



Dinner Symposium 2 - GH e cuore



Bari,
7-10 novembre 2013



La cardiopatia nell' ipopituitarico

E. De Menis

Dipartimento Medicina Clinica - Montebelluna



ORMONI E CUORE



Bari,
7-10 novembre 2013

TIROIDE

CORTICOSTEROIDI

ORMONI SESSUALI

GH/IGF-I

CONSEGUENZE

Compromissione capacità di esercizio fisico, riduzione Qualità di vita

Cardiovascolare globale: rischio eventi cardiovascolari

PROBLEMI METODOLOGICI

Età insorgenza del deficit (CoGHD vs. AoGHD)

Causa del deficit

Durata del deficit

Severità del deficit

Dose di rhGH, durata del trattamento

Terapie concomitanti



Funzione cardiaca



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METODOLOGIA

- ECOCARDIOGRAFIA
- METODICHE ANGIOGRAFICHE
RADIONUCLEARI
- MRI
- TC

PARAMETRI ANALIZZATI

- VOLUMI E MASSE VENTRICOLARI
- FUNZIONE SISTOLICA
(CONTRATTILITA', FRAZIONE
EIEZIONE, GITTATA SISTOLICA)
- FUNZIONE DIASTOLICA
(RIEMPIMENTO VENTRICOLARE)

A RIPOSO, DOPO SFORZO

LVMI

- RIDUZIONE

FRAZIONE DI EIEZIONE basale e da esercizio

- RIDUZIONE

FUNZIONE DIASTOLICA

- RIDOTTA

GITTATA CARDIACA

- RIDUZIONE

CAPACITA' ESERCIZIO FISICO

- RIDOTTA



FUNZIONE CARDIACA



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Colao JCEM 2002 179

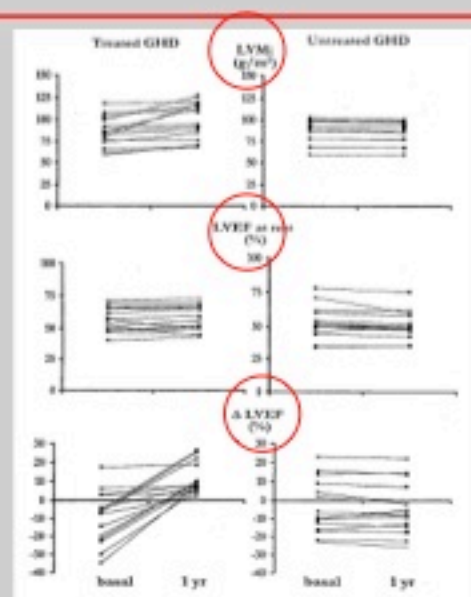
AoGHD

12 mesi: 15 Untreated vs. 15 treated. vs. 30 controls

TREATED: miglioramento dei parametri

UNTREATED: peggioramento della Left Ejection

Fraction da sforzo e capacità di esercizio



Colao JCEM 2002 180

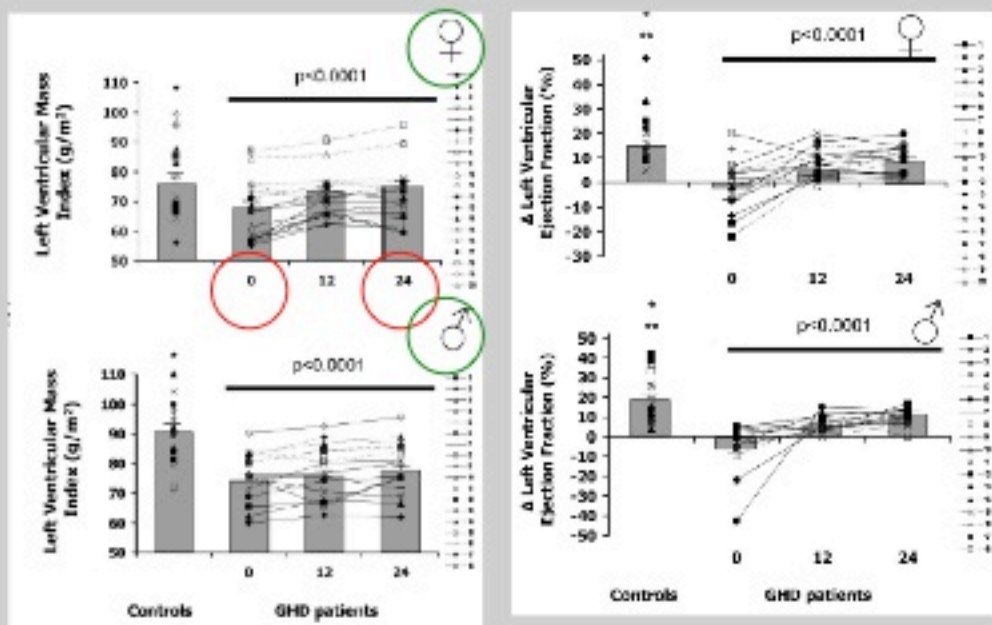
AoGHD

24 mesi: 36 giovani VS. 36 controlli

LVM i ridotto rispetto ai controlli, ma si normalizza dopo 2 anni di terapia

Delta fra Left Ejection fraction basale e durante esercizio ridotta, migliora ma rimane ancora ridotta

Non differenze significative seso





CORRELAZIONE FRA SEVERITA' DEFICIT DI GH E FUNZIONE CARDIACA



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Colao JCEM 2004 167

100 ipopituitarici

LVEF: ridotta a riposo e dopo sforzo

LVEF a picco di esercizio normale:

- 21% GHD severo
- 56% GHD parziale
- tutti in non GHD

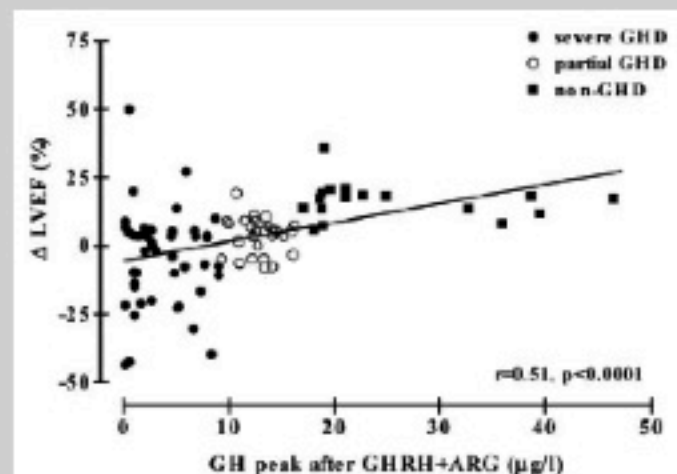
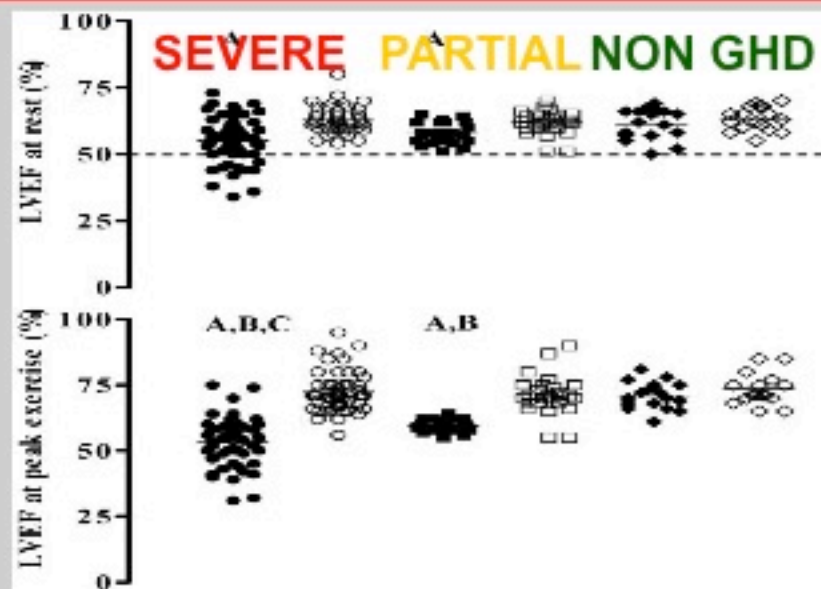
Correlazione con picco GH

PFR diastolico (peak filling rate: riempimento diastolico): ridotta a riposo e dopo sforzo

CAPACITA' DI ESERCIZIO: ridotta capacità (watts) e durata (sec)

Capalbo JCEM 2009 151

Anche in GHD pediatrici conferma correlazione fra severità del deficit di GH e alterazioni cardiache (massa e contrattilità)





TRANSIZIONE



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Colao JCEM 2002 187

0 = TRATTAMENTO CON rhGH

Normali LVMI e LVEF

Lieve deficit diastolico

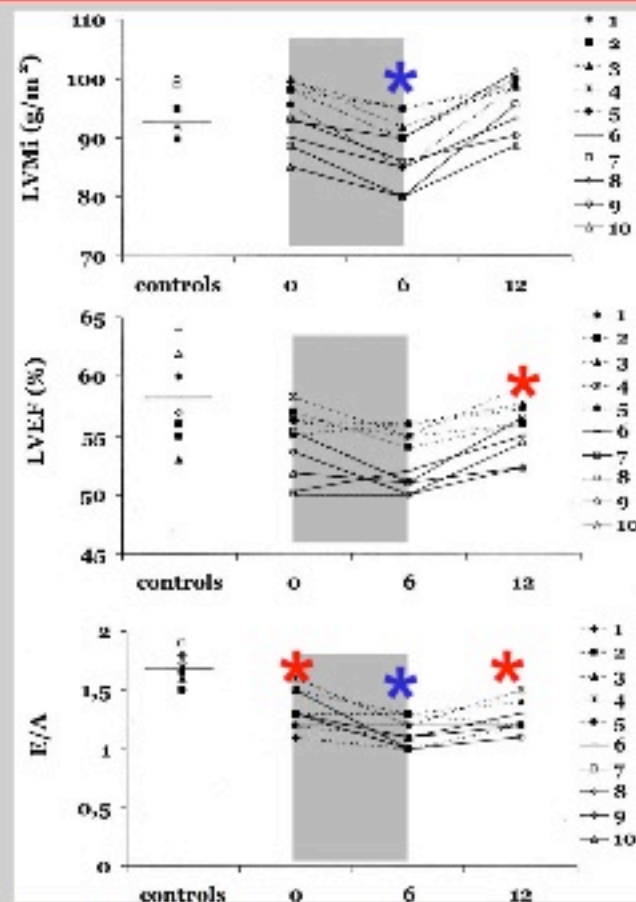
6 = MESI DI SOSPENSIONE

Peggioramento dei parametri

Riduzione LVMI;

12 = RIPRESA TRATTAMENTO

Miglioramento, anche se mancata normalizzazione funzione diastolica



Growth Horm IGF Res. 2011 April ; 21(2): 81-88. doi:10.1016/j.ghr.2011.01.003.

Early-onset Growth Hormone Deficiency Results in Diastolic Dysfunction in Adult-life and is Prevented by Growth Hormone Supplementation

L. Groban^{1,2}, M. Lin¹, K.A. Kassik¹, R.L. Ingram², and W.E. Sonntag³

MODELLO SPERIMENTALE

Colao JCEM 1999 69

11 pazienti con deficit di GH di (60-72 aa) comparati con 11 controlli

	Controls (n = 11)	Patients (n = 11)	P value
Mean age (yr)	63.5 ± 0.9	64.7 ± 1.0	0.4
BMI (kg/m ²)	24.9 ± 1.2	26.1 ± 0.6	0.4
Peak GH levels after ARG+GHRH test (μg/L)	23.2 ± 2.3	2.2 ± 0.7	0.000
Plasma IGF-I (μg/L)	71.8 ± 7.5	49.2 ± 8.5	0.06
Disease duration (yr)		10.5 ± 1.0	
Echocardiography study			
Left ventricular mass index (g/m ²)	99.9 ± 1.5	97.6 ± 1.8	0.3
Interventricular septum thickness (mm)	9.1 ± 0.2	9.1 ± 0.2	1
Left ventricular posterior wall thickness (mm)	9.0 ± 0.2	9.1 ± 0.2	0.7
Equilibrium radionuclide angiography study			
Systolic blood pressure (mm Hg)			
At rest	125.4 ± 1.2	127.3 ± 7.1	0.8
Exercise	150.4 ± 2.1	176.4 ± 9.3	0.01
Diastolic blood pressure (mm Hg)			
At rest	80.9 ± 1.5	80.9 ± 4.1	1.0
Exercise	100.4 ± 4.4	101.8 ± 3.9	0.8
Heart rate (beats/min)			
At rest	72.0 ± 3.9	66.7 ± 2.3	0.3
Exercise	130.0 ± 6.2	127.8 ± 7.2	0.8
Left ventricular ejection fraction (%)			
At rest	63.2 ± 2.5	57.1 ± 2.1	0.07
Exercise	73.3 ± 3.0	51.0 ± 2.5	0.000
Exercise-induced changes (%)	15.8 ± 3.5	-10.2 ± 4.0	0.000
Left ventricular peak ejection rate (EDV/s)	3.7 ± 0.4	3.3 ± 0.2	0.4
Peak rate of left ventricular filling			
Peak filling rate (EDV/s)	2.6 ± 0.2	2.5 ± 0.2	0.7
Peak filling rate (SV/s)	4.0 ± 0.3	4.3 ± 0.3	0.5
Peak filling rate/peak ejection rate	0.7 ± 0.000	0.7 ± 0.000	0.999
Exercise duration (min)	9.1 ± 0.2	7.2 ± 0.1	0.000
Exercise capacity (watts)	97.7 ± 5.3	76.3 ± 4.0	0.004

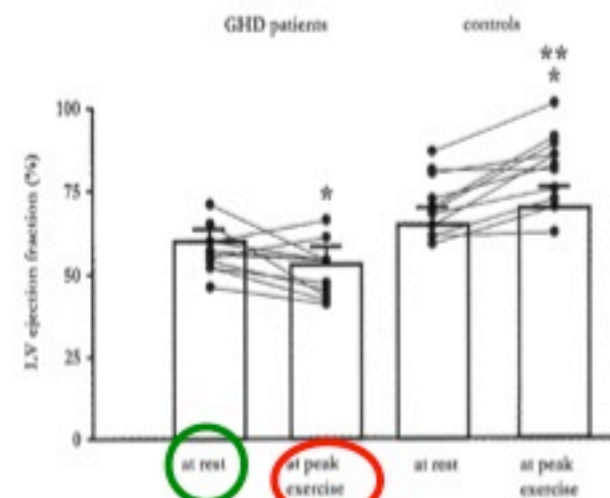


FIG. 1. LV ejection fraction at rest and at peak exercise in GHD patients and controls measured by radionuclide angiography. The bars represent the mean ± SEM. *, $P < 0.05$ compared to LV ejection fraction at rest; **, $P < 0.001$ to LV ejection fraction in GHD patients.

Massa cardiaca e funzione diastolica sovrapponibili

La performance cardiaca (frazione di eiezione ventricolare sx) durante esercizio fisico e capacità di esercizio fisico ridotte



ELDERLY GHD: EFFECT OF GH THERAPY



Bari,
7-10 novembre 2013

Effects of GH replacement therapy on cardiac parameters in GH-deficient elderly patients during a 6-month placebo-controlled period

	Placebo			GH		
	Basal	Month 6	P basal vs month 6	Basal	Month 6	P basal vs month 6
VTE, cm	23 (13-31)	20 (14-28)	NS	22 (17-28)	22 (14-27)	NS
AV-plane movement, mm	12.7 (8.9-15.2)	12.3 (7-16.7)	NS	12.6 (10-15.3)	12.2 (10-14)	NS
Fractional shortening percentage	35 (26-48)	36 (14-47.6)	NS	34 (15.6-45)	36 (20.5-48)	NS
EF slope, mm/s ²	283 (161-1000)	256 (152-684)	NS	250 (152-402)	167 (176-492)	NS
E-wave, cm/s	66 (47-117)	71 (48-120)	NS	64 (48-80)	60 (45-80)	NS
E/A ratio	0.9 (0.6-1.2)	0.9 (0.7-1.3)	NS	0.9 (0.6-1.2)	0.8 (0.7-1.0)	NS
S/D ratio	1.4 (0.9-1.7)	1.3 (0.7-1.6)	NS	1.6 (1-2.4)	1.4 (1.1-1.8)	NS
LVIDd, mm	50 (40-62)	51 (40-61)	NS	50 (41-62)	50 (42-62)	NS
LVIDs, mm	33 (23-45)	34 (25-49)	NS	34 (25-42)	33 (26-44)	NS
Posterior wall dimension, mm	9 (7-13)	11 (6-13)	NS	11 (7-15)	11 (7-15)	NS
Septum dimension, mm	11.2 (9-13.6)	11 (9-14.4)	NS	11.6 (7-14.2)	11.3 (7-14.5)	NS
Left atrial dimension, mm	37 (30-44)	36 (27-44)	NS	36 (31-43)	36 (31-43)	NS
Heart rate at rest, bpm	70 (47-102)	66 (45-101)	NS	76 (48-101)	67 (50-85)	0.029
Heart rate at max exercise, bpm	147 (112-179)	138 (113-177)	NS	142 (102-162)	148 (107-166)	0.405
Max work load, Watts	126 (76-210)	140 (80-200)	NS	120 (103-190)	169 (110-230)	0.012

VTE, mitral outflow tract integral; EF slope, the diastolic closing motion of the mitral valve leaflets; E-wave, rapid filling wave; E/A ratio, rapid filling wave/atrial filling wave; S/D ratio, pulmonary vein systolic wave/pulmonary vein diastolic wave; LVIDd and LVIDs, left ventricular interior diameter at diastole and systole, respectively. Values are given as median and range.

Elgzyri Clin Endocrinol 2004 68

Dopo 6 e 12 mesi di terapia nessuna variazione significativa della morfologia e funzione cardiaca, della frequenza cardiaca, della pressione arteriosa, ma miglioramento della capacità di esercizio fisico (almeno a 6 mesi)

Table 3 The effects on cardiac parameters of GH replacement for 12 months to GH-deficient elderly patients

	Basal	Month 6	P basal vs. month 6	Month 12	P basal vs. month 12	ANOVA
AV-plane movement, mm	12.5 ± 4	12.3 ± 0.3	NS	12.2 ± 0.3	NS	NS
Fractional shortening percentage	33 ± 2	36 ± 2	NS	41 ± 3	NS	NS
EF slope, mm/s ²	313 ± 23	291 ± 14	NS	325 ± 18	NS	NS
E/A ratio	1 ± 0.04	0.9 ± 0.05	NS	1 ± 0.05	NS	NS
S/D ratio	1.4 ± 0.07	1.4 ± 0.06	NS	1.4 ± 0.08	NS	NS
LVIDd, mm	50 ± 1	50 ± 1	NS	50 ± 1	NS	NS
LVIDs, mm	33 ± 1	31 ± 1	NS	32 ± 1	NS	NS
Posterior wall dimension, mm	10 ± 0.3	10 ± 0.3	NS	11 ± 0.3	NS	NS
Septum dimension, mm	11 ± 0.3	11 ± 0.3	NS	11 ± 0.3	NS	NS
Left atrial dimension, mm	37 ± 1	37 ± 1	NS	36 ± 1	NS	NS
Max work load, Watts	142 ± 6	151 ± 7	0.014	150 ± 8	NS	0.017
Diastolic BP at rest, mmHg	84 ± 2	83 ± 2	NS	83 ± 2	NS	NS
Systolic BP at rest, mmHg	147 ± 4	148 ± 4	NS	148 ± 4	NS	NS
Systolic BP at max workload, mmHg	212 ± 6	218 ± 5	NS	215 ± 5	NS	NS

E/A ratio, rapid filling wave/atrial filling wave ratio; S/D ratio, pulmonary vein systolic wave/pulmonary vein diastolic wave ratio; LVIDd and LVIDs, left ventricular interior diameter at diastole and systole, respectively. Values are given as mean ± SEM.

Andreassen Pituitary 2013 170

16 pz. AoGHD

Comparazione a controlli

Comparazione dopo 12 mesi terapia
(dosi fisiologiche)

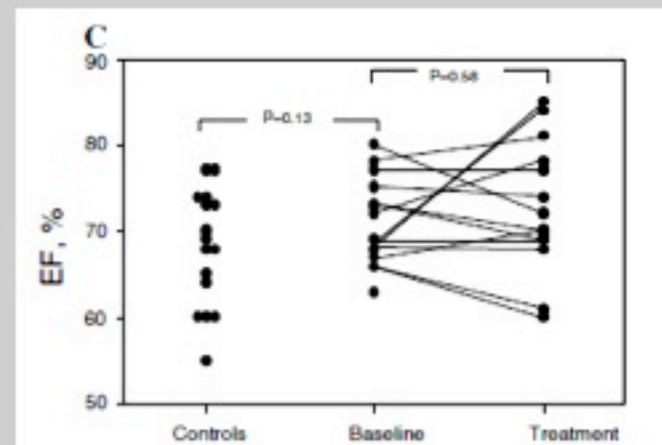
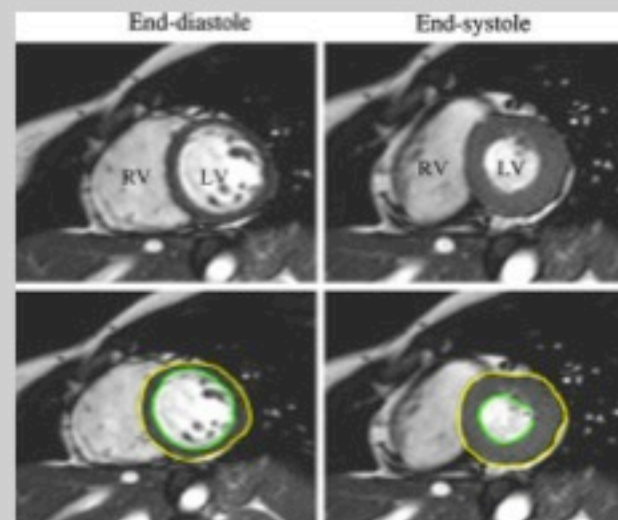
MRI

LVM index: nessuna differenza

Ejection Fraction: nessuna differenza

Cardiac Output: nessuna differenza

BNP: nessuna differenza





FUNZIONE CARDIACA: pretrattamento



Bari,
7-10 novembre 2013

RIDUZIONE

**AMATO (JCEM 1993); COLAO (2001 JCEM); COLAO (JCEM 2005) SALERNO
(156, 2006); CAPALBO (151, 2009)**

SARTORIO (1997)

PINCELLI (SCACCHI JEI 2003)

FEINBERG (2003)

ERDOGAN (2004)

VALCAVI 1995

FORT 1995

LINK 2001

NON VARIAZIONI

THUESEN (1994),

CLIMENT (2006);

DE GREGORIO (2006)

ANDREASSEN (170, 2013)



FUNZIONE CARDIACA: dopo trattamento



Bari,
7-10 novembre 2013

MIGLIORAMENTO

AMATO 1993; COLAO 2001; SALERNO 156, 2006 E CAPALBO 151, 2009

CUNEO 1991

SARTORIO 1997

CIDAHLL 1994

VALCAVI 1995

FORT 1995

LINK 2001

NON EFFETTI

THUESEN 1994

BESHYAM 1994

NASS 1995

BAUM 1996

TER MAATEN 1999

EZZAT 2002

ANDREASSEN 170, 2013



FUNZIONE CARDIACA: SHORT TERM TREATMENT



Bari,
7-10 novembre 2013

MAISON Circulation 2003 100

METANALISI 16 studi

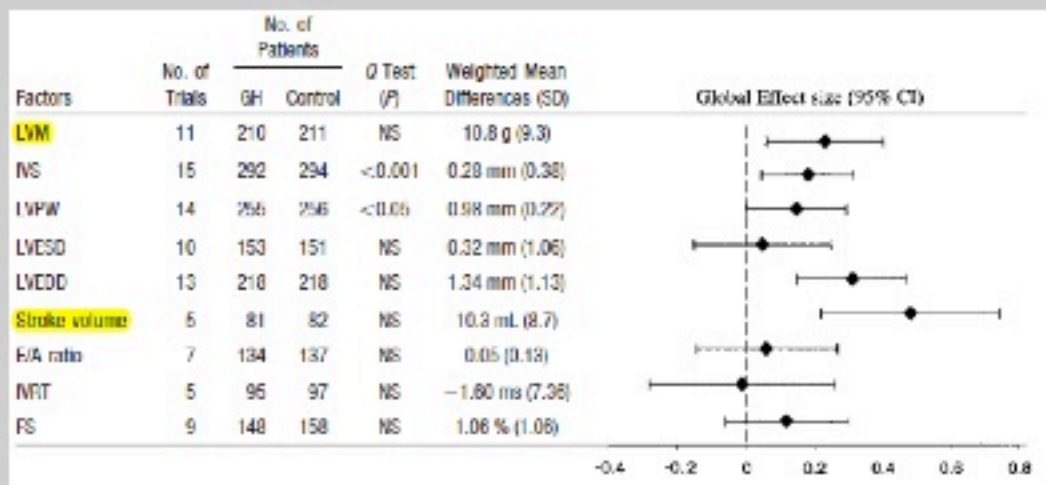
Aumento modesto **LVM** (10 g),
del setto, della parete posteriore

Aumento modesto **cardiac output**
(10 ml)

Tendenza a miglioramento della
contrattilità

Non variazioni della **funzione diastolica**

Risultati dipendenti dalla dose sostitutiva: dosi fisiologiche l'unico parametro realmente modificato è un lieve aumento della massa ventricolare sx.





FUNZIONE CARDIACA: LUNGO TERMINE (> 5 anni)



Bari,
7-10 novembre 2013

Appelman-Dijkstra EJE 2013

GIBNEY JCEM 1999

10 pz. trattati vs.

10 non trattati

10 anni

	GH-treated group		Untreated group	
	Baseline	10 yr	Baseline	10 yr
Systolic blood pressure (mm Hg)	113.7 ± 2.9	123.0 ± 3	118.0 ± 4.6	123.4 ± 7.8
Diastolic blood pressure (mm Hg)	78.5 ± 4.3	79.2 ± 2.8	77.2 ± 2.5	74.2 ± 3.5
End diastolic diameter (cm)	4.9 ± 0.1	5.1 ± 0.2	5.0 ± 0.2	5.1 ± 0.1
End systolic diameter (cm)	3.3 ± 0.2	3.2 ± 0.2	3.1 ± 0.1	3.2 ± 0.1
Left ventricular mass (g)	193.8 ± 15.6	225.7 ± 22.7	222.0 ± 16.2	234.3 ± 22.2

Ecocardiografia (eseguita con due strumenti diversi)

end-systolic, end-diastolic diameters e LVM

nessuna differenza fra trattati e no: nessuna differenza fra valori prima e dopo trattamento riguardo

CHRISOULIDOU JCEM 2000

12 trattati vs.

10 non trattati

> 7 anni

TABLE 7. Echocardiographic data

	Group A (n = 12)		Group D (n = 10)	
	Baseline	Repeat	Baseline	Repeat
IVRT (ms)	97.8 ± 17.1	89.1 ± 14.4	103.0 ± 20.4	103.8 ± 29.3
LVMI (g/m ²)	96.7 ± 18.8	97.7 ± 14.3	89.7 ± 14.7	100.4 ± 23.5
E/A	1.31 ± 0.28	1.07 ± 0.33 ^a	1.06 ± 0.36	0.92 ± 0.39
Exercise time (min)	11.0 ± 3.0	10.8 ± 2.7	8.2 ± 3.0	9.5 ± 2.4

Data are the mean ± SD. IVRT, isovolumic relaxation time; LVMI, left ventricular mass index; E/A, peak early to late left ventricular filling ratio.

^a P < 0.05 for baseline vs repeat in each group.

LV MASS INDEX non varia nei trattati (gruppo a);

DEFICIT DIASTOLICO si riduce, ma non differisce rispetto ai non trattati (gruppo D)

TREADMILL: non variazioni di durata, mentre rate-pressure product si riduce con terapia, ma non differenze con i non trattati



ARITMIE-VALVULOPATIE CARDIOPATIA ISCHEMICA



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ARITMIE- VALVULOPATIE: non dati

CARDIOPATIA ISCHEMICA

FRAMINGHAM SCORE

**Aumentato e si riduce con terapia (Abdu Clin Endocrinol
2004): ruolo assetto lipidico**

CORONARY CALCIFICATIONS (CT)

**Aumento, anche rispetto a controlli con medesime
comorbidity, ed anche in pazienti con basso FS
(Cannavò JEI 2011)**



CRANIOPHARINGIOMA



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Mortality

Pediatric series: survival 65–100% at 10 yr

Adult/mixed series: survival 40–93% at 10 yr

SMR 3-9 (*Sherlock End Rev 2010*)

70 pts: expected 2.4 deaths - observed 24 deaths

(*Crowley, Clin End 2009*)

Causes

Tumor itself

Cardio-cerebrovascular

(hormonal replacement: oestrogens, GH, cortisol;

radiotherapy...)

Respiratory

(SAS, infections, embolism..)

ADVERSE METABOLIC PROFILE

SLEEP RELATED DISORDERS

**INTENSIVE
DIAGNOSTIC
WORK-UP**



ARTERIE PERIFERICHE



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DISFUNZIONE ENDOTELIALE

IMT (INTIMA-MEDIA THICKNESS)

PLACCHE ATEROSCLEROTICHE



DISFUNZIONE ENDOTELIALE

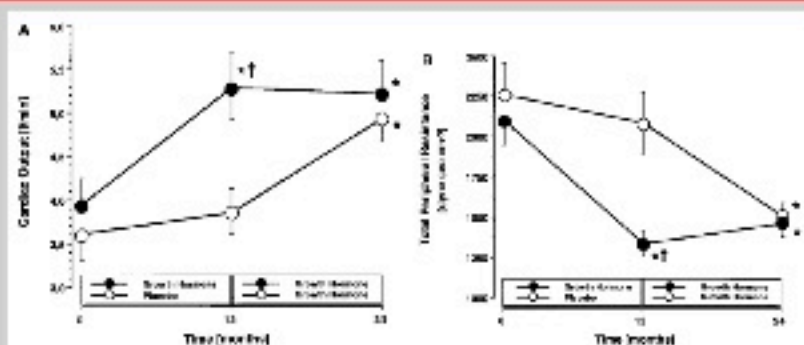
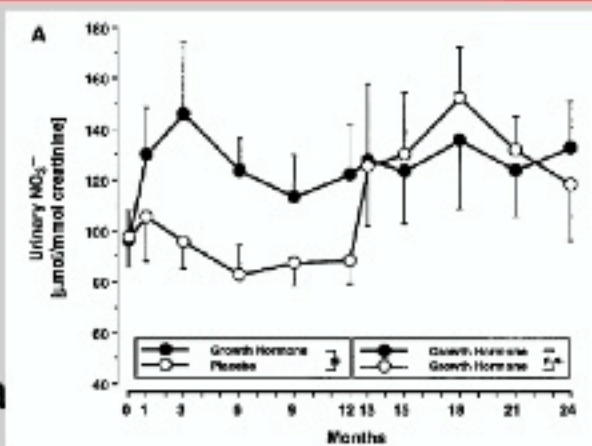


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Boger JCI 1996

Produzione NO

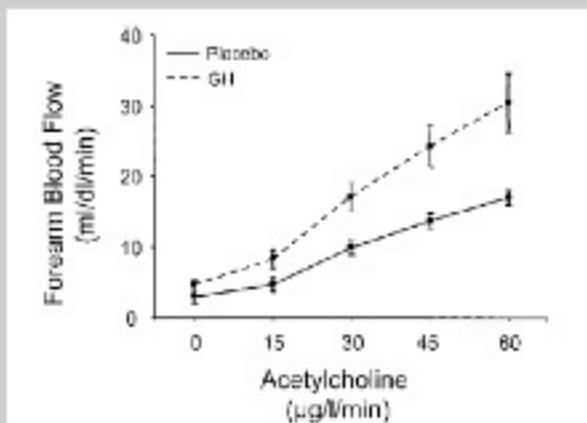
Effetto della terapia



Napoli JCEM 2003

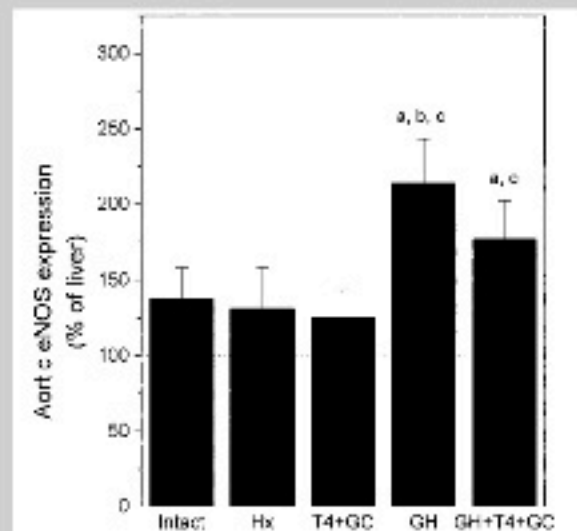
Infusione periferica

GH: produzione NO e flusso



Wickman EJE 2002

Espressione eNOS





DISFUNZIONE ENDOTELIALE



Bari,
7-10 novembre 2013

CoGHD

Lanes JCEM 2005 92

12 Untreated

10 Treated

14 Controls

TABLE 2. Interventricular septal thickness, left ventricular posterior wall thickness, left ventricular mass, left ventricular ejection fraction, and systolic and diastolic volumes, carotid artery intima-media thickness, increase in brachial artery diameter and blood flow, and epicardial tissue in untreated and GH-treated GHID adolescents and healthy controls

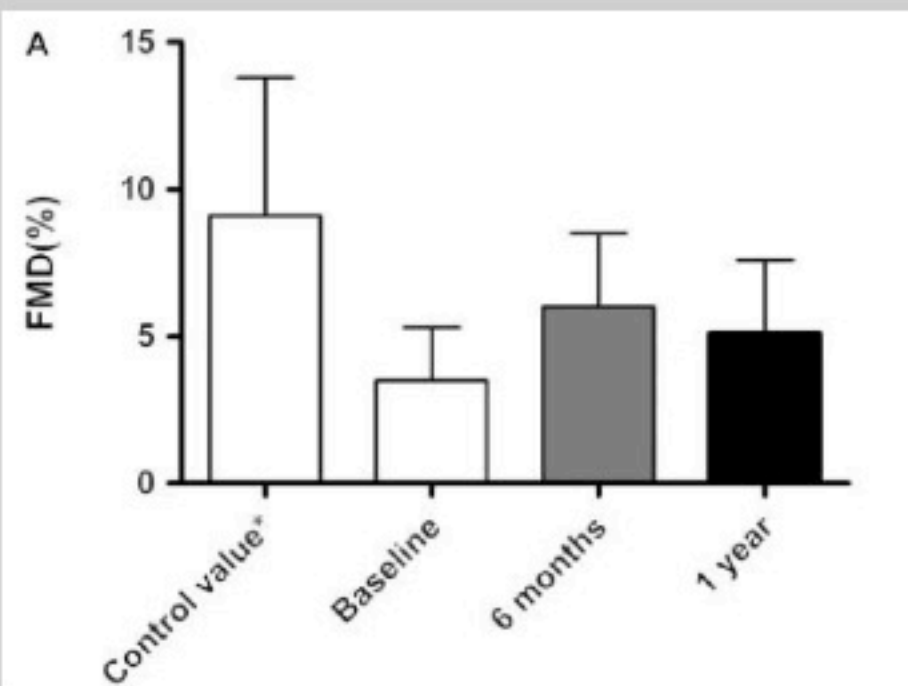
	Untreated GHID (n = 12)	Treated GHID (n = 10)	Non-GHID controls (n = 14)	P
Interventricular septal thickness (mm)	6.9 ± 1.1	6.9 ± 0.6	7.0 ± 1.1	NS
Left ventricular posterior wall thickness (mm)	6.5 ± 1.1	6.6 ± 1.3	6.9 ± 1.3	NS
Left ventricular mass (g/m ²)	42.2 ± 2.4	43.5 ± 6.3	49.9 ± 9.0	<0.05*
Left ventricular ejection fraction (%)	64.9 ± 5.4	68.6 ± 8.0	65.0 ± 5.0	NS
End systolic volumes (ml)	19.0 ± 7.9	16.5 ± 3.7	24.2 ± 8.7	<0.05*
End diastolic volumes (ml)	55.0 ± 25.2	52.1 ± 8.6	68.2 ± 21.0	<0.05*
Carotid artery intima-media thickness (mm)	0.9 ± 0.2	0.7 ± 0.1	0.8 ± 0.2	NS
Increase in brachial artery diameter (%)	15.4 ± 1.1	23.7 ± 1.3	29.8 ± 2.1	<0.02*
Increase in brachial artery blood flow (%)	179 ± 69.0	253.2 ± 43.1	144 ± 70.7	<0.001
Epicardial adipose tissue (mm)	0.76 ± 1.06	0.62 ± 0.51	0.65 ± 0.75	<0.001

AoGHD

Pfeifer JCEM 1999 190

VAN DER KLAUW EJE 2008 199

12 pazienti trattati per 1 anno



(FMD: flow-mediated dilatation)



IMT (INTIMA-MEDIA THICKNESS)



Bari,
7-10 novembre 2013

CoGHD Non differenza

Lanes JCEM 2005 92

Treated vs. Untreated

Colao JCEM 2005 181

Transizione: dopo 6 mesi di terapia

TABLE 2. Interventricular septal thickness, left ventricular posterior wall thickness, left ventricular mass, left ventricular ejection fraction, end systolic and diastolic volumes, carotid artery intima-media thickness, increase in brachial artery diameter and blood flow, and epicardial tissue in untreated and GH-treated GHD adolescents and healthy controls

	Untreated GHD (n = 12)	Treated GHD (n = 10)	Non-GHD controls (n = 14)	P
Interventricular septal thickness (mm)	6.9 ± 1.1	6.9 ± 0.6	7.0 ± 1.1	NS
Left ventricular posterior wall thickness (mm)	6.5 ± 1.1	6.6 ± 1.3	6.9 ± 1.3	NS
Left ventricular mass (g/m ²)	42.2 ± 2.4	48.6 ± 6.8	49.9 ± 9.0	<0.05*
Left ventricular ejection fraction (%)	64.9 ± 5.4	68.8 ± 3.0	65.0 ± 5.0	NS
End systolic volume (ml)	19.0 ± 7.9	18.6 ± 3.7	24.2 ± 9.7	<0.05*
End diastolic volume (ml)	55.0 ± 25.2	52.1 ± 8.6	68.2 ± 21.0	<0.05*
Carotid artery intima-media thickness (mm)	0.9 ± 0.2	0.7 ± 0.1	0.8 ± 0.2	NS
Increase in brachial artery diameter (%)	16.4 ± 1.1	28.7 ± 1.8	29.8 ± 2.1	<0.02*
Increase in brachial artery blood flow (%)	179 ± 60.0	268.2 ± 43.1	164 ± 70.7	<0.001*
Epicardial adipose tissue (mm)	2.76 ± 1.36	2.39 ± 0.51	2.25 ± 0.75	<0.02*

AoGHD Riduzione

Colao JCEM, 2008 102

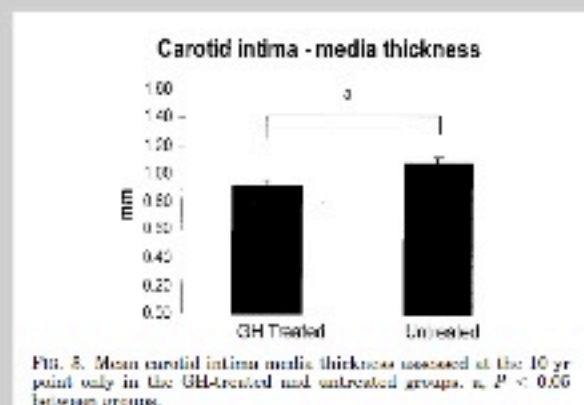
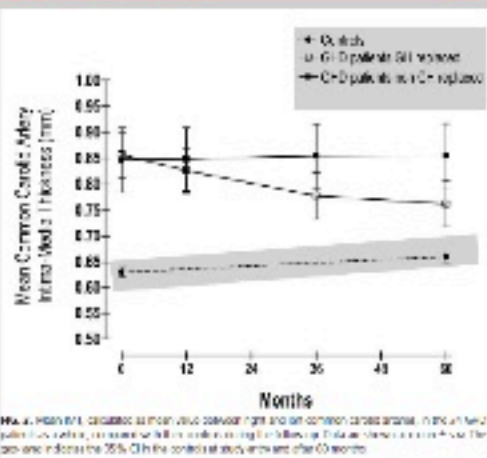
22 trattati 13 untreated

5 anni

Gibney JCEM 1999 164

10 pz. trattati vs. 10 non trattati

10 anni





PLACCHE ATEROSCLEROTICHE



Bari,
7-10 novembre 2013

Markussis Lancet 1992

Colao JCEM 2008 102

- non variazioni delle placche a 5 anni di terapia

Pfeiffer JCEM 1999 190

- non trova placche

Leonsson Clin Endoc 2002 186

- nessuna differenza nelle placche (e IMT) se si considera BMI dei controlli



FATTORI DI RISCHIO CARDIOVASCOLARE



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ISSN 1120-8479
Printed in Italy

The Journal of Clinical Endocrinology & Metabolism (JCEM) 2013
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doi:10.1210/1.2013-0001

European Journal of Endocrinology (2013) 169 R1–R14

ISSN 0954-6820

Impact of Growth Hormone (GH) Treatment on Cardiovascular Risk Factors in GH-Deficient Adults: A Metaanalysis of Blinded, Randomized, Placebo-Controlled Trials

PATRICK MAISON, SIMON GRIFFIN, MAHMOUD NIEHLIK-BIGLALI, NABILA HADDAD, BEVERLY BALKAU, and PHILIPPE CHANSON

REVIEW
THERAPY OF ENDOCRINE DISEASE

Long-term effects of recombinant human GH replacement in adults with GH deficiency: a systematic review

Natasha M Appelman-Dijkstra*, Kim M J A Claessen*, Ferdinand Roelfsema, Alberto M Pereira and Niels R Biermas

PRESSIONE ARTERIOSA

GHD: aumento pressione diastolica e sistolica (?)

GHD TREATMENT

- short term: no variation of systolic BP, slight decrease of diastolic BP (-1.8 mmHg)
- long-term: no variation of systolic BP, no significant effect on diastolic BP (except 1 study: *CHRISOULIDOU JCEM 2000*)

ASSETTO LIPIDICO

METABOLISMO GLUCIDICO

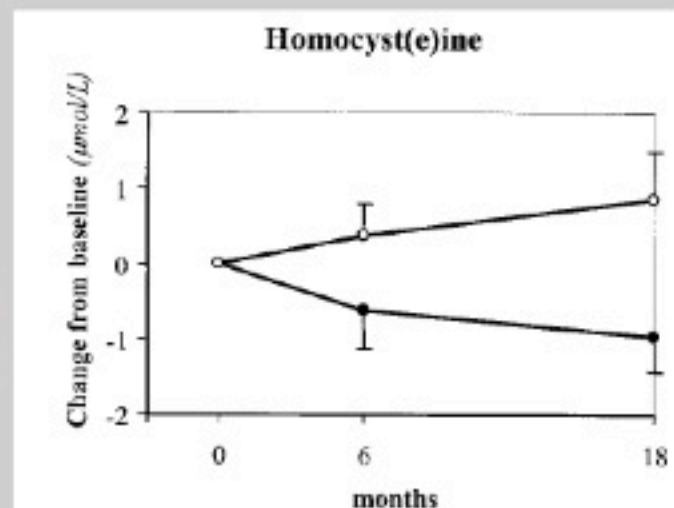
ALTRI MARKERS

OMOCISTEINA

AoGHD males

Sesmi 95 JCEM, 2001

- aumentati nel GHD e si riducono nei trattati



G. I. Changes in homocyst(e)ine levels in the two treatment groups. ●, GH-treated patients; ○, placebo-treated. The *P* value

AoGHD females

Beauregard 177 JCEM
2008

- nessun effetto



MARKERS RISCHIO CV



Bari,
7-10 novembre 2013

Markers di *acute phase reaction*: PCR, SAA
Citochine: ILE-1; ILE-6; TNF α

Dati sperimentali

Molecole di *adesione*: VCAM; E-Selectin

Fattori della *coagulazione*: ridotta fibrinolisi,
correzione con terapia

Growth hormone replacement normalizes impaired fibrinolysis:
New insights into endothelial dysfunction in patients with
hypopituitarism and growth hormone deficiency Growth Hormone & IGF Research 23 (2013) 243-248

D. Miljic ^{a,*}, P. Miljic ^b, M. Doknic ^a, S. Pekic ^a, M. Stojanovic ^a, G. Cvijovic ^a, D. Micic ^a, V. Popovic ^a



MARKERS RISCHIO CV



Bari,
7-10 novembre 2013

PCR

AoGHD males

Sesmi Ann I Med 2000 141



AoGHD females

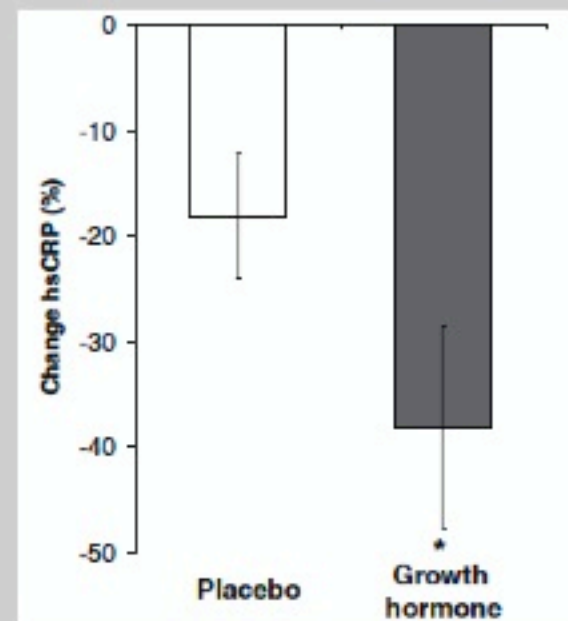
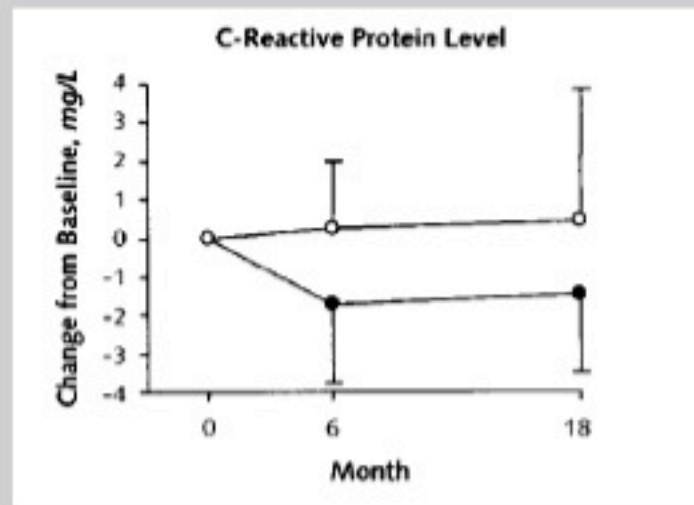
Beauregard JCEM 2008 177

Bollerslev EJE 2006 183 : riduzione del 40% (correlazione con IGF-I)

Leonsson CE 2003 192

- aumento rispetto ai controlli non obesi, ma non agli obesi

Bona





MARKERS RISCHIO CV



Bari,
7-10 novembre 2013

ILE-1

ILE-6

AoGHD

Sesmiolo Ann Int Med 2000

Serri JCEM 1999

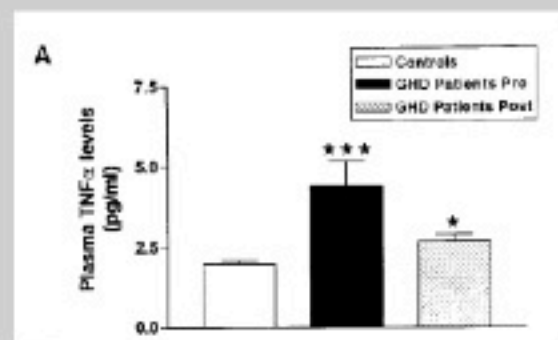
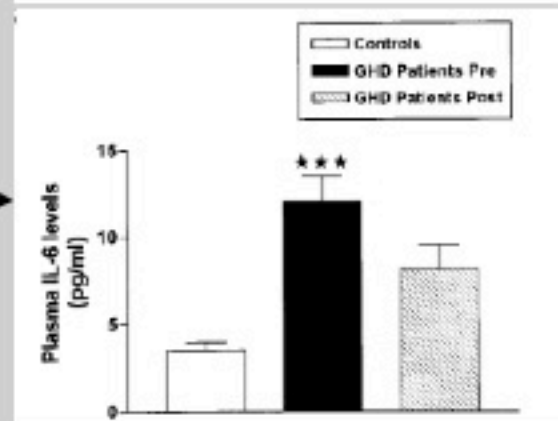
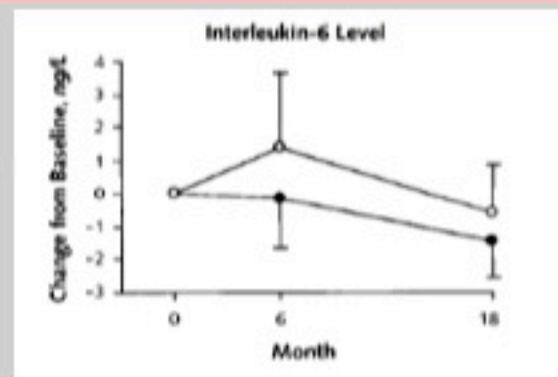
Leonsson CE 2003

Non dipende da BMI

TNF- α

AoGHD

Serri JCEM 1999





MORTALITA IPOPITUITARISMO prima di rhGH



Bari,
7-10 novembre 2013

ROSEN 1990

Bulow Clin End 1997

SMR cardiovascolare globale 1.7

SMR cardiaca 1.4

SMR cerebrovascolare 3.39 (femmine 4.9)

Tomlinson Lancet 2001

SMR 1.87

SMR cardiovascolare 1.8

SMR respiratoria 2.7

SMR cerebrovascolare 2.4

Ipotesi eccesso mortalità: **RT**, scorretta t. sostitutiva con **corticosteroidi**, mancata terapia sostitutiva con **steroidi sessuali**, mancata sostituzione con **GH**



MORTALITA' IPOPIUITARISMO dell' Adulto in trattamento con rhGH



Bari,
7-10 novembre 2013

Erfurth JCEM 2013 (NATIONAL REGISTRIES + PMS)

Van Buderen *Dutch Reg. JCEM 2011*

Gaillard *KIMS EJE 2012*

Burman *KIMS Swed JCEM 2013*

Hartman *Hypoccs USA JCEM 2013*

Mortalità normale nei maschi, lievemente aumentata nelle **femmine**

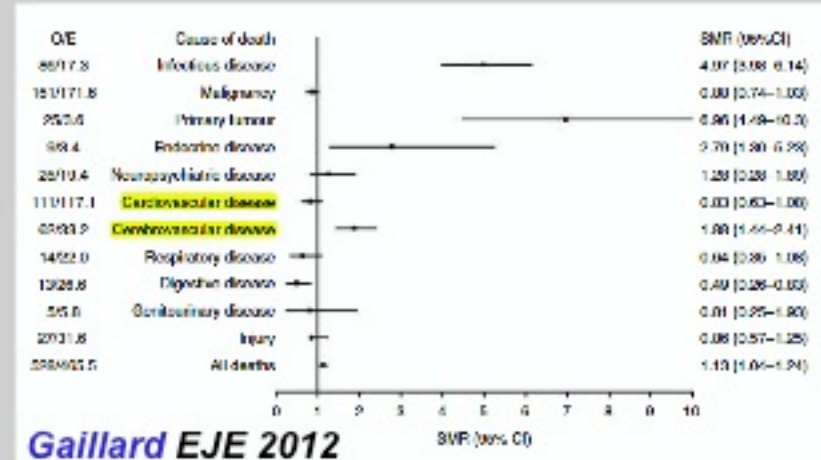
Aumento eventi **cerebrovascolari** (correlazione con RT)

Aumento mortalità **infettiva** in ACTH deficient

Mortalità legata a tipo di **neoplasia** (estensione tumore, craniofaringioma)

Non aumento di mortalità legata a neoplasie, eccetto **neoplasie intracraniche** RT

Overall Mortality, SMR (95% CI)	Higher Mortality in Females vs Males/Young Age at Disease Onset	Increased Mortality in Cerebrovascular Disease/SMR (95% CI)
NP, 1.27 (1.04-1.56)	Yes/yes	Yes/2.54 (1.41-4.59)
GP, 1.13 (1.04-1.24)	Yes/yes	Yes/1.88 (1.44-2.41)
NP, 1.42 (1.18-1.70)	Yes/yes	No
NP, 0.86 (0.59-1.21)	No/no	No



FATTORI CORRELATI A MIGLIOR SOPRAVVIVENZA

Terapia **neurochirurgica** - Minor utilizzo di **radioterapia**

Farmaci **anti-ipertensivi** e **ipolipemizzanti**

Miglior terapia **sostitutiva** con estrogeni, corticosteroidi - Terapia con **rhGH** ?



LINEE GUIDA e CUORE



Bari,
7-10 novembre 2013

SPECIAL FEATURE

Clinical Practice Guideline

Evaluation and Treatment of Adult Growth Hormone Deficiency: An Endocrine Society Clinical Practice Guideline

JCEM 2011

Mark E. Molitch, David R. Clemmons, Saul Malozowski, George R. Merriam, and Mary Lee Vance

3.1 We recommend that GH therapy of GH-deficient adults offers significant clinical benefits in body composition and **exercise capacity** (1/⊕⊕⊕⊕).

3.4 We suggest that GH therapy of GH-deficient adults improves several **cardiovascular surrogate outcomes**, including **endothelial function**, **inflammatory cardiovascular biomarkers**, **lipoprotein metabolism**, **carotid intima-media thickness (IMT)**, and **aspects of myocardial function**, but tends to increase **insulin resistance** (2/⊕⊕⊕⊕).