

Renato Cozzi

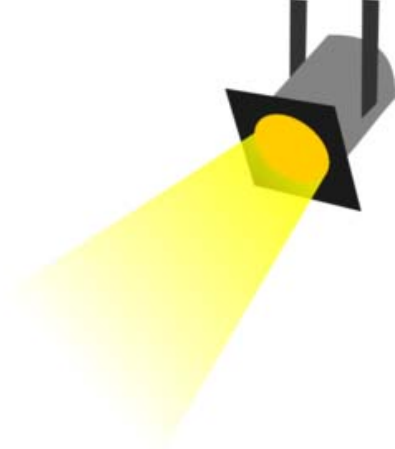
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Simposio 15

Dal diabete mellito al diabete secondario ad
endocrinopatie

Casi clinici in acromegalia



Caso no 1. Mirco, 46 aa.





Caso no 1. Mirco - storia clinica

- Goloso (dolci)
- BMI 27
- Poliuria, polidipsia, calo ponderale (- 12 kg)
- Glicemia 400 mg/dl, HbA1C 14.6%
- Fenotipo acromegalico
- 2000: tunnel carpale bilaterale
- Sleep apnea
- Normoteso

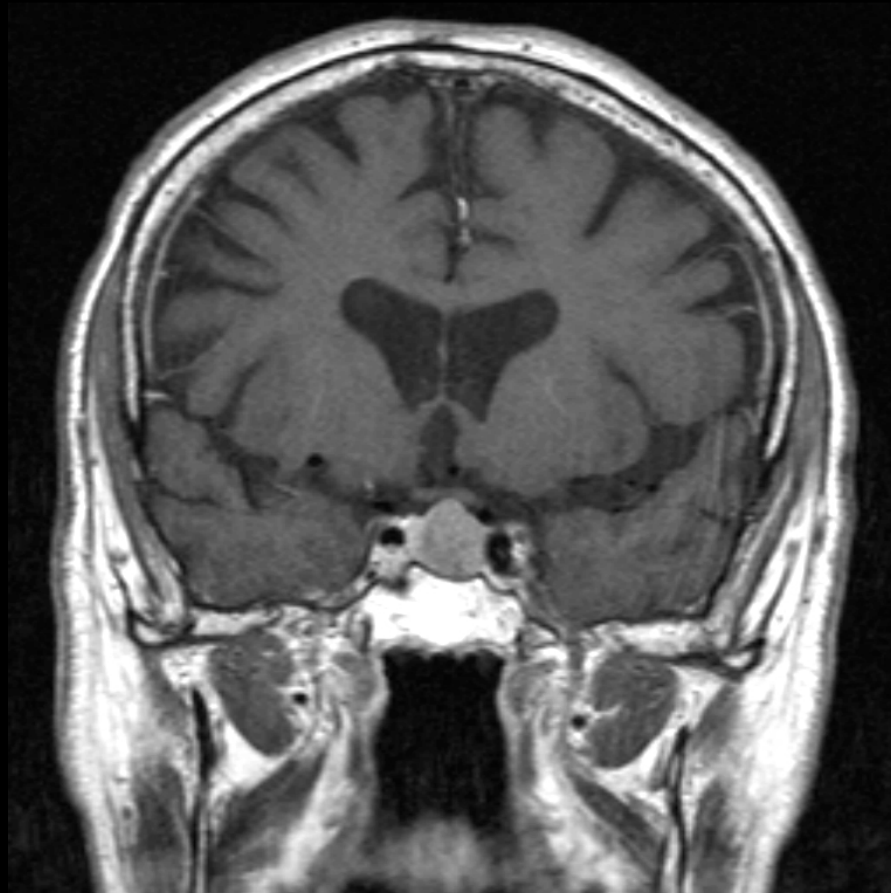


Caso no 1. Mirco - laboratorio

- GH 44 ng/ml
- IGF-1 550% ULNR
- PRL 13 ng/ml
- Testosterone 1.7 ng/ml (vn 2.8-9)
- C-Peptide (post-prandiale) 5.7 ng/ml

Caso no 1. Mirco - RM sellare

7



W 1596 : L 777



Caso no 1. Mirco - terapia

- Dieta per diabetici
- Inizia Octreotide LAR 30 mg/28 gg
- Consigliata insulinoterapia (23 U/die)



Caso no 1. Mirco - follow up

▪ Dopo 1 mese

- ❖ GH 4.1 ng/ml. IGF-1 200% ULNR
- ❖ Glicemia 120 mg/dl. HbA1C 11.2%
- ❖ Ha fatto solo dieta
- ❖ Benessere soggettivo. Non più SA

▪ Dopo 3 mesi

- ❖ GH 4 ng/ml. IGF-1 220% ULNR
- ❖ Glicemia 116 mg/dl. HbA1C 6.5%
- ❖ RM sellare: riduzione tumorale modesta



Caso no 1. Mirco - follow up

- Inviato a NCH ipofisario
- OK per intervento
- Asportazione radicale
- OGTT post-Tx: GH nadir 0.1 ng/ml
- Glicemia 120 min: 200 ng/ml
- HbA1C 6.5%



Caso no 2. Vincenzina, 70 aa.



Caso no 2. Vincenzina

- DMT2 da circa 20 anni: 4 insuline/die (110 U)
- HbA1C 9.5%
- BMI 32
- Menopausa a 52 anni
- Ipertesa (3 farmaci): controllo scadente
- Cardiopatia ischemica



Caso no 2.Vincenzina

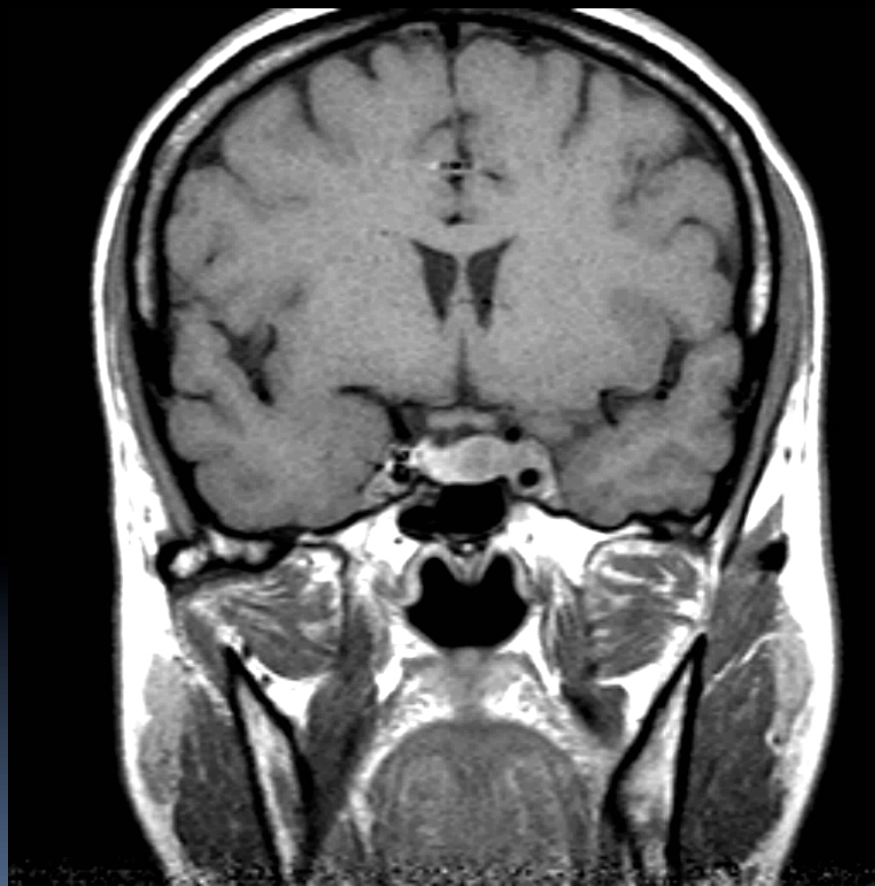
- Cefalea quotidiana cronica
- Roncopatia
- Sleep apnea
- Aspetto grossolano

Acromegalia da circa 15 anni

Laboratorio: GH 32 ng/ml. IGF-1 420%

Caso no 2.Vincenzina - RM sellare

6



W 1115 : L 704



Caso no 2.Vincenzina - Terapia

- **Figlia:** intervento
- «la mamma ha un tumore nel cervello»
- **Endocrinologo:**
terapia
farmacologica



Caso no 2. Vincenzina - Octreotide LAR

▪ Dopo 1 mese

- GH 7 ng/ml.
- IGF-1 280% ULNR
- Ipoglicemie frequenti
- Insulina: 90 U/die

▪ Dopo 3 mesi

- GH 5 ng/ml.
- IGF-1 200% ULNR
- Ipoglicemie rare
- HbA1C 8.0%
- Insulina: 80 U/die



Caso no 2. Vincenzina - Follow up

▪ Dopo 6 mesi

- GH 3 ng/ml.
- IGF-1 130% ULNR
- HbA1C 7.8%
- Insulina 70 U/die

▪ Dopo 12 mesi

- GH 1.5 ng/ml.
- **IGF-1 90% ULNR**
- HbA1C 7.6%
- Insulina 50 U/die
- RM sellare:
riduzione
tumorale (-30%)



Caso no 2. Vincenzina. Oggi (dopo 5 aa)

- GH 1.2 ng/ml. IGF-1 80% ULNR
- HbA1C 7.4%
- Insulina: 34 U/die
- BMI 32
- RM sellare: ulteriore riduzione (-70%). Il tumore mantiene caratteristiche invasive



Caso no 3. Giovanni, 70 anni



Caso no 3. Giovanni. 2009

- ◆ DMT2 di vecchia data
- ◆ BMI 28
- ◆ Recente scompenso glicemico, dopo iperpiressia.
- ◆ Sospetto TIA arto superiore sin
- ◆ RICOVERO



Caso no 3. Giovanni - storia clinica

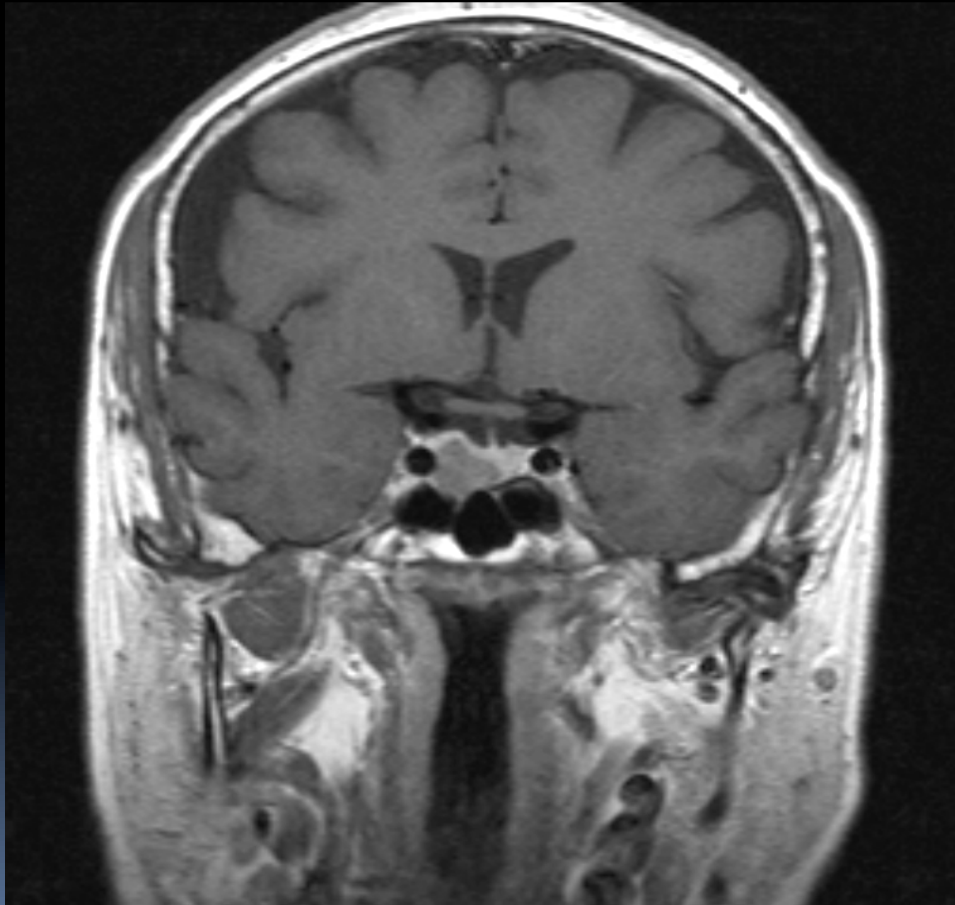
- ◆ Ex fumatore
- ◆ Cardiopatia ischemica
- ◆ 1995 sostituzione valvolare aortica. TAO
- ◆ Ipertensione arteriosa
- ◆ Roncopatia
- ◆ PSA 5.8
- ◆ Fenotipo indifferente

Terapia

- ◆ Antiipertensivi (tre farmaci)
- ◆ Insulina (40 U/die) + ADO
- ◆ Statine
- ◆ TAO

Caso no 3. Giovanni - RM sellare

6



W 1707 : L 774



Caso no 3. Giovanni - laboratorio

- ◆ GH 2.6 ng/ml (media di 5 campioni)
- ◆ IGF-1 170% ULNR
- ◆ HbA1C 8.3%



Caso no 3. Giovanni - Octreotide LAR

▪ Dopo 1 mese

- ◆ GH 1.7 ng/ml. IGF-1 110%
- ◆ HbA1C 8.1%
- ◆ DMT2: profilo invariato

▪ Dopo 3 mesi

- ◆ GH 2.2 ng/ml. IGF-1 120%
- ◆ HbA1C 7.9%
- ◆ Insulina 36 U/die
- ◆ RM sellare: invariata

▪ Dopo 12 mesi

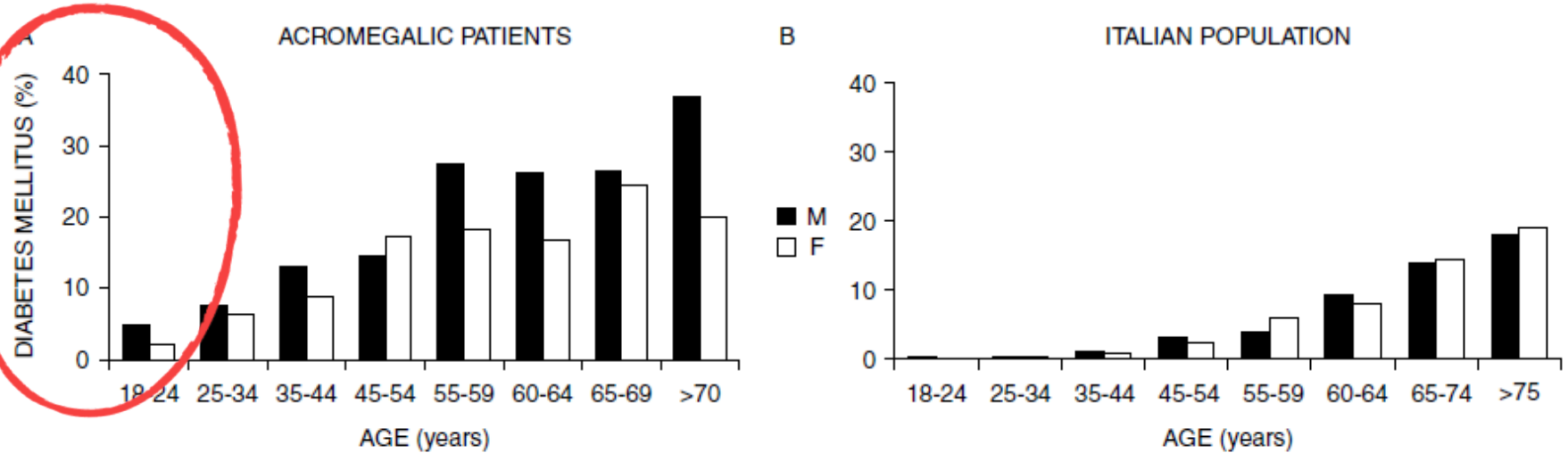
- ◆ GH 1.2 ng/ml. IGF-1 115%
- ◆ HbA1C 7.2%
- ◆ RM sellare invariata



Caso no 3. Giovanni - oggi

- Mantiene octreotide LAR 30 mg/28 gg
- Controlli clinici e di laboratorio annuali
- RM sellare stabile
- GH 1.8 ng/ml. IGF-1 125%
- HbA1C 7.2%
- Insulina 40 U/die

Predictors of morbidity and mortality in acromegaly: an Italian survey



Prevalenza di DM in acromegalia nei registri europei

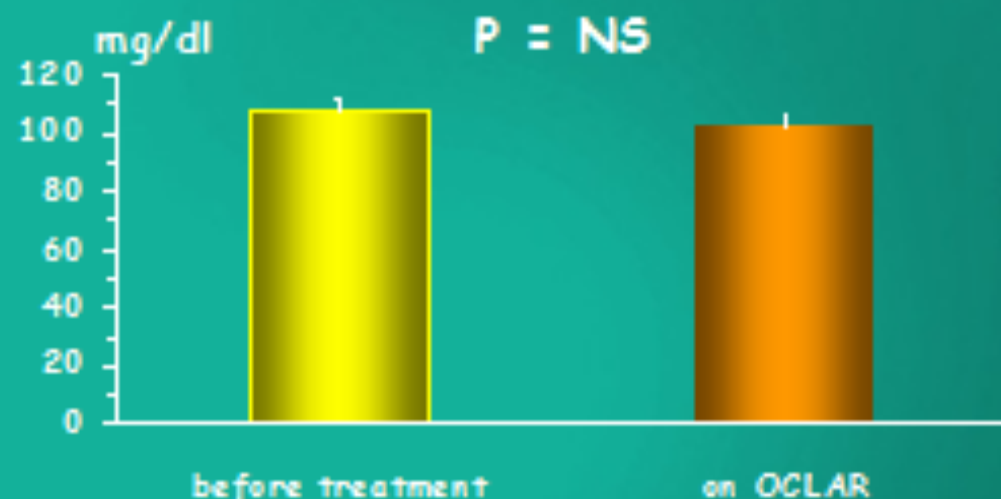


	Number of patients (M/F)	Age at diagnosis mean (M/F)	Macro- adenomas (%)	Diabetes mellitus (%)	Hypertension (%)	Disease control (%)	SMR (95% CI)
(9)	419 (178/241)	47	—	—	—	46	1.26 (1.03–1.54)
(19)	1219 (478/741)	45	75	37.6	39.1	31	—
(13)	208 (125/83)	42	54	29.7	54.4	—	2.70 (2.10–3.50)
(11)	334 (161/173)	47.5 (45/49)	61	—	—	55	1.16 (0.85–1.54)
(20)	418 (213/205)	44 (42/46)	79	25.3	39.4	49	1.39 (0.96–2.03)
(21)	1485 (677/808)	44 (41/47)	79	—	—	—	—
Present study	1512 (624/888)	45 (43/47)	70	16	33	65	1.13 (0.87–1.46)

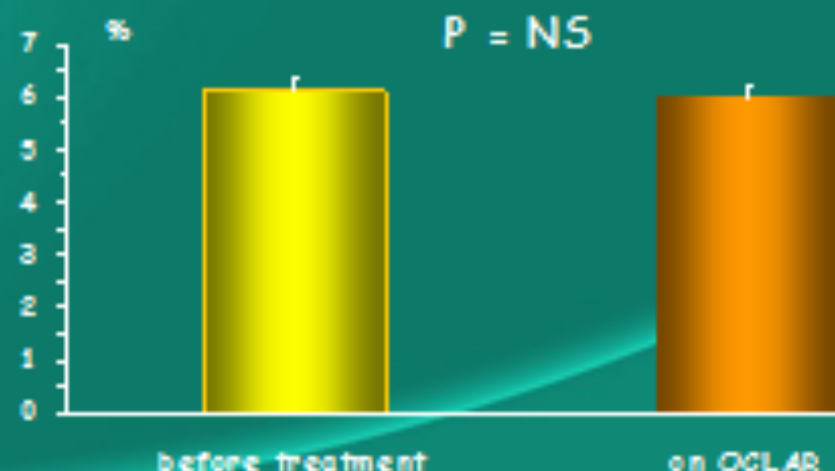
Predittori di DM in acromegalia

Variables	OR	95% CI	<i>P</i> value
<u>Age</u>	2.26	1.68–3.05	0.001
<u>Male sex</u>	1.64	1.08–2.52	0.02
GH at diagnosis	0.99	0.95–1.03	NS
<u>IGF1 at diagnosis (SDS)</u>	1.11	1.00–1.24	0.05
<u>Delay of diagnosis</u>	1.14	0.92–1.41	NS

Octreotide LAR chronic treatment and fasting glucose



HbA1c



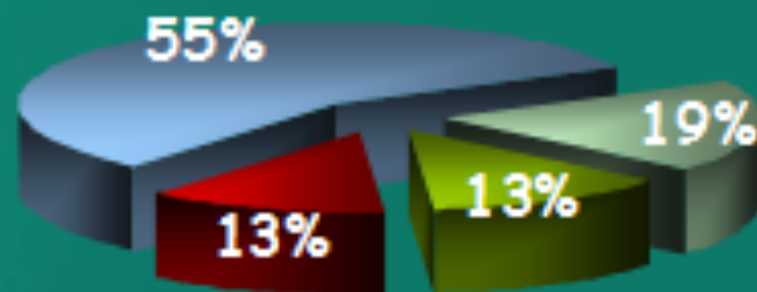
HbA1c: individual values

pre-treatment



■ normal
■ pathologic

during OC-LAR



■ no change
■ improved
■ normalized
■ worsened

Outcome glicometabolico in acromegalici con DM/IGT durante SA



Studies	Patients with diabetes or IGT/overall group	Overall group, biochemical control of acromegaly		Patients with diabetes or IGT, glycometabolic outcome during SSA treatment		
		Safe GH, %	Normal IGF-I, %	Worsened, %	Unchanged, %	Improved, %
Ho <i>et al.</i> , 1992 (33)	5 of 7	43	43	NA	NA	80
Koop <i>et al.</i> , 1994 (39)	35 of 90	NA	NA	23	40	37
Arosio <i>et al.</i> , 1995 (44)	13 of 68	20	57	31	54	15
Fløgstad <i>et al.</i> , 1997 (5)	2 of 14	64	64	0	100	0
Giusti <i>et al.</i> , 1997 (47)	5 of 57	54	35	20	80	0
Ambrosio <i>et al.</i> , 2002 (55)	4 of 16	90	40	0	50	50
Ayuk <i>et al.</i> , 2002 (56)	8 of 22	NA	67	NA	NA	62
Ronchi <i>et al.</i> , 2002 (59)	2 of 10	50	20	50	50	0
Gutt <i>et al.</i> , 2005 (66)	6 of 11	NA	54	83	17	0
Jallad <i>et al.</i> , 2005 (68)	22 of 80	74	54	23	54	23
All studies	107 of 375	54	50	25	46	29

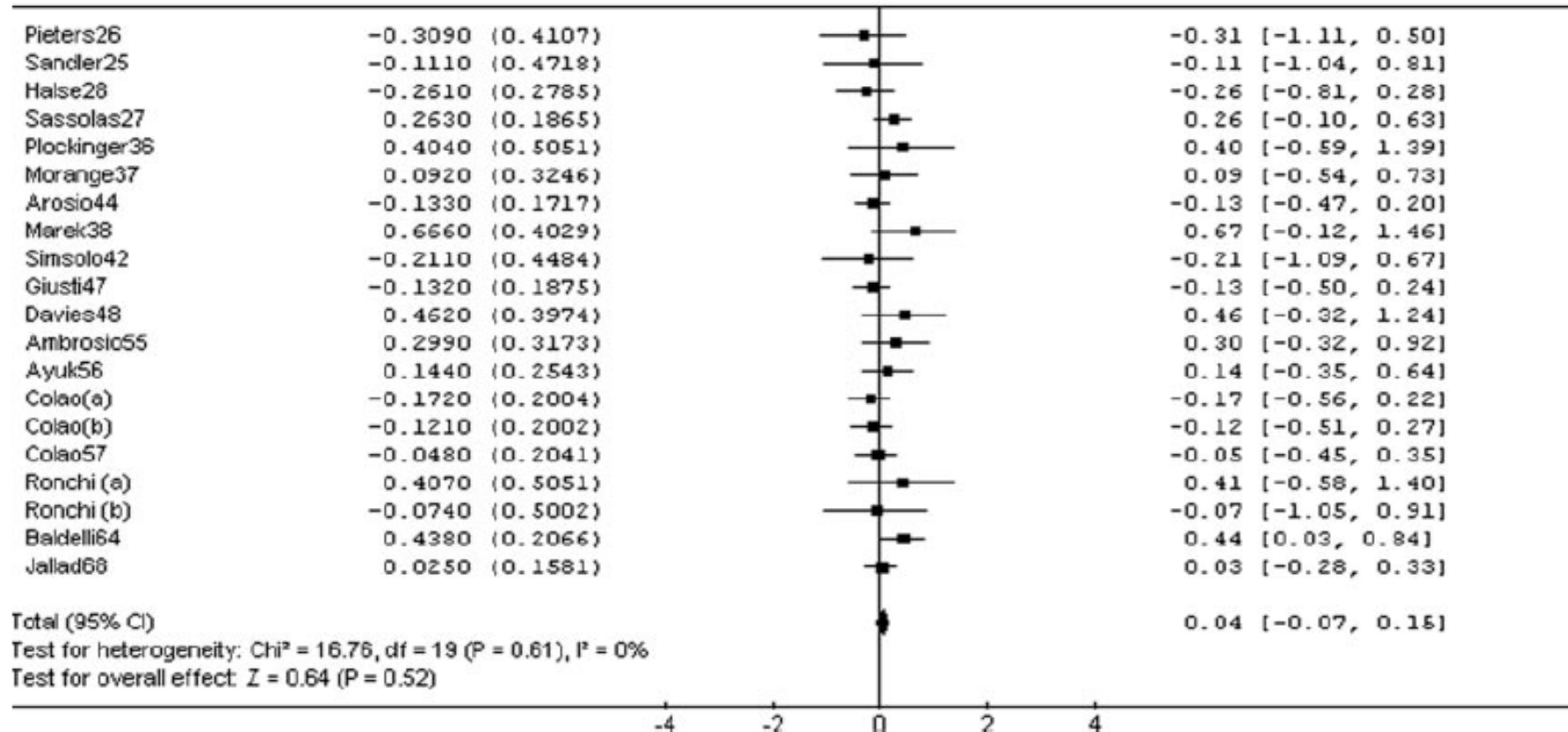
Effects of Somatostatin Analogs on Glucose Homeostasis: A Metaanalysis of Acromegaly Studies

Study
or sub-category

Effect size (SE)

Effect size (fixed)
95% CI

Effect size (fixed)
95% CI

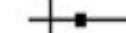
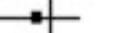
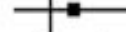


Study
or sub-category

Effect size (SE)

Effect size (fixed)
95% CI

Effect size (fixed)
95% CI

Halse28	-0.1310 (0.2780)		-0.13 [-0.68, 0.41]
Lam35	-0.0400 (0.3650)		-0.04 [-0.76, 0.68]
Arosio44	-0.0810 (0.1720)		-0.08 [-0.42, 0.26]
McKnight40	0.5060 (0.4540)		0.51 [-0.38, 1.40]
Simsolo42	-0.5210 (0.4550)		-0.52 [-1.41, 0.37]
Flogstad5	-0.2670 (0.3800)		-0.27 [-1.01, 0.48]
Diez53	0.1580 (0.4480)		0.16 [-0.72, 1.04]
Ambrosio55	-0.3130 (0.3180)		-0.31 [-0.94, 0.31]
Colao(a)	0.2830 (0.2010)		0.28 [-0.11, 0.68]
Colao(b)	0.3770 (0.2020)		0.38 [-0.02, 0.77]
Colao57	0.2890 (0.2050)		0.29 [-0.11, 0.69]
Ronchi (a)	0.3930 (0.5050)		0.39 [-0.60, 1.38]
Ronchi (b)	0.0000 (0.5000)		0.00 [-0.98, 0.98]
Baldelli64	0.5770 (0.2080)		0.58 [0.17, 0.98]
Gutt66	0.0750 (0.4270)		0.08 [-0.76, 0.91]
Jallad68	0.0000 (0.1580)		0.00 [-0.31, 0.31]
Maiza72	-0.1430 (0.2360)		-0.14 [-0.61, 0.32]

Total (95% CI)

Test for heterogeneity: $\chi^2 = 17.89$, $df = 16$ ($P = 0.33$), $I^2 = 10.6\%$

Test for overall effect: $Z = 1.69$ ($P = 0.09$)

0.11 [-0.02, 0.23]

-4 -2 0 2 4

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GRAZIE PER L'ATTENZIONE

Simposio 15

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