 1


1922
Case VII
Before Insulin
Case VII
After Insulin

Un garçon diabétique de type 1, avant et après la thérapie par insuline.

Source : Greylin

Diabète de type 2

Metabolic Factors Contributing to Increased Resting Metabolic Rate and Decreased Insulin-Induced Thermogenesis During the Development of Type 2 Diabetes

Christian Weyer, Clifton Bogardus, and Richard E. Pratley

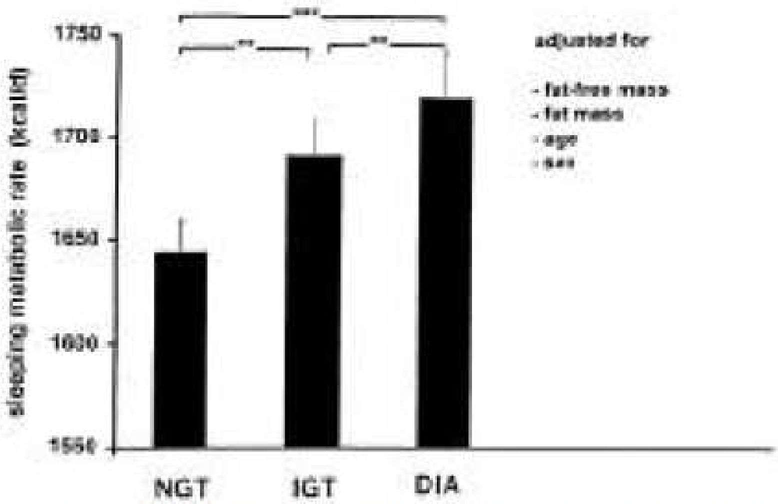


FIG. 1. SMR in 560 Pima Indian subjects with NGT, IGT, or diabetes (DIA). SMR is adjusted for age, sex, FFM, and FM (least-square mean ± SE). Asterisks indicate significant differences among the three groups (**$P < 0.01$, ***$P < 0.001$).

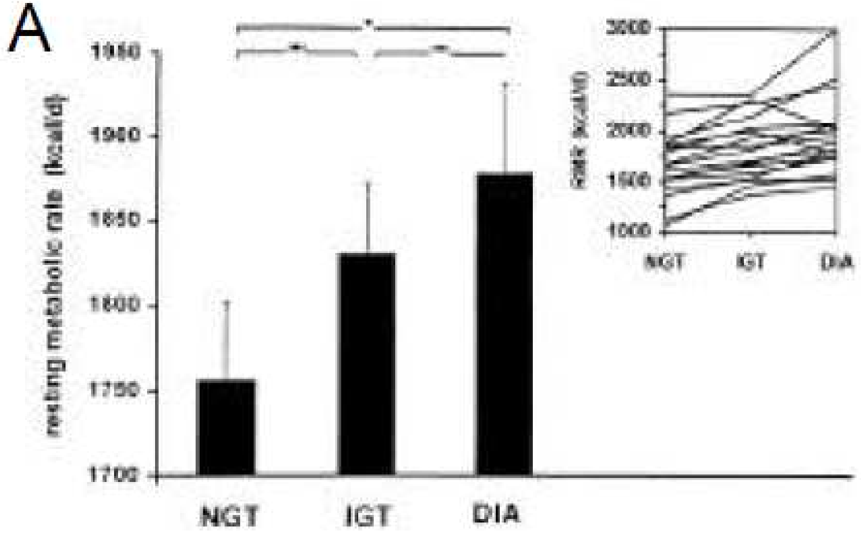


FIG. 2. Longitudinal changes in RMR (*A*) ($n = 17$) and IIT (*B*) ($n = 15$) in Pima Indians, in whom glucose tolerance deteriorated from NGT to IGT to diabetes (DIA) over 5.1 ± 1.4 years (25). RMR and IIT are

that increases in RMR and decreases in IIT occur early in the development of type 2 diabetes, and that both changes are related to the progressive metabolic abnormalities that occur during the development of the disease. *Diabetes* 48:1607–1614, 1999

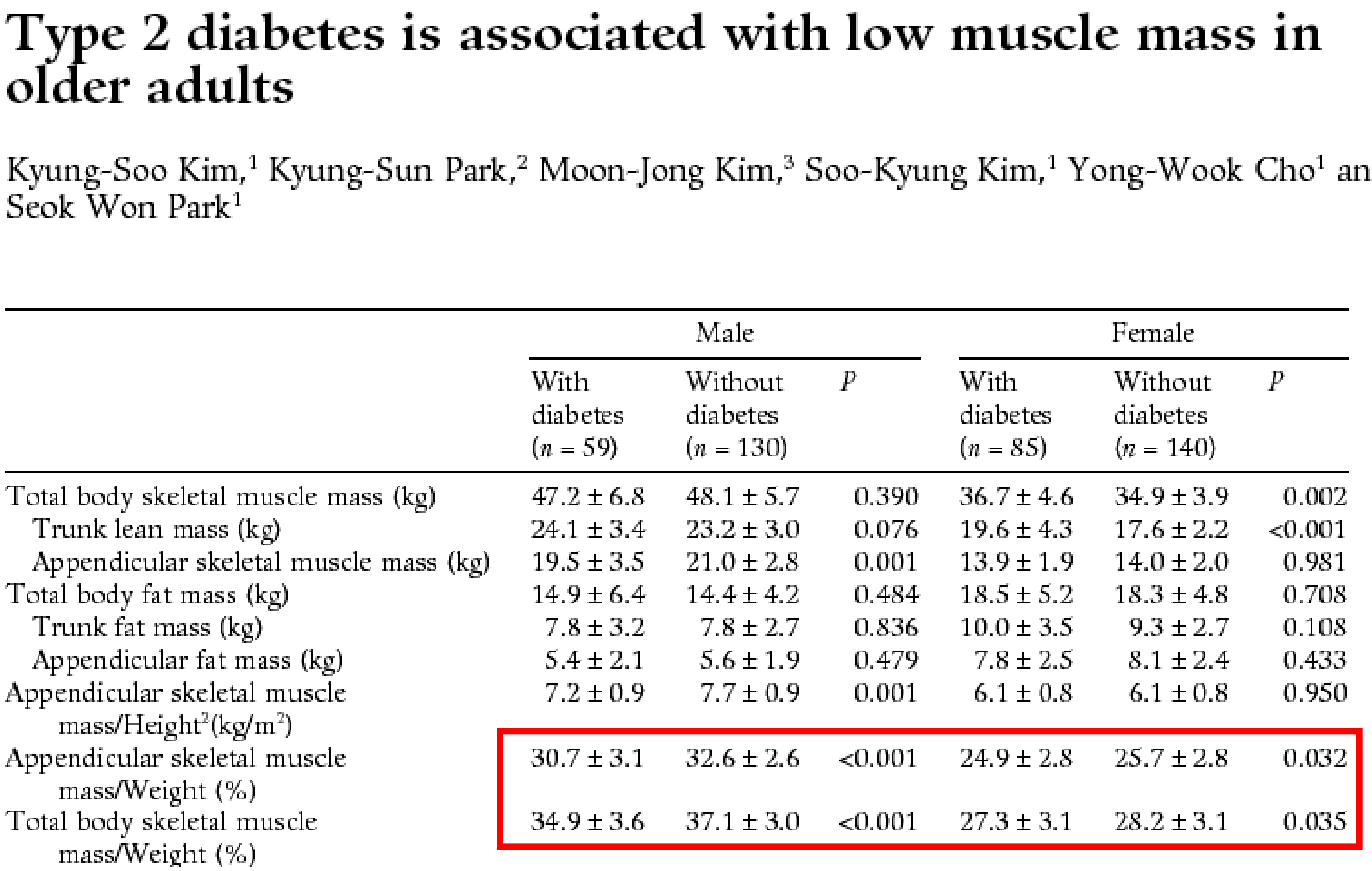
DT2 et sarcopénie

Né en 1955
Retraite 1988
« physiquement usé »

Né en 1960
Retraite 1997
« aurait dû arréter plus tôt »

Sarcopénie

- **« Perte musculaire au profit du tissu adipeux, avec l'âge »**



Type 2 diabetes is associated with low muscle mass in older adults

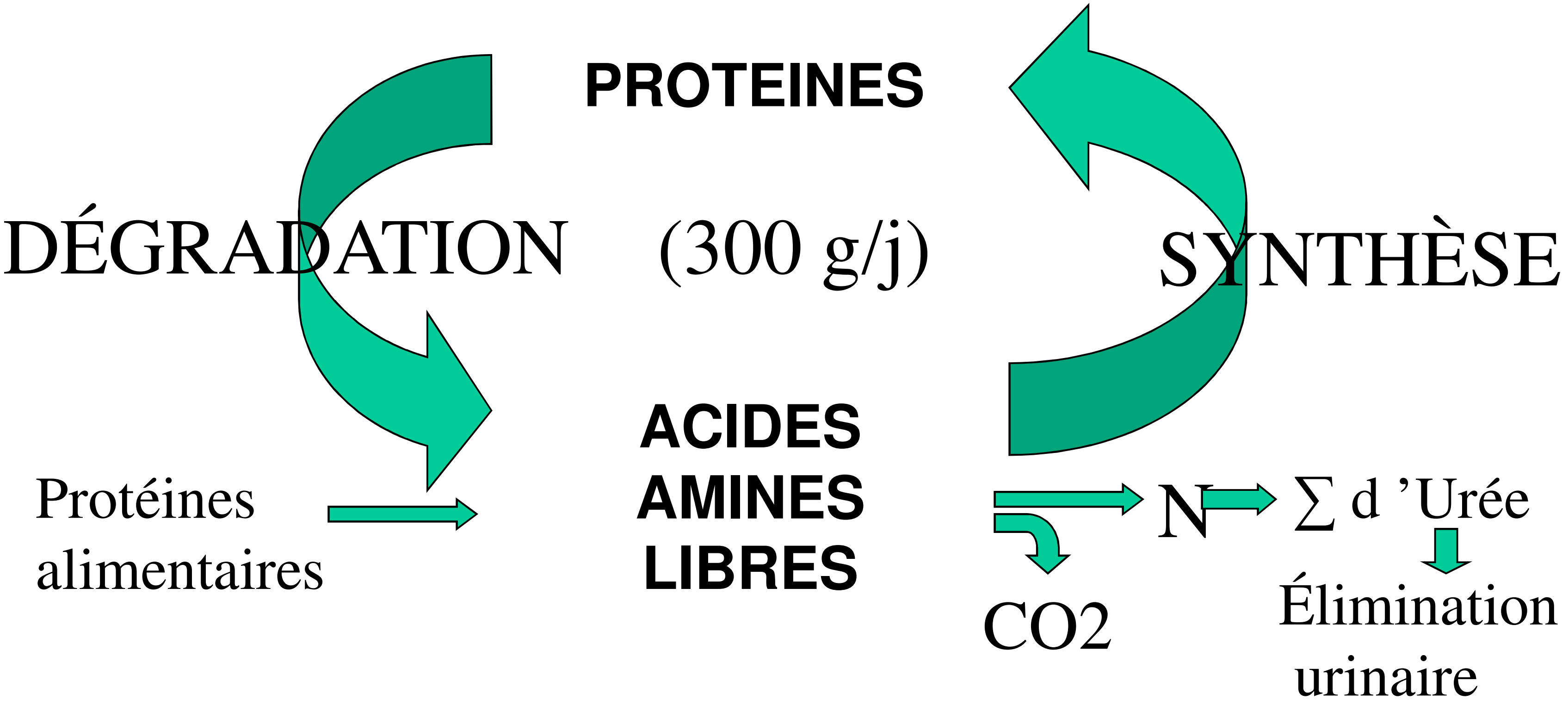
Kyung-Soo Kim,[1] Kyung-Sun Park,[2] Moon-Jong Kim,[3] Soo-Kyung Kim,[1] Yong-Wook Cho[1] and Seok Won Park[1]

	Male			Female		
	With diabetes (*n* = 59)	Without diabetes (*n* = 130)	*P*	With diabetes (*n* = 85)	Without diabetes (*n* = 140)	*P*
Total body skeletal muscle mass (kg)	47.2 ± 6.8	48.1 ± 5.7	0.390	36.7 ± 4.6	34.9 ± 3.9	0.002
Trunk lean mass (kg)	24.1 ± 3.4	23.2 ± 3.0	0.076	19.6 ± 4.3	17.6 ± 2.2	<0.001
Appendicular skeletal muscle mass (kg)	19.5 ± 3.5	21.0 ± 2.8	0.001	13.9 ± 1.9	14.0 ± 2.0	0.981
Total body fat mass (kg)	14.9 ± 6.4	14.4 ± 4.2	0.484	18.5 ± 5.2	18.3 ± 4.8	0.708
Trunk fat mass (kg)	7.8 ± 3.2	7.8 ± 2.7	0.836	10.0 ± 3.5	9.3 ± 2.7	0.108
Appendicular fat mass (kg)	5.4 ± 2.1	5.6 ± 1.9	0.479	7.8 ± 2.5	8.1 ± 2.4	0.433
Appendicular skeletal muscle mass/Height^2(kg/m^2)	7.2 ± 0.9	7.7 ± 0.9	0.001	6.1 ± 0.8	6.1 ± 0.8	0.950
Appendicular skeletal muscle mass/Weight (%)	30.7 ± 3.1	32.6 ± 2.6	<0.001	24.9 ± 2.8	25.7 ± 2.8	0.032
Total body skeletal muscle mass/Weight (%)	34.9 ± 3.6	37.1 ± 3.0	<0.001	27.3 ± 3.1	28.2 ± 3.1	0.035

Geriatr Gerontol Int 2014

- *Kim et al., Korean Sarcopenic Obesity Study, DiabetesCare 2010:*
- Sarcopénie:
- **15,7%** chez 414 DT2,
- vs **6,9%** chez 396 contrôles

Métabolisme protéique



PROTEINES

DÉGRADATION (300 g/j) SYNTHÈSE

Protéines
alimentaires

ACIDES
AMINES
LIBRES

N ∑ d 'Urée

Élimination
urinaire

CO2

Perfusion AA*
(*CLeucine)
→
mesures d'enrichissement
(plasma, CO2 expiré)
→
Calcul du TurnOver
-protéolyse
-synthèse protéique

Insulin Resistance of Protein Metabolism in Type 2 Diabetes

Sandra Pereira, Errol B. Marliss, José A. Morais, Stéphanie Chevalier, and Réjeanne Gougeon

Hommes

Femmes

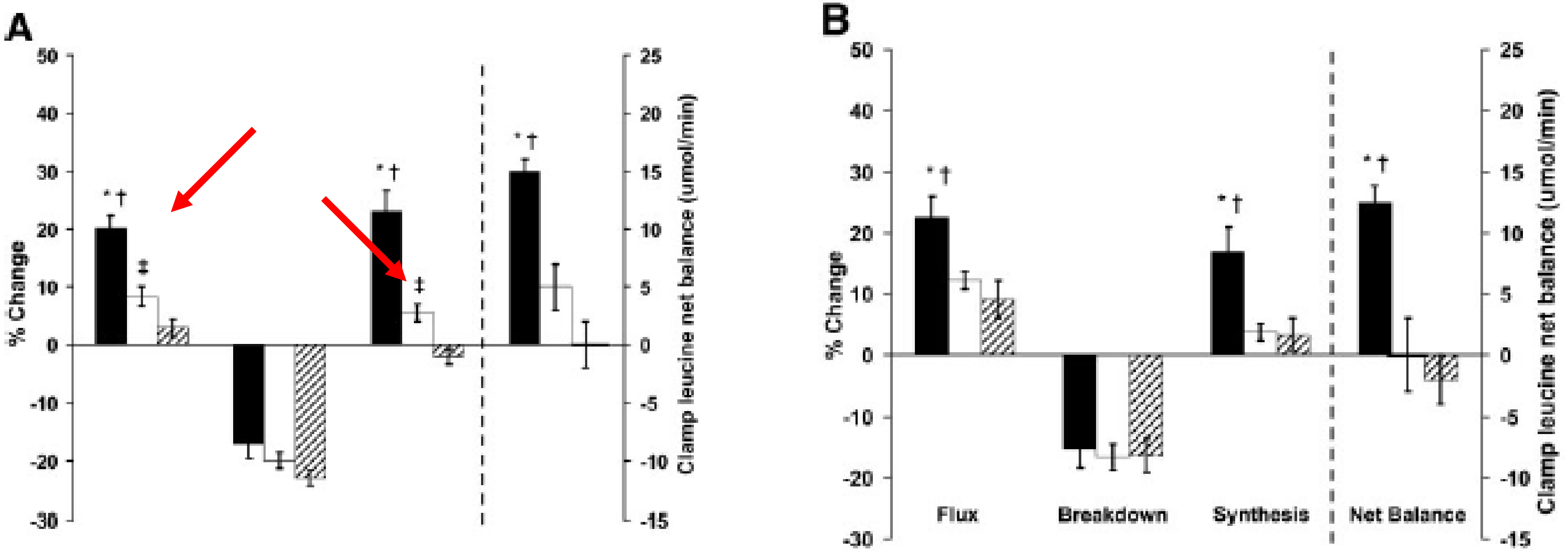
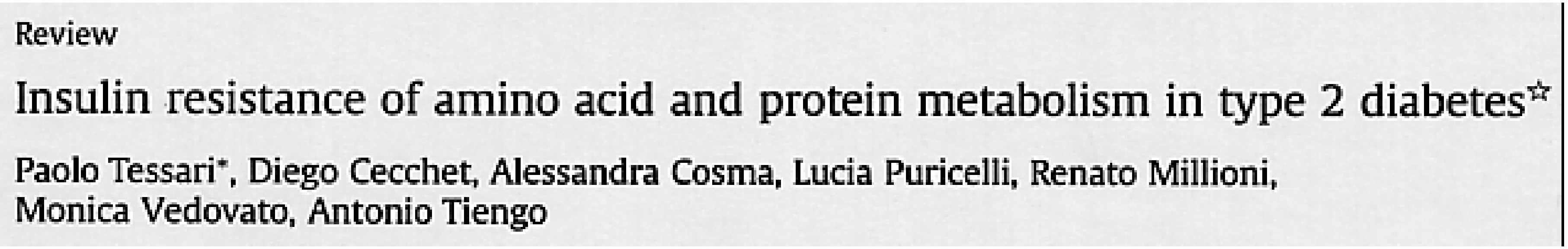


FIG. 2. Percent change in protein flux, breakdown, and synthesis from baseline to clamp and clamp net leucine balance: ■, lean subjects; □, control subjects; ▨, type 2 diabetic subjects. *$P < 0.05$ type 2 diabetic vs. lean subjects, †$P < 0.05$ control vs. lean subjects, ‡$P < 0.05$ type 2 diabetic vs. control subjects. Unpaired *t* tests were used for these comparisons.



Review

Insulin resistance of amino acid and protein metabolism in type 2 diabetes☆

Paolo Tessari*, Diego Cecchet, Alessandra Cosma, Lucia Puricelli, Renato Millioni,
Monica Vedovato, Antonio Tiengo

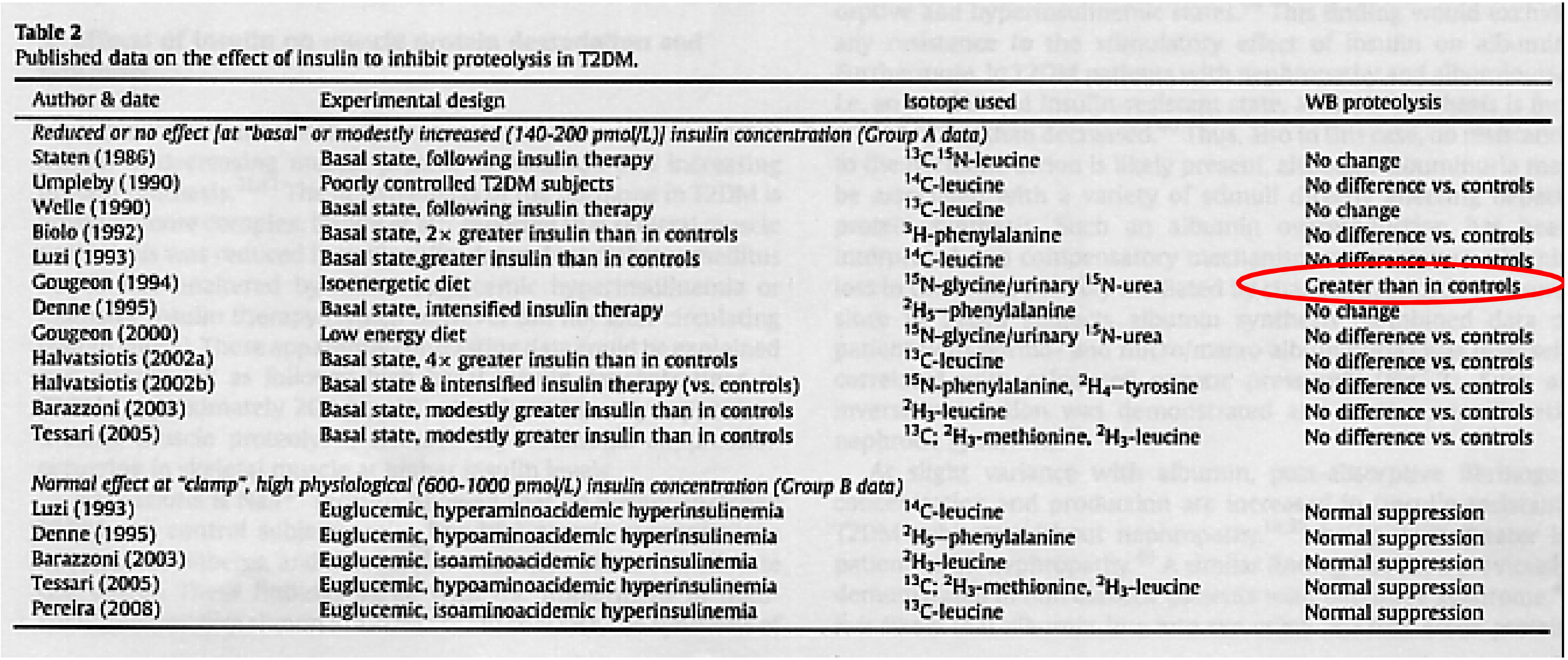
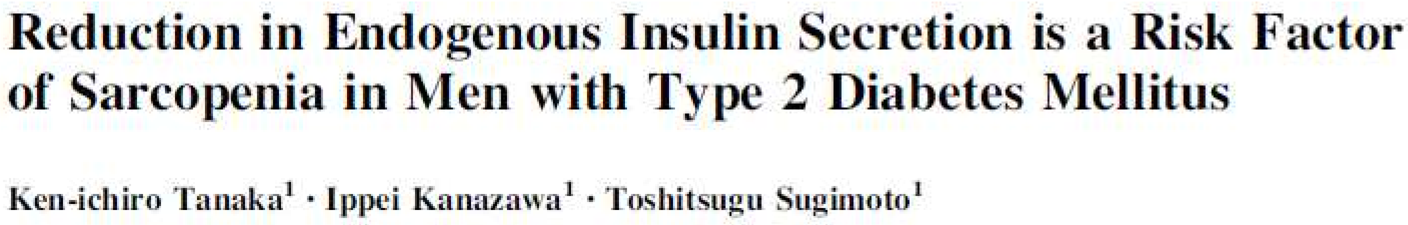


Table 2
Published data on the effect of insulin to inhibit proteolysis in T2DM.

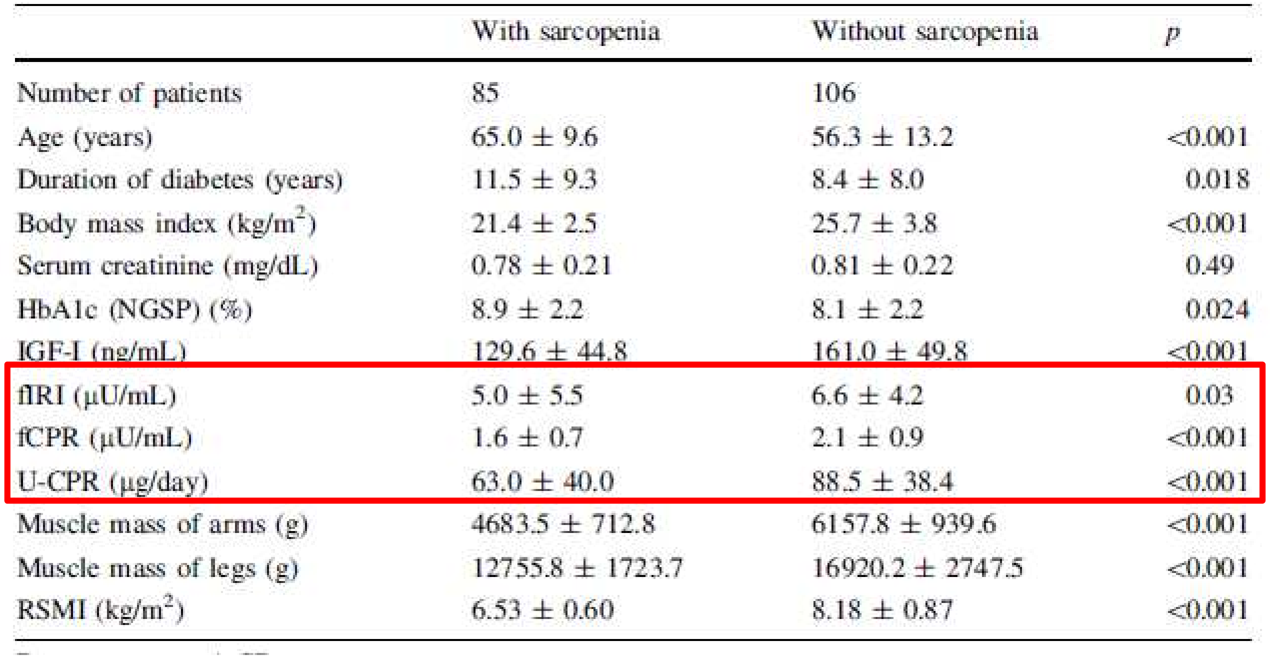
Author & date	Experimental design	Isotope used	WB proteolysis
Reduced or no effect [at "basal" or modestly increased (140-200 pmol/L)] insulin concentration (Group A data)			
Staten (1986)	Basal state, following insulin therapy	^{13}C,^{15}N-leucine	No change
Umpleby (1990)	Poorly controlled T2DM subjects	^{14}C-leucine	No difference vs. controls
Welle (1990)	Basal state, following insulin therapy	^{13}C-leucine	No change
Biolo (1992)	Basal state, 2× greater insulin than in controls	^{3}H-phenylalanine	No difference vs. controls
Luzi (1993)	Basal state,greater insulin than in controls	^{14}C-leucine	No difference vs. controls
Gougeon (1994)	Isoenergetic diet	^{15}N-glycine/urinary ^{15}N-urea	Greater than in controls
Denne (1995)	Basal state, intensified insulin therapy	$^{2}H_5$–phenylalanine	No change
Gougeon (2000)	Low energy diet	^{15}N-glycine/urinary ^{15}N-urea	No difference vs. controls
Halvatsiotis (2002a)	Basal state, 4× greater insulin than in controls	^{13}C-leucine	No difference vs. controls
Halvatsiotis (2002b)	Basal state & intensified insulin therapy (vs. controls)	^{15}N-phenylalanine, $^{2}H_4$–tyrosine	No difference vs. controls
Barazzoni (2003)	Basal state, modestly greater insulin than in controls	$^{2}H_3$-leucine	No difference vs. controls
Tessari (2005)	Basal state, modestly greater insulin than in controls	^{13}C; $^{2}H_3$-methionine, $^{2}H_3$-leucine	No difference vs. controls
Normal effect at "clamp", high physiological (600-1000 pmol/L) insulin concentration (Group B data)			
Luzi (1993)	Euglucemic, hyperaminoacidemic hyperinsulinemia	^{14}C-leucine	Normal suppression
Denne (1995)	Euglucemic, hypoaminoacidemic hyperinsulinemia	$^{2}H_5$–phenylalanine	Normal suppression
Barazzoni (2003)	Euglucemic, isoaminoacidemic hyperinsulinemia	$^{2}H_3$-leucine	Normal suppression
Tessari (2005)	Euglucemic, hypoaminoacidemic hyperinsulinemia	^{13}C; $^{2}H_3$-methionine, $^{2}H_3$-leucine	Normal suppression
Pereira (2008)	Euglucemic, isoaminoacidemic hyperinsulinemia	^{13}C-leucine	Normal suppression

Clinical Nutrition 2010



Reduction in Endogenous Insulin Secretion is a Risk Factor of Sarcopenia in Men with Type 2 Diabetes Mellitus

Ken-ichiro Tanaka[1] · Ippei Kanazawa[1] · Toshitsugu Sugimoto[1]



	With sarcopenia	Without sarcopenia	p
Number of patients	85	106	
Age (years)	65.0 ± 9.6	56.3 ± 13.2	<0.001
Duration of diabetes (years)	11.5 ± 9.3	8.4 ± 8.0	0.018
Body mass index (kg/m^2)	21.4 ± 2.5	25.7 ± 3.8	<0.001
Serum creatinine (mg/dL)	0.78 ± 0.21	0.81 ± 0.22	0.49
HbA1c (NGSP) (%)	8.9 ± 2.2	8.1 ± 2.2	0.024
IGF-I (ng/mL)	129.6 ± 44.8	161.0 ± 49.8	<0.001
fIRI (µU/mL)	5.0 ± 5.5	6.6 ± 4.2	0.03
fCPR (µU/mL)	1.6 ± 0.7	2.1 ± 0.9	<0.001
U-CPR (µg/day)	63.0 ± 40.0	88.5 ± 38.4	<0.001
Muscle mass of arms (g)	4683.5 ± 712.8	6157.8 ± 939.6	<0.001
Muscle mass of legs (g)	12755.8 ± 1723.7	16920.2 ± 2747.5	<0.001
RSMI (kg/m^2)	6.53 ± 0.60	8.18 ± 0.87	<0.001

Calcif Tissue Int 2015

Diabètes type 3

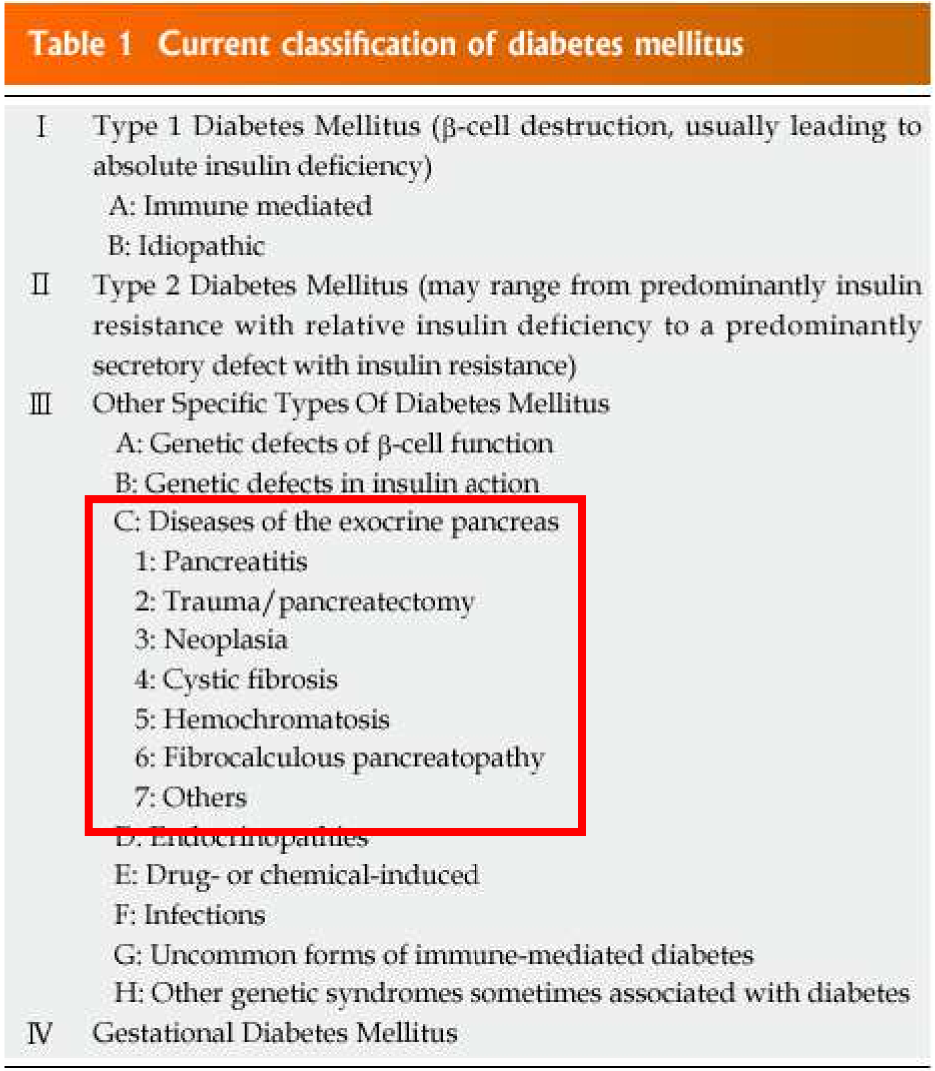


Table 1 Current classification of diabetes mellitus

I	Type 1 Diabetes Mellitus (β-cell destruction, usually leading to absolute insulin deficiency)
	A: Immune mediated
	B: Idiopathic
II	Type 2 Diabetes Mellitus (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)
III	Other Specific Types Of Diabetes Mellitus
	A: Genetic defects of β-cell function
	B: Genetic defects in insulin action
	C: Diseases of the exocrine pancreas
	1: Pancreatitis
	2: Trauma/pancreatectomy
	3: Neoplasia
	4: Cystic fibrosis
	5: Hemochromatosis
	6: Fibrocalculous pancreatopathy
	7: Others
	D: Endocrinopathies
	E: Drug- or chemical-induced
	F: Infections
	G: Uncommon forms of immune-mediated diabetes
	H: Other genetic syndromes sometimes associated with diabetes
IV	Gestational Diabetes Mellitus

-Fréquence: 1% ?
-5-10% dans les CHU allemands
-80% : pancréatites chroniques
Ewald, DMRR 2012

Mécanismes

- Destruction des ilôts --> insulinodéficience
    - Mais aussi déficit en glucagon
- Maldigestion =
    - Malnutrition
    - Hypovitaminose D
    - Baisse de secrétion d ’incrétines
        - *(Ebert, diabetologia 1980)*

Am J Physiol Endocrinol Metab 292: E324–E330, 2007.
First published September 5, 2006; doi:10.1152/ajpendo.00059.2006.

Increased postprandial responses of GLP-1 and GIP in patients with chronic pancreatitis and steatorrhea following pancreatic enzyme substitution

**Filip K. Knop,[1,5] Tina Vilsbøll,[1] Steen Larsen,[2] Patricia V. Højberg,[1]
Aage Vølund,[3] Sten Madsbad,[4] Jens J. Holst,[5] and Thure Krarup[1]**

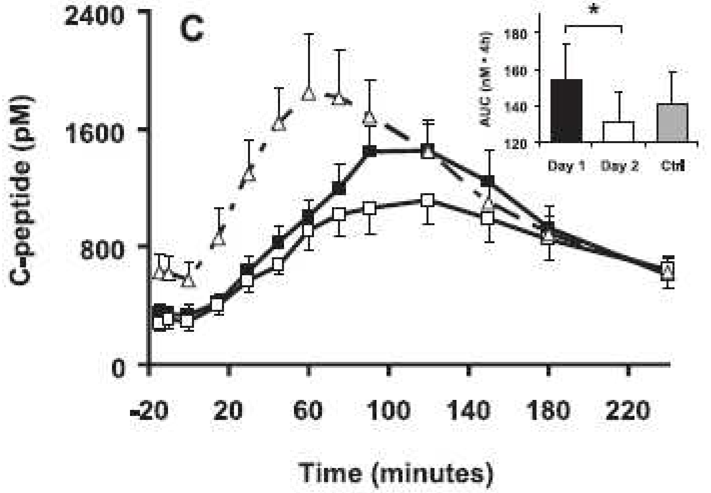
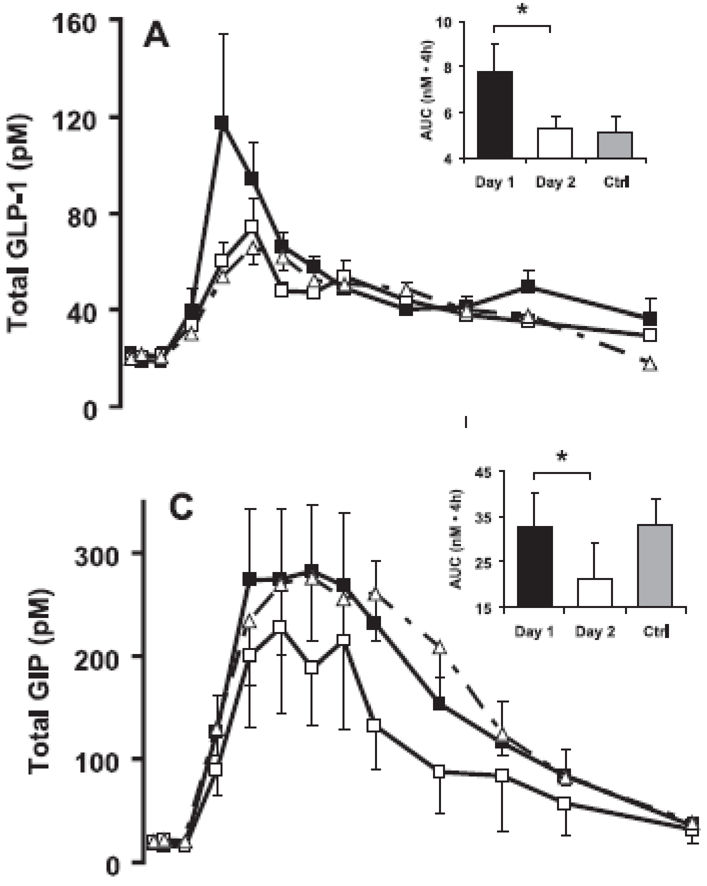
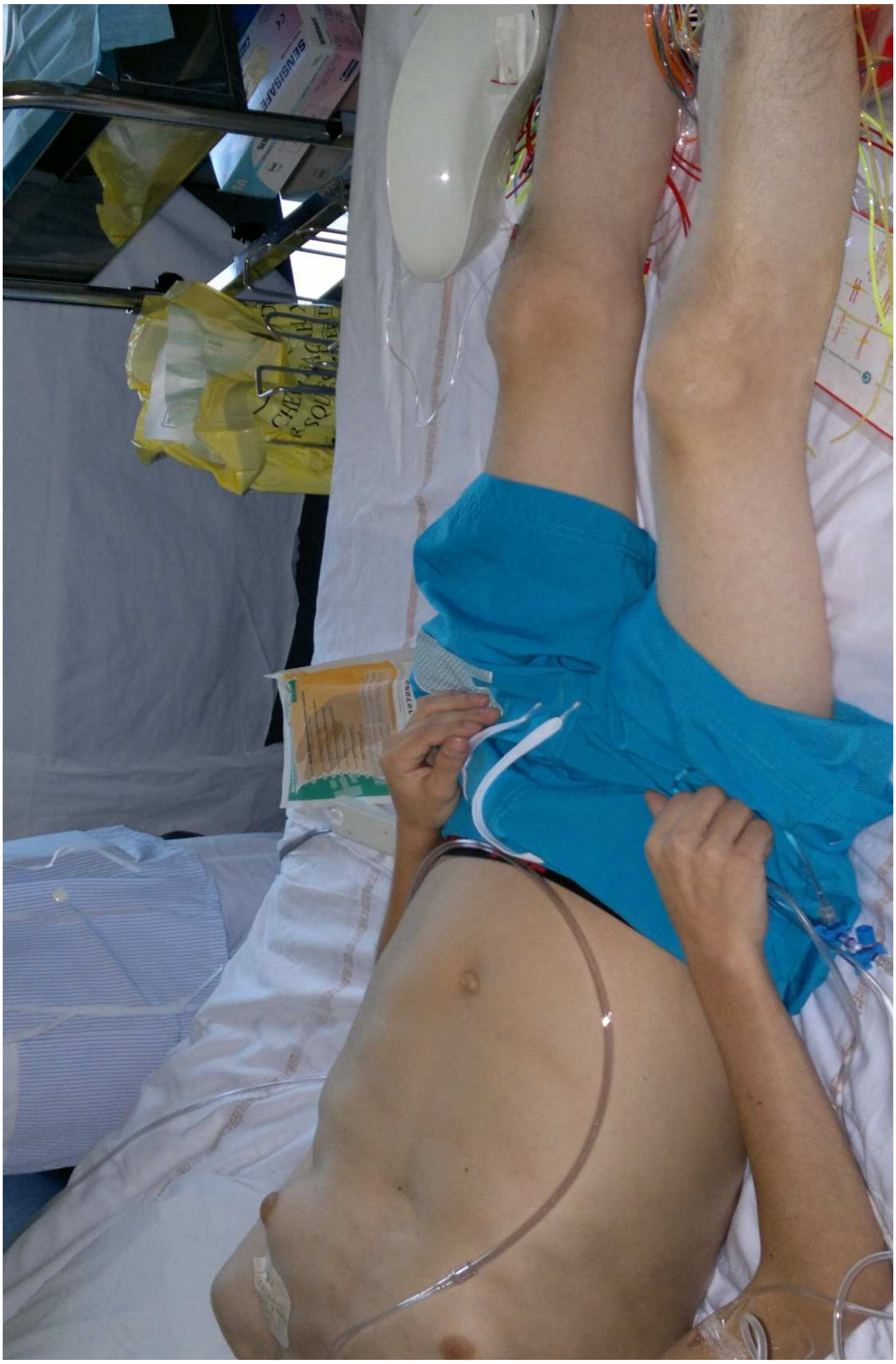


Fig. 1. Plasma glucose (*A*), plasma insulin (*B*), and plasma C-peptide (*C*) concentrations in patients with chronic pancreatitis (CP) and pancreatic exocrine insufficiency (PEI) following ingestion of a liquid meal over 15 min (0–15 min) with pancreatic enzyme substitution (PES; *day 1*, ■) and without PES (*day 2*, □). Punctuated curves (△) represent healthy control subjects (Ctrl)





Cas clinique

- Homme 61 ans
- Diabète depuis 20 ans
  - Familial ++
  - BMI 31
  - Diététique, ADOs
- Eté 1996: perte de poids
- Janvier 1997: sinusite, drainage chirurgical, TTT ADO accru
- Juin 1997: Hospitalisation -20kg, HbA1C 13%
- Pas de plainte, examen clinique normal
- CA 19-9: 179O U/mL

Gonzalez C, Diabète & Obésité 2008

① Diabète secondaire à un cancer du pancréas

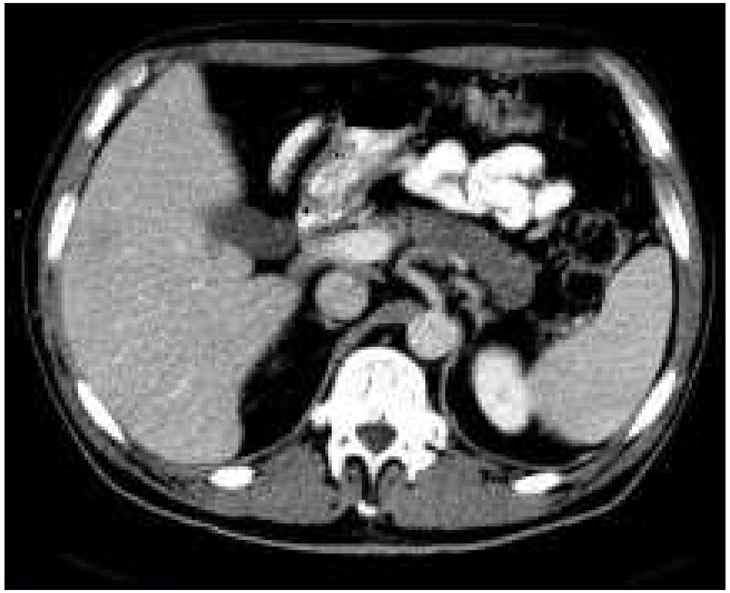


Figure 1 - Scanner pancréatique : aspect moins lobulé et hypodense de la queue du pancréas.

Cancer

Diabète

Dépression réactionnelle

DENUTRITION

ChimioTTT

Chirurgie digestive lourde

Insuffisance pancréatique exocrine

Soutien nutritionnel - Extraits pancréatiques - TCM -Insuline

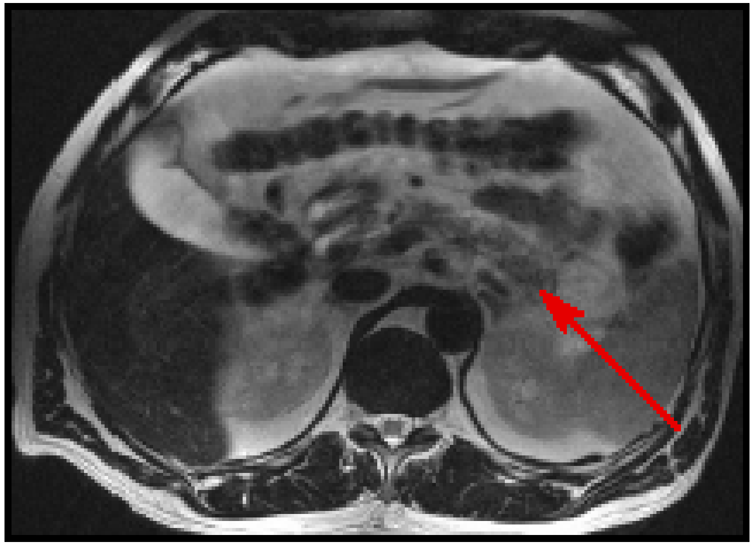


Figure 2 - IRM pancréatique : tumeur infiltrante de la queue du pancréas.

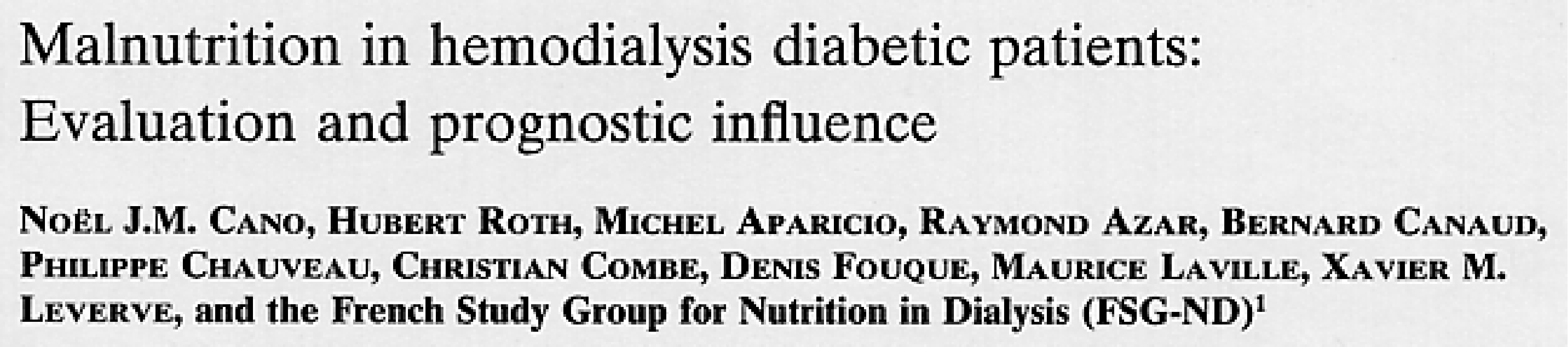
InsulinoTTT: --> +12 kg

6 semaines après l 'admission: laparotomie

Carcinose péritonéale

ChimioTTT pendant un an, puis décès

Diabète compliqué



Malnutrition in hemodialysis diabetic patients: Evaluation and prognostic influence

Noël J.M. Cano, Hubert Roth, Michel Aparicio, Raymond Azar, Bernard Canaud, Philippe Chauveau, Christian Combe, Denis Fouque, Maurice Laville, Xavier M. Leverve, and the French Study Group for Nutrition in Dialysis (FSG-ND)[1]

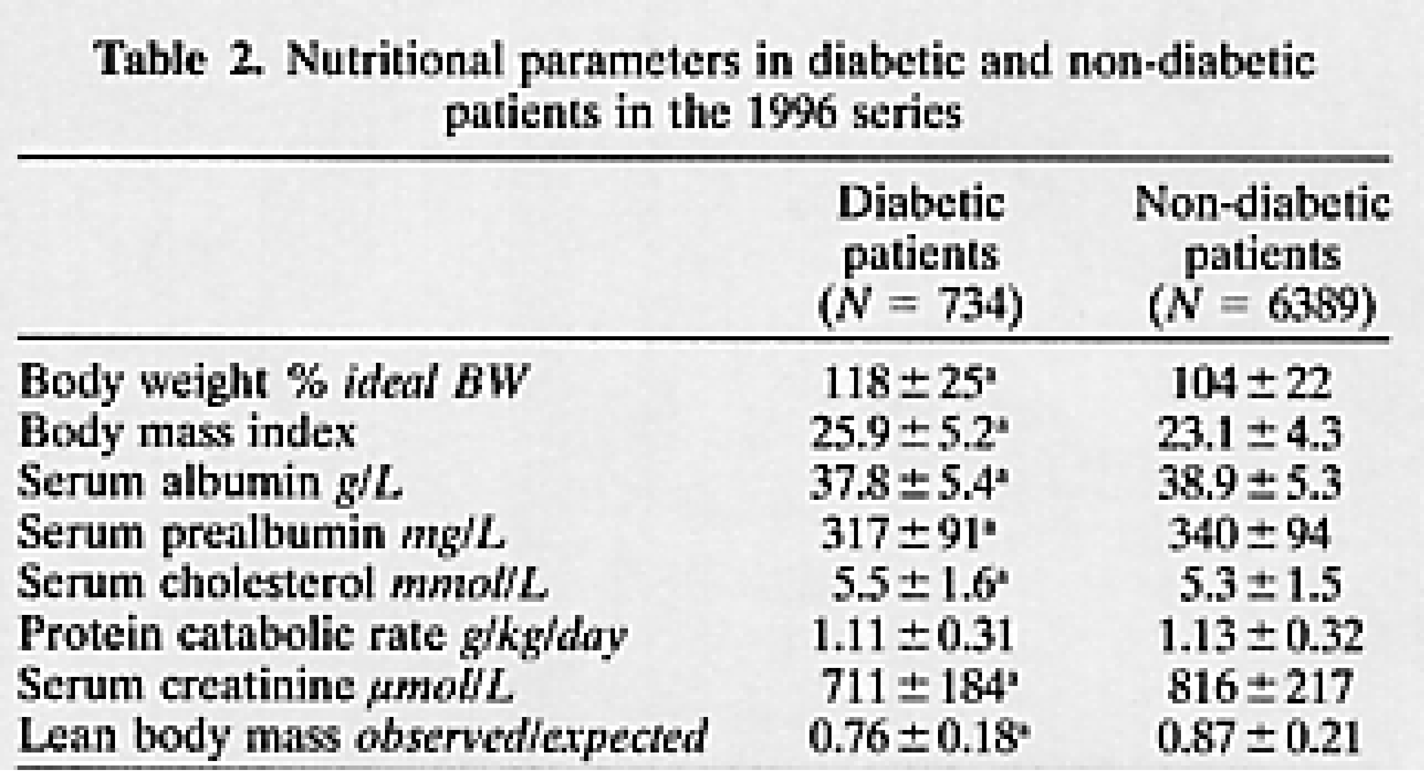
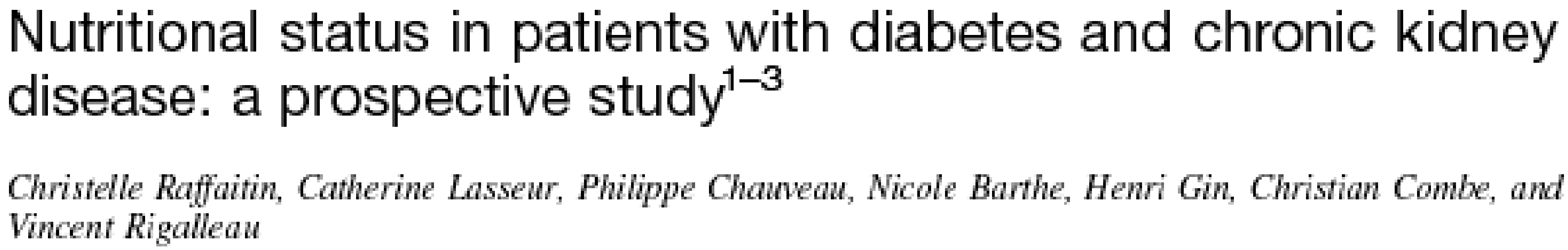


Table 2. Nutritional parameters in diabetic and non-diabetic patients in the 1996 series

	Diabetic patients ($N = 734$)	Non-diabetic patients ($N = 6389$)
Body weight % *ideal BW*	118 ± 25[a]	104 ± 22
Body mass index	25.9 ± 5.2[a]	23.1 ± 4.3
Serum albumin *g/L*	37.8 ± 5.4[a]	38.9 ± 5.3
Serum prealbumin *mg/L*	317 ± 91[a]	340 ± 94
Serum cholesterol *mmol/L*	5.5 ± 1.6[a]	5.3 ± 1.5
Protein catabolic rate *g/kg/day*	1.11 ± 0.31	1.13 ± 0.32
Serum creatinine *μmol/L*	711 ± 184[a]	816 ± 217
Lean body mass *observed/expected*	0.76 ± 0.18[a]	0.87 ± 0.21



Nutritional status in patients with diabetes and chronic kidney disease: a prospective study[1–3]

Christelle Raffaitin, Catherine Lasseur, Philippe Chauveau, Nicole Barthe, Henri Gin, Christian Combe, and Vincent Rigalleau

- **Coopératif:**
- Néphrologie
    - C Lasseur,
    - P Chauveau,
    - C Combe
- Diabéto-Nutrition
    - V Rigalleau
    - C Raffaitin
    - H Gin
- Médecine Nucléaire
    - N Barthe

- **Structuré:**
    - Cs alternées
    - Hospit de jour
- **Suivant les recommandations:**
    - HbA1C
    - TA
    - Lipides
- **Nutritionnel:**
    - ++ Composition corporelle

Am J Clin Nutr 2007

Patients

- Caractéristiques initiales des 35 patients:
  - 23 hommes et 12 femmes
  - âge moyen: 66,5 ± 10,8 ans
  - 67,0 % DT2
  - GFR 41.6±20.9 ml/min/1,73m^2
  - HbA1C: 8,0±1,3%

- Résultats à 2 ans:
  - Déclin GFR: - 3,3 ± 8,4 ml/min/1,73m^2 par an (p = 0,028)
  - amélioration de l'HbA1C = - 0,7 ± 1,1 %   (p = 0,001)

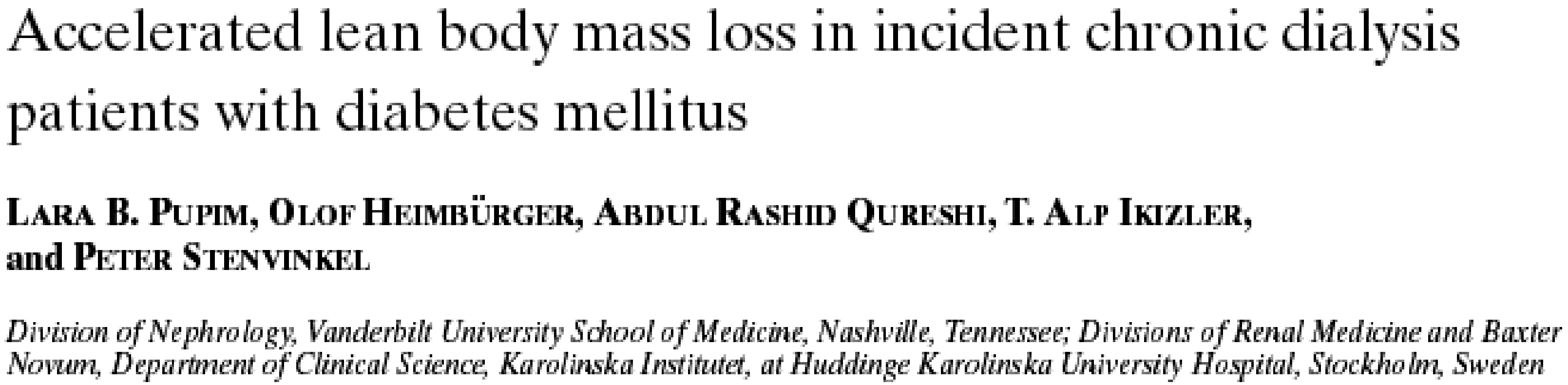
Évolution de l ’état nutritionnel, en l ’absence de dialyse

Variable	Inclusion T0	T 2 ans	*P* value
BMI	26,7 ± 4,2	27,4 ± 4,7	**0,048**
Masse maigre (kg)	50,8 ± 7.9	52,3 ± 8,8	**0,013**
Masse grasse (kg)	20,1 ± 7,2	21,3 ± 8,3	0,218
Albumine (g/l)	36,3 ± 3,3	39,4 ± 3,5	**0,001**

Evolution des sujets dialysés (HD) ou non (IRCS) à la 2ème évaluation

Variable	2ème évaluation *vs* inclusion			
	HD	*P* value	IRCS	*P* value
Poids (kg)	- 3,4 ± 6,2	NS	- 0,5 ± 7,0	NS
Masse maigre (kg)	- 4,2 ± 5,7 *	**0,046**	+ 1,6 ± 2,8	NS
Albumine (g/l)	+ 1,3 ± 4,1 **	NS	+ 3,9 ± 3,5	**0,01**
VEC (l)	- 2,4 ± 4,7 ¤	NS	+ 2,3 ± 5,9	NS
VT (l)	- 4,7 ± 8,3 ¤	NS	+ 2,5 ± 10,0	NS
HbA1c (%)	- 0,36 ± 1,2	NS	- 1,0 ± 1,4	NS

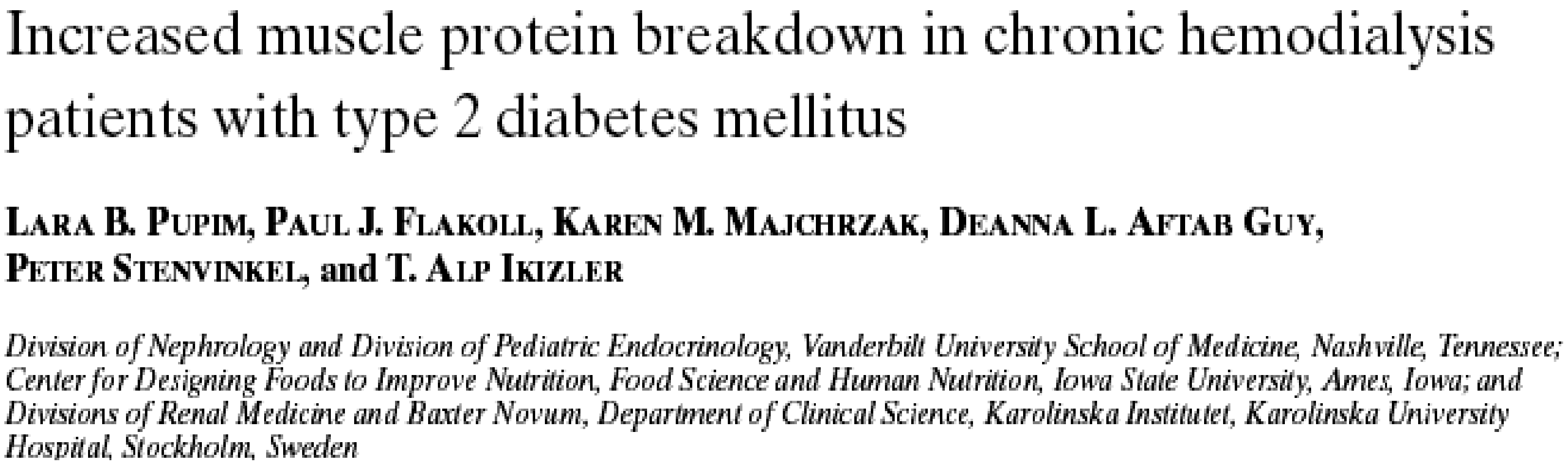
Le DT2 se dénutrit en dialyse
(Kidney Int 2005)



Accelerated lean body mass loss in incident chronic dialysis patients with diabetes mellitus

Lara B. Pupim, Olof Heimbürger, Abdul Rashid Qureshi, T. Alp Ikizler, and Peter Stenvinkel

Division of Nephrology, Vanderbilt University School of Medicine, Nashville, Tennessee; Divisions of Renal Medicine and Baxter Novum, Department of Clinical Science, Karolinska Institutet, at Huddinge Karolinska University Hospital, Stockholm, Sweden



Increased muscle protein breakdown in chronic hemodialysis patients with type 2 diabetes mellitus

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Profound weight loss in a type 2 diabetic patient with diabetic neuropathic cachexia: A case report

T. Al-Hajeri*, S. El-Gebely, N. Abdella

T. Al-Hajeri et al. / Diabetes & Metabolism 35 (2009) 422–424 423

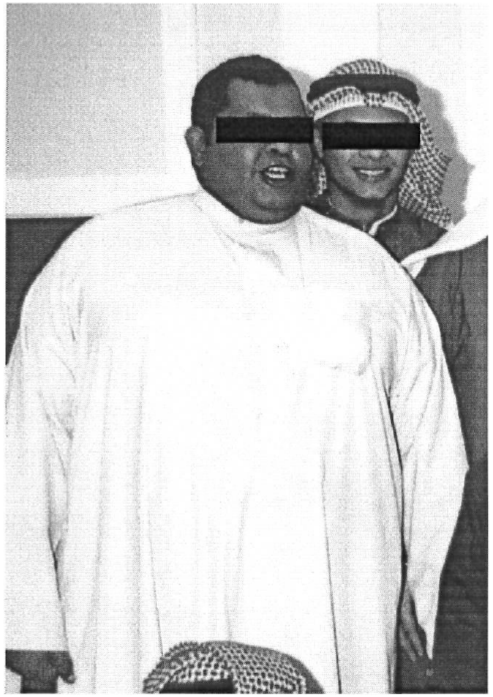


Fig. 1. The patient prior to the illness.

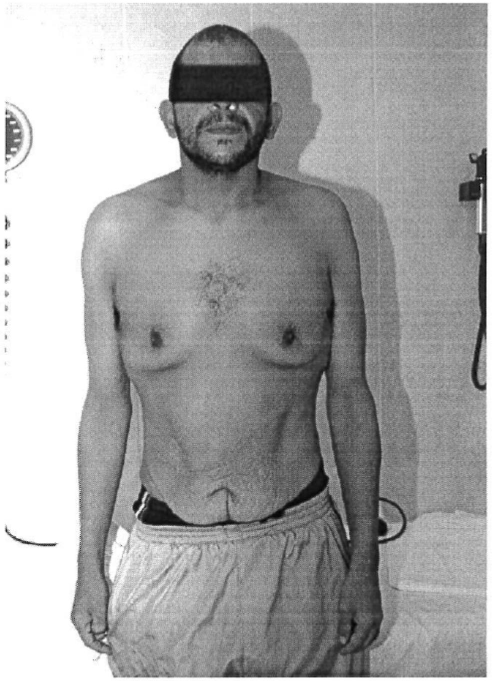


Fig. 2. The patient on admission to hospital.

A 35-year-old morbidly obese man, diagnosed with type 2 diabetes in 2006, lost nearly 100 kg extremely rapidly soon after the diagnosis, with dramatic painful paraesthesia and autonomic neuropathy, and poor diabetes control. Investigations to find a tumour, or an infectious, endocrinological or digestive disease, to explain his clinical features were all negative. However, with insulin and analgesic treatment, the patient's symptoms improved markedly within a few months; the patient gained 50 kg, while insulin was tapered and then withdrawn, to be replaced by metformin, which maintained perfect diabetes control. Also, the analgesic therapies could be discontinued. This case report is typical of diabetic neuropathic cachexia, first described by Ellenberg in 1974.

Muscle Strength in Type 2 Diabetes

Henning Andersen,[1] Søren Nielsen,[2] Carl E. Mogensen,[2] and Johannes Jakobsen[1]

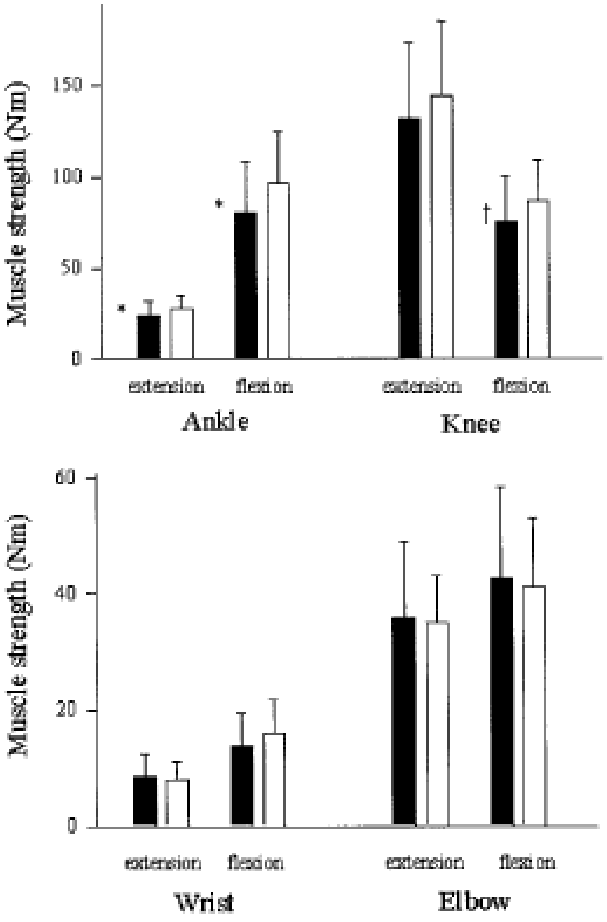
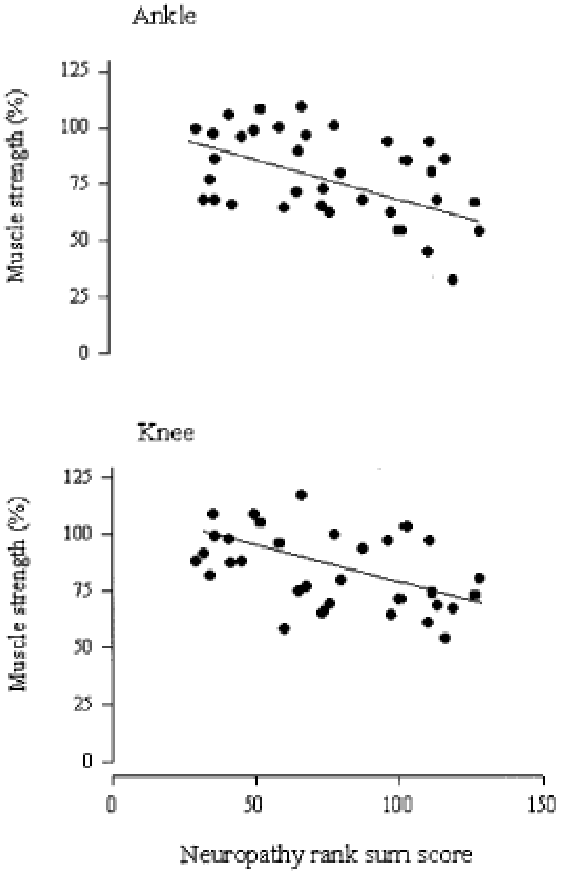


FIG. 1. Isokinetic muscle strength of extensors and flexors at the ankle, knee, wrist, and elbow in type 2 diabetic patients (■) and control subjects (□). Values are mean ± SD. *$P < 0.03$; †$P < 0.05$.



Diabetes 2004

Traitements

INVOLUNTARY WEIGHT LOSS SECONDARY TO METFORMIN USE IN ELDERLY ADULTS

JAGS 2016

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José María González-Pérez, MD, PhD
Antonio Martínez-Riera, MD, PhD
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mean age was 74.0 ± 9.1, and 11 were male. Sixteen were aged 65 and older. All had previously been diagnosed with type 2 diabetes mellitus and were being treated with metformin. The average daily dose was 1838.2 ± 483.3 mg.

glomerular filtration rate (GFR) was 68.9 ± 37.1 mL/min, estimated using the Cockcroft-Gault formula. Ten subjects had a stable GFR of less than 60 mL/min. All subjects reported anorexia, but only six had gastrointestinal symptoms, including nausea, vomiting, abdominal pain, and diarrhea.

baseline weight, which corresponds to a weight loss of 12.4 ± 6.5 kg. This weight loss was involuntary and was a cause for alarm to the individuals, their families, and their physicians. Weight loss occurred over a mean 61.2 ± 59.8 weeks. After metformin was stopped, no subject continued to lose weight, and 11 regained more than

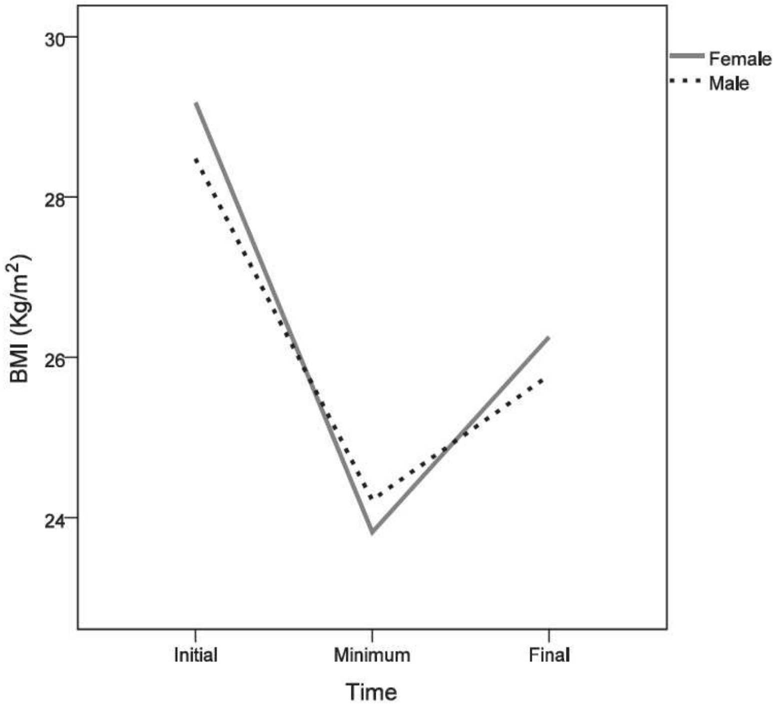
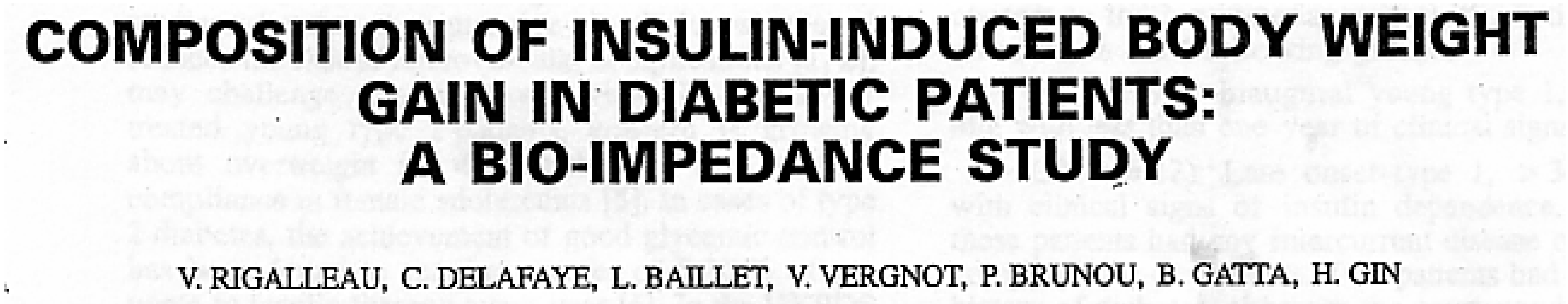


Figure 1. Evolution of body mass index (BMI; kg/m^2). *Initial* indicates when metformin was introduced, *minimum* indicates when metformin was suspended, and *final* indicates when monitoring was over.



COMPOSITION OF INSULIN-INDUCED BODY WEIGHT GAIN IN DIABETIC PATIENTS: A BIO-IMPEDANCE STUDY

V. RIGALLEAU, C. DELAFAYE, L. BAILLET, V. VERGNOT, P. BRUNOU, B. GATTA, H. GIN

D&M 1999

- N=72 patients diabétiques
  - 12 DT1 juvéniles
  - 12 DT1 à marche lente
  - 12 DT2 avec pathologie intercurrente
  - 12 DT2 avec complication microvasculaire
  - 12 DT2 « insulino-requérants »
  - 12 DT2 avant/après sevrage insulinique

- Étudiés par bio-impédancemétrie
- avant après mise sous insuline

Prises de poids sous insuline

	G1	G2	G3	G4	G5	G6
^{2} HbA1C (%)	-7.3±1.1 **vs G4,5	-5.8±1.0 *vs G4,**vs G5	-5.2±1.1 *vs G5	-3.6±0.4	-2.7±0.6	-0.6±0.4 ***vs AO
^{2} body weight (kg/30d)	+3.0±1.0 * vs G3,4,5,	±2.0±0.9	+0.5±0.4	+0.5±0.3	+1.0±0.3	-1.3±0.7
^{2} fat-free mass (kg/30d)	+2.8±1.1 ** vs G3,4,5,6,	+2.2±0.9 * vs G3,4,5,6	+0.6±0.4	+0.5±0.2	+0.4±0.3	-0.4±0.3
^{2} fat mass (kg/30d)	+0.2±0.4	-0.2±0.2 * vs G5,6	-0.1±0.4 * vs G6	+0.0±0.3	+0.6±0.3	-0.9±0.4

Dans les indications les plus évidentes,
la prise de poids est constituée de masse maigre.

Conclusions

- Hyperglycémie = hypermétabolisme
- Défaut de secrétion/d ’action de l ’insuline
- **--> Risque de dénutrition**

- Diabète = symptôme
  - Maladies variées: DT1, DT2, D 2aires
  - Situations variées: complications, agression
- **--> Expression variable**