Chirurgie bariatrique et diabète de type 1 : vraie solution ou fausse bonne idée ?

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Madame H... 41 ans

Diabète de type 1 depuis l'âge de 18 ans

Mère : obésité, diabète de type 2

Obésité ancienne, IMC 37 kg/m², poids stable en dépit de ses efforts sur la diététique et l'activité physique

Hypertriglycéridémie autour de 3,50 g/l, HDL-c autour de 0,30 g/l

SAOS modéré, non appareillé

Rétinopathie diabétique débutante

HbA1c entre 8 et 9% depuis 1 an, sous pompe externe (environ 100 U d'insuline/j) et metformine

Chirurgie bariatrique ?

Prévalence du surpoids et de l'obésité chez les patients présentant un DT1

Table 1. Summary of recent overweight and obesity rates among individuals with type 1 diabetes mellitus								
	Site of study	Age of cohort (years)	Size of cohort	Rates of overweight and obesity				
T1D Exchange ^a [2]	USA, Germany, Austria	NR	NR	US: 35% overweight or obese				
				Germany and Austria: 20% overweight or obese				
Liu et al.ª [3]	USA	3-19	3524	22.1% overweight				
				12.6% obese				
Islam <i>et al.</i> ª [4]	Australia	<16	1975	33% overweight or obese				
Pinhas-Hamiel <i>et al.</i> ^a [5]	Israel	5-30	326	19% overweight				
				5.2% obese				
Baskaran <i>et al.</i> ª [6]	USA	8-16	507	22% overweight				
				10% obese				
Frölich-Reiterer et al. ^b [7]	Austria and Germany	<20	12774	12.5% overweight				
				2.8% obese				
Fourlanos et al. ^c [8]	Australia	30-75	62	37.1% obese				
Holt et al. ^c [9]	USA	35-67	641	42.4% overweight				
				35.9% obese				
Price <i>et al.</i> ^c [10]	Australia	≥18	501	38.3% overweight				
				17.2% obese				
Vestberg et al. ^c [11]	Sweden	≥18	20985	35.1% overweight				
				8.9% obese				

NR, not reported. ^aUS Centers for Disease Control and Prevention or International Obesity Task Force criteria for overweight (BMI 85th to <95th percentile) and obesity (BMI \geq 95th percentile). ^bGerman Working Group of Obesity in Childhood and Adolescence (AGA) criteria for overweight (BMI 90th to 97th percentile) and obesity (BMI \geq 97th percentile). ^bGerman Working Group of Obesity in Childhood and Adolescence (AGA) criteria for overweight (BMI 90th to 97th percentile) and obesity (BMI \geq 97th percentile). ^bGerman Working Group of Obesity (BMI 25–30 kg/m²) and obesity (BMI \geq 30 kg/m²).

En 2017, en Suède, parmi les patients DT1 : surpoids 55%, obésité 18%

> Obésité de l'adulte # 9 à 37% selon les séries!

Polsky S, Ellis SL. Curr Opin Endocrinol Diabetes Obes 2015;22:277-82. Höskuldsdottir G et al. Diabetes Care 2020, published on line October 6, 2020

Prévalence du surpoids et de l'obésité chez les patients présentant un DT1

Pittsburgh Epidemiology of Diabetes Complications Study



Déterminants de la prise de poids chez les patients DT1



Figure 1: Drivers of overweight and obesity in people living with type 1 diabetes

Insulinothérapie et prise de poids : un cercle vicieux



Figure 2: The vicious cycle of insulin-associated weight gain



« Diabète double » ou diabète de type X : une population à haut risque

« Diabète double » = DT1 + surpoids/obésité, antécédents familiaux de DT2 et/ou stigmates d'insulinorésistance

Augmentation du risque de complications, indépendamment du contrôle glycémique

	Cleland et al, 2012 ⁶
	Features additional to presence of T1D
Family history	Family history of T2D, especially in ≥2 relatives
Weight gain/obesity and metabolic syndrome	 Hypertension or borderline high blood pressures Weight gain while receiving insulin Low HDL (compared with high levels typically found in people with T1D)
Atypical features for T1D ^a or features of insulin resistance	Features of insulin resistance Relatively high total insulin dose

Prévalence accrue des complications vasculaires dans le « double diabète »

WILEY

5.00



DD, compared to T1D without MS





(B) Prevalence of macrovascular complications



⁽D) Risk ratios of macrovascular complications in DD, compared to T1D without MS





Prevalence of diabetes complications in individuals with type 1 diabetes (T1D) and metabolic syndrome. Complication rates (A,B) FIGURE 4 and risk ratios (C,D) of diabetes complications are shown in the presence and absence of metabolic syndrome in individuals with T1D. ALB, albuminuria; CHD, coronary heart disease; DR, diabetic retinopathy; MI, myocardial infarction; PAD, peripheral arterial disease; PDR, proliferative retinopathy. Data were modified from Merger et al⁵⁴

Insulino-résistance et risque de mortalité chez les patients DT1



FIGURE 1 Estimated glucose disposal rate (eGDR) and mortality in type 1 diabetes (T1D). All-cause mortality was related to eGDR, calculated using waist circumference, in 17 050 individuals with T1D diabetes. Data were adapted from Nyström et al³⁹

Chirurgie bariatrique chez les patients DT1 : les enseignements des méta-analyses

13 études, 86 patients DT1 & IMC > 35 kg/m²

Âge 41 ±7 ans IMC 42,50 ±2,7 kg/m² Insuline 98 ±26 U/j HbA1c 8,46 ±0,78%

> RYGBP 69% SG 15% BPD 14% LAGB 2%

	Pre		Post		Mean difference	Mean difference
Study or subgroup	Mean SD 7	otal Mean	SD Tota	Weight	IV, random, 95% CI	IV, random, 95% CI
1.4.1 BMI, end Subtotal (95% CI)		86	86	62.3%	13.42 [8.53, 18.32]	•
Heterogeneity: $\tau^2 = 61.41$; χ Test for overall effect: $Z = 5.2$	P = 340.69, df = 12 88 ($P < 0.00001$)	(P < 0.0000)	(1); $I^2 = 96\%$			
1.4.2 BMI, 12 M					IMC 12 mois	
Subtotal (95% CI)		40	40	37.7%	15.18 [10.86, 19.50]	•
Test for overall effect: $Z = 6$. <u>1.1.1 Insulin/day, end</u>	38 (<i>P</i> < 0.00001)					
Subtotal (95% CI)	5	9	59	58.9% 4	9.98 [38.61, 61.36]	•
Heterogeneity: $\tau^2 = 80.18$; χ Test for overall effect: $Z = 8.0$ 1.1.2 Insulin/day, 12 M	$f^{2} = 12.54, df = 9 (P$ 51 ($P < 0.00001$)	$= 0.18); I^2$	= 28%	Do	ses d'insuline 12 mois	
Subtotal (95% CI)	3	3	33	41.1% 6	0.91 [38.12, 83.71]	•
Heterogeneity: $\tau^2 = 492.00$; Test for overall effect: $Z = 5$.	$\chi^2 = 17.23, df = 6 ($ 24 (<i>P</i> < 0.00001)	P = 0.008);	$I^2 = 65\%$			
Subtotal (95% CI) Heterogeneity: $\tau^2 = 0.66$; χ^2	e 52.91, df = 12 (F	36 9 < 0.00001)	86); <i>I</i> ² = 77%	62.3%	0.64 [0.06, 1.23]	•
Test for overall effect: $Z = 2$. 1.3.2 HbA1c, 12M	16 (P = 0.03)				HbA1c 12 mois	
Subtatal (05% CI)	2	40	40	37.7%	0.44 [0.09, 0.79]	 ▲

Chow A et al. Arch Journal of Obesity 2016

Chirurgie bariatrique chez les patients DT1 : les enseignements des méta-analyses

10 études retenues, 84 patients

Âge moyen 40,8 ans IMC 42,06 kg/m² Insuline 100,45 U/j (0,91 U/kg/j) Suivi moyen 31,8 mois

By-pass (RYGBP) +++ Sleeve (SG) ++ Anneau gastrique (LAGB) + Diversion bilio-pancréatique (BPD) +

IMC -11,04 kg/m² p<0,00001

Amélioration des paramètres tensionnels et lipidiques



Chirurgie bariatrique chez les patients DT1 : des bénéfices confirmés dans des études plus récentes

Study	Vear	Number	HbA _{1c} (%)		Insulin requirement (units/kg/ day)		Insulin requirement (units)		BMI (kg/m ²)		Follow-up
Study	Tear		Pre-op	Postop	Pre-op	Postop	Pre-op	Postop	Pre-op	Postop	(montus)
Vilarrasa et al. (47) Al Sabab <i>et al.</i> (48)	2017 2017	32	8.5±1.3 8.6+1.2	7.9±1.4 8.3±1.4	0.8±0.3	0.5±0.2	92±40 76±68	41±18 18+18	41.3 ± 4.8 41.9 ± 5.4	32 (CI NA) 31.5+8.4	12 18
Rottenstreich <i>et al.</i> (49) Faucher <i>et al.</i> (50)	2016 2016	13 13	8.4±1.5 8.3 (7.8–9.0)	7.6±0.8 7.6 (CI NA)	0.7±0.3 0.8 (0.7–1.0)	0.5±0.3 0.4 (0.3–0.5)	84±40	46±33	39.9±4.1 40.6 (37.9–41.9)	30.1±3.9 29.1 (CI NA)	24 12

Amélioration de l'HbA1c et réduction des doses d'insuline...



... s'estompant avec le temps et la reprise de poids

Yeung KTD et al. Diabet Med 2019;36:414-23. Vilarrasa N et al. Obes Surg 2017;27:856-63.

Bénéfices de la chirurgie bariatrique chez les patients DT1 : quels mécanismes ?⁽¹⁾



Chirurgie bariatrique chez les patients DT1 : des résultats parfois mitigés sur l'HbA1c

Table 1

Clinical outcomes before and after bariatric surgery (N = 37).

Clinical outcome*	Before bariatric		After	r bariatric	P-values [†]
	N	$\text{Mean} \pm \text{SD}$	N	$\text{Mean} \pm \text{SD}$	
HbA1c – % (mmol/mol)	27	8.8 ± 1.3 (73 ± 14.2)	34	$8.1 \pm 1.1 \ (65 \pm 12.0)$	0.05
Weight – kg	14	108 ± 24	30	91 ± 20	0.006
BMI – kg/m ²	12	$\textbf{38.8} \pm \textbf{9.1}$	30	33.3 ± 6.7	0.006
Blood pressure – mmHg					
Systolic	14	121 ± 7	30	121 ± 12	0.94
Diastolic	14	72 ± 6	30	73 ± 7	0.74
Lipid profile – mg/dL					
Total cholesterol	7	160 ± 27	17	169 ± 31	-
LDL-C	15	88 ± 22	26	80 ± 17	0.23
HDL-C	14	64 ± 24	25	71 ± 21	0.74
Triglyceride	14	106 ± 60	25	84 ± 23	0.15

* For each variable the mean of each subject was calculated and then the mean of the entire group was recorded.

[†] P-values adjusted for age, gender, household income, CGM use, and pump use as fixed effects and participant as a random effect. *P*-values were only determined if there were at least 10 individuals with data available before and after bariatric surgery. P-values adjusted using the Benjamini-Hochberg procedure.



Chirurgie bariatrique chez les patients DT1 : des résultats parfois mitigés sur l'HbA1c

Table 1. Baseline characteristics of patients with type 1 diabetes.

Characteristic	Surgery group ($N = 26$)	Nonsurgery group ($N = 26$)	p value
Sex (M/F)			0.05
Male n (%)	7 (27)	14 (54)	
Female n (%)	19 (73)	12 (46)	
Age (years) mean \pm SD	40.4 ± 9.8	33.1 ± 9.6	0.01
Age at diagnosis of T1D: mean \pm SD	20.2 ± 11.2	23.1 ± 11.9	NS
Duration of diabetes (years)	20.2 ± 8.6	11.1 ± 9.2	0.001
BMI (kg/m²)	39.5 ± 4.4	33.6 ± 3.9	0.001
HbA1c (%)	8.5 ± 0.9	7.9 ± 1.9	0.02
Comorbidities			
Hypertension	13 (50%)	5 (19.2%)	0.02
Retinopathy	1 (3.8%)	0 (0%)	NS
Neuropathy	0 (0%)	0 (0%)	NS
Proteinuria	4 (15.3%)	0 (0%)	NS
Coronary artery disease	0 (0%)	2 (7.7%)	NS
Medications n (%)			
Insulin pump	12 (46)	14 (54)	NS
Multiple daily injections	14 (54)	12 (46)	NS
Lipid-lowering agents	13 (50.0%)	7 (26.9%)	0.09
Antihypertensive agent	13 (50%)	5 (19.2%)	0.02
Metformin	3 (11.5%)	13 (50%)	0.003



4 acidocétoses (15%) - 6 hypoglycémies sévères (23%)

Landau Z et al. Ther Adv Endocrinol 2019;10:1-8.

Chirurgie bariatrique chez les patients DT1 : des résultats parfois mitigés sur l'HbA1c

Bariatric Surgery in Patients With Obesity and Latent Autoimmune Diabetes in Adults (LADA)

10 patients (9 femmes et 1 homme) Âge médian : 52 ans, ancienneté du diabète : 12 ans Peptide-C détectable : 2 patients sur 10

IMC : 34,8-53,7 kg/m² RYGBP, n= 5 & SG, n= 5

IMC médian : 38,6 kg/m² \rightarrow 30,3 kg/m² à un an* \rightarrow 33,1 kg/m² suivi médian 5 ans*

HbA1c médiane : 9,4 ±1,7% → 8,6 ±1,2% à un an (ns) → 9,0 ±1,5% suivi médian 5 ans (ns)

Absence d'amélioration des paramètres lipidiques et tensionnels





Figure 1—Changes in BMI (kg/m²) (*A*), HbA_{1c} (%) (*B*), and daily insulin requirement (*C* and *D*) before and after bariatric surgery in patients with obesity and LADA. Data are presented as mean \pm SEM. Number of patients with data at each time point is shown beneath *x*-axis. **P* < 0.05.

Chirurgie bariatrique et complications métaboliques aiguës chez les patients DT1⁽¹⁾

References	Patients (n)	Mean duration of T1DM (years)	Mean duration of follow-up	Procedures (n)	DKA before surgery	DKA after surgery	Hypoglycemia before surgery	Hypoglycemia after surgery
Chuang et al. (18)	2	5.5	20 months	RYGB (1) SG (1)	Patient 1: 1 episode Patient 2: (-)	Patient 1: (-) Patient 2: 1 episode	()	Patient 1: Mild hypoglycemic episodes 2 to 5 times per week Patient 2: Mild hypoglycemic episodes 2 to 5 times per week
Aminian et al. (39)	12	NA	90 days	RYGB (6) SG (4) AGB (2)	3 patients (25%)	Severe: 3 Moderate: 3 Mild: 6	NA	NA
Maraka et al. (30)	7	20.6	2 years	RYGB (9) SG (1)	NA	2 patients	NA	7 patients
Vilarrasa et al. (23)	32	20	4.6 years	SG (15) RYGB (11) BPD (6)	(-)	2 patients (one had a recurrent episode)	(-)	3 patients (9.3%)—severe
Landau et al. (22)	26	20.2	3.5 years	SG (19) RYGB (4) AGB (3)	NA	4 patients (within 48 h after surgery)	NA	6 patients shortly after discharge–2 patients hospitalized
Faucher et al. (31)	13	21	12 months	SG (7) RYGB (6)	NA	NA	(-)	Median number of minor episodes at 6 months: RYGB: 3.5 SG: 6 2 severe episodes
Al Sabah et al. (32)	10	NA	4 years	SG (10)	NA	NA	NA	2 patients (18.2%)

TABLE 3 | Incidence of diabetic ketoacidosis and hypoglycemia after bariatric surgery in patients with type 1 diabetes mellitus and obesity.

DKA, diabetic ketoacidosis; NA, not applicable; RYGB, R-n-Y gastric bypass; SG, sleeve gastrectomy; BPD, biliopancreatic diversion; AGB, adjustable gastric banding.

Chirurgie bariatrique chez les patients DT1 : source de variabilité glycémique ?

Variations +++ de l'absorption du glucose après chirurgie malabsorptive (RYGB, DBP)



Basal Bolus Injections après repas

Figure 1: Continuous monitoring of blood glucose (mmol/l) with multiple-dose insulin injections and prandial insulin administered 15 minutes after the start of meals. Solid lines represent the record of six individuals and consecutive days. The dotted line is the average of the six recorded days. The shaded zone represents the target glucose value.



Basal Bolus Injections avant repas

Despite considerable weight loss with a concomitant decrease in insulin requirement, glycaemic control remained difficult after surgery. Due to their different impacts on glucose kinetics, the type of surgical operation should be part of the assessment. These patients might benefit from sensor-augmented insulin pump therapy with automated insulin suspension after bariatric surgery. The decision for surgical intervention in these patients should be carefully weighed against the difficulties in achieving adequate glycaemic control.

Figure 2: Continuous monitoring of blood glucose (mmol/l) with multiple-dose insulin injections and prandial insulin administered 15 minutes before the start of meals. Solid lines represent the record of six individuals and consecutive days. The dotted line is the average of the six recorded days. The shaded zone represents the target glucose value.



Pompe + capteur avec 'arrêt avant hypo'

Figure 3: Continuous glucose monitoring with continuous subcutaneous insulin infusion via a sensor-augmented insulin pump with automated insulin suspension. Insulin boluses administered 15 minutes before the start of the meals. Solid lines represent the record of six individuals and consecutive days. The dotted line is the average of the six recorded days. The shaded zone represents the target glucose value.

Chirurgie bariatrique dans le DT1 : une étude cas-témoins avec un suivi prolongé

Etude suédoise - Appariement âge, sexe, IMC, année d'inclusion

Table 1—Clinical charac	teristics and	l pharm	acological	treatment	s at base	eline (in
addition to insulin)						
	a /	207)	DVCD /	207)	-	C1 45

	Control ($n = 387$)	RYGB $(n = 387)$	Р	SMD
Female sex	345 (89.1)	298 (77.0)	<0.001	0.33
Age (years)	41.1 ± 14.5	41.7 ± 10.3	0.586	0.04
Diabetes duration (years)	18.7 ± 13.2	18.8 ± 11.4	0.940	0.01
BMI (kg/m ²)	$39.5~\pm~7.0$	40.8 ± 5.4	0.005	0.21
HbA _{1c} (mmol/mol)	67.5 ± 16.7	70.1 ± 16.5	0.052	0.15
HbA _{1c} (%)	$8.4~\pm~1.53$	8.6 ± 1.50	0.052	0.15

Comorbidités et traitements identiques

Table 3—Changes in metabolic variables							
	Со	ntrol group	RYGB group				
	N	Mean (SD)	N	Mean (SD)			
HbA _{1c} (%)		\frown		\frown			
Baseline	380	8.4 (1.53)	277	8.6 (1.50)			
After 1 year	306	8.3 (1.41)	293	7.6 (1.42)			
After 2 years	310	8.3 (1.50)	259	7.8 (1.45)			
BMI (kg/m ²)		\sim		$\tilde{\frown}$			
Baseline	387	39.5 (7.0)	387	40.8 (5.4)			
After 1 year	296	37.5 (7.0)	370	30.6 (5.7)			
After 2 years	288	37.5 (7.1)	322	28.8 (4.9)			
Weight (kg)		\smile		Ŭ			
Baseline	201	111.4 (21.8)	387	116 (20.2)			
After 1 year	149	106.1 (21.7)	362	86.2 (19.2)			
After 2 years	142	105.8 (19.3)	293	82.3 (17.1)			



Suivi moyen #5 ans

Chirurgie bariatrique chez les patients DT1 : attention à la rétinopathie

Worsening of diabetic retinopathy with rapid improvement in systemic glucose control: A review

The effect of bariatric surgery on DR and early worsening remains debatable. Existing data support positive, neutral and negative effects of bariatric surgery on DR.⁵² The potential risk factors for DR progression following bariatric surgery may include pre-operation DR severity, magnitude of post-surgery HbA1c reduction and, in some cases, gender and ethnicity.^{53,54}

> Acta Ophthalmol. 2020 Jan 7. doi: 10.1111/aos.14342. Online ahead of print.

Bariatric surgery might aggravate proliferative diabetic retinopathy

Ozkan Sever¹, Fatih Horozoglu¹

Conclusion: Patients with PDR who received BS showed more severe retinopathy than patients who were matched for age, sex, HbA1c levels and follow-up duration and who did not receive BS.

Troubles des conduites alimentaires et diabète(s)



Comportements alimentaires problématiques et DT1

Au-delà des TCA recensés par le DSM-V, les (jeunes) patients DT1 présentent fréquemment des **comportements alimentaires problématiques** (disturbed eating behaviors, DEB).

Ils renvoient à la présence d'au moins un symptôme en lien avec l'alimentation dans le dernier mois :

- régimes restrictifs
- jeûne
- activité physique excessive
- « orgies » alimentaires après hypoglycémie
- omission des injections d'insuline à visée compensatoire +++



La prévalence des comportements alimentaires problématiques est très élevée chez les adolescents et jeunes adultes DT1 (20 à 50% chez les filles, 5 à 25% chez les garçons)

Chirurgie bariatrique chez les patients DT1 : pour résumer



Van der Schueren B et al. Lancet Diabetes Endocrinol 2021

- SG > RYGBP ? (moindre variabilité de l'absorption des glucides)
- Encadrer la période pré et post-opératoire +++ (FO, équilibre glycémique, suivi psychologique...)
- Décision individuelle, au cas par cas, sans attendre de résultats 'miraculeux' sur les glycémies