

Clinical relevance of cardiac structure and function abnormalities in patients with Cushing's syndrome before and after cure.

Toja PM, Branzi G, Ciambellotti F, Radaelli P, De Martin M, Lonati LM, Scacchi M, Parati G, Cavagnini F, Pecori Giraldi F.

Clin Endocrinol (Oxf) 2012, 76: 332-338

comorbidità cardiovascolari

Cushing's Syndrome is associated with an increased risk for abnormalities of cardiac mass, which ameliorates, but does not fully disappear after remission.

Diastolic blood pressure (mm Hg)	15.9 ± 2.6	14.9 ± 2.9	13.4 (7-15)	82.2 ± 2.5	82.0 ± 2.5	<0.05	NS
Diastolic blood pressure (mm Hg)	1.71 (1.07-2.28)	1.61 (1.12-2.12)	1.21 (0.79-1.47)	94.7 ± 2.0	94.7 ± 2.0	<0.001	NS
Fasting blood glucose (mg/dL)	2.92 ± 0.55	2.97 ± 0.54	2.74 (1.62-3.59)	120.5 ± 1.8	120.5 ± 1.8	NS	NS
Serum triglycerides levels (mg/dL)	0.5 ± 0.1	0.44 ± 0.1	0.3 (0.07-0.48)	189.5 ± 8.9	189.5 ± 8.9	<0.05	NS
Total blood cholesterol levels (mg/dL)	5.2 ± 1.2	5.2 ± 1.2	4.9 ± 0.9	120.5 ± 1.8	120.5 ± 1.8	NS	NS
LDL cholesterol levels (mg/dL)	1.6 ± 0.3	1.6 ± 0.3	1.09 (0.36-1.36)	34.8 ± 0.5	34.8 ± 0.5	<0.05	NS
HDL cholesterol levels (mg/dL)	1.6 ± 0.3	1.6 ± 0.3	1.7 (0.8-2.0)	3.5 ± 0.2	3.5 ± 0.2	<0.05	NS
Prothrombin time (%)	1.10 ± 0.21	1.0 ± 0.14	0.8 (0.4-1.0)	103.5 ± 2.0	103.5 ± 2.0	NS	<0.05
Activated partial thromboplastin time (s)	28.7 ± 0.7	27.9 ± 0.7	27.9 ± 0.4	27.9 ± 0.4	27.9 ± 0.4	NS	NS
Systolic blood pressure (mm Hg)	130.0 ± 3.2	135.2 ± 4.6	120 (96-146)	280.4 ± 18.4	280.4 ± 18.4	<0.05	NS
Plasma reninogen levels (mg/dL)	70.1 ± 5.0	77.5 ± 10.2	70 (59-82)	147.0 ± 3.5	147.0 ± 3.5	NS	NS
Serum lipoprotein a levels (mg/dL)	25.2 ± 4.3	29.6 ± 3.9	25.4 (19-32)	33.4 ± 5.0	33.4 ± 5.0	NS	NS
Plasma ACTH levels (pg/mL)	55.9 ± 6.1	42.3 ± 5.6	50 ± 1	156.2 ± 10.4	156.2 ± 10.4	NS	<0.05
Diastolic blood pressure (mm Hg)	14.8 ± 1.5	14.0 ± 1.9	NS	120.4 ± 9.5	120.4 ± 9.5	NS	<0.05
Serum cortisol levels (µg/L)	399.1 ± 28.5	185.5 ± 17.9	<NS01	18.7 ± 4.2	18.7 ± 4.2	NS	NS
Urinary cortisol levels (µg/24 h)	25.1 ± 5.8	10.5 ± 3.1	<0.05	34.5 ± 2.0	34.5 ± 2.0	<0.05	<0.05
Fasting serum insulin levels (microPa/mL)	26.9 ± 3.5	38.0 ± 1.9	<0.005	35.2 ± 2.0	35.2 ± 2.0	<0.05	<0.05
Right	27.3 ± 3.8	38.2 ± 2.9	<0.05				
Left							

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REVIEW
MANAGEMENT OF ENDOCRINE DISEASE

The burden of Cushing's disease: clinical and health-related quality of life aspects

R A Feelders, S J Pulgar¹, A Kempel² and A M Pereira³

Table 2 Comorbidities, prevalence at diagnosis, and reversibility in patients with CD.

Morbidity	Prevalence at diagnosis	Reversibility
Hypercoagulopathy/hemostatic abnormalities	Hemostatic abnormalities (53.6%) (53) Vascular morbidity (10%) (49) VTE (incidence 2.5–3.1 per 1000 persons per year) (57)	Adequate prophylaxis with anticoagulants can reverse the prothrombotic state and greatly reduce the risk of postoperative thromboembolic events (49)
Kidney disease	Nephrolithiasis: 50% (116)	Prevalence in patients achieving remission 27% (116)
Osteoporosis/compression fractures	Osteoporosis: 38–50% (6, 71) Fractures ^b : 15.8% (71)	Only partially reversible 2 years after normalization of cortisol levels (67)

altre comorbidità

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Effect of 2 years of cortisol normalization on the impaired bone mass and turnover in adolescent and adult patients with Cushing's disease: a prospective study

Di Somma C, Pivonello R, Loche S, Faggiano A, Klain M, Salvatore M, Lombardi G , Colao A

Clin Endocrinol '03, 58: 302-308

Conclusions Bone impairment in childhood- and adulthood-onset Cushing's disease patients can be partly, but not completely, reversed 2 years after normalization of cortisol levels. Longer recovery times or additive therapeutic approaches are necessary to maximize peak bone mass in children and restore bone mass in adults with Cushing's disease

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Table 2 Comorbidities, prevalence at diagnosis, and reversibility in patients with CD.

Morbidity	Prevalence at diagnosis	Reversibility
Major depression/psychopathology ^c	MDD/MD/MAD: 54–81% (10, 72, 73) Overall psychopathology: 67% (5) Atypical depression: 51.5% (5)	Prevalence of MD at 3 months: 54%; at 6 months: 36%; at 12 months: 24% (5) About 70% of patients fully recovered from their depression (75)
Cognitive deficits/loss of brain volume	Subjective loss of brain volume: 86% (80)	Partially reversible (based on retrospective study in 38 patients only) (80)
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comorbidità psichiatriche

comorbidità psichiatriche

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Problemi da risolvere



- Deficit ipofisario
- ΔΕΦΙCΙΤ ΙΠΟΦΙΣΑΡΙΟ
- Imaging negativo
- ΙΜΑΓΙΝΙΝΓ ΝΕΓΑΤΙΒΟ
- Reintervento terapeutico
- ΡΕΙΝΤΕΡΛΕΝΤΟ ΤΕΡΑΠΕΥΤΙCΟ
- Comorbidità
- Cοmοrβιdιtα



Razionale della terapia medica



- Conoscenza della malattia e dei danni indotti dallo ipercortisolismo

ipercortisolismo
e dei danni indotti dallo

- Conoscenza della malattia

- Inizio precoce del trattamento

trattamento

- Inizio precoce del



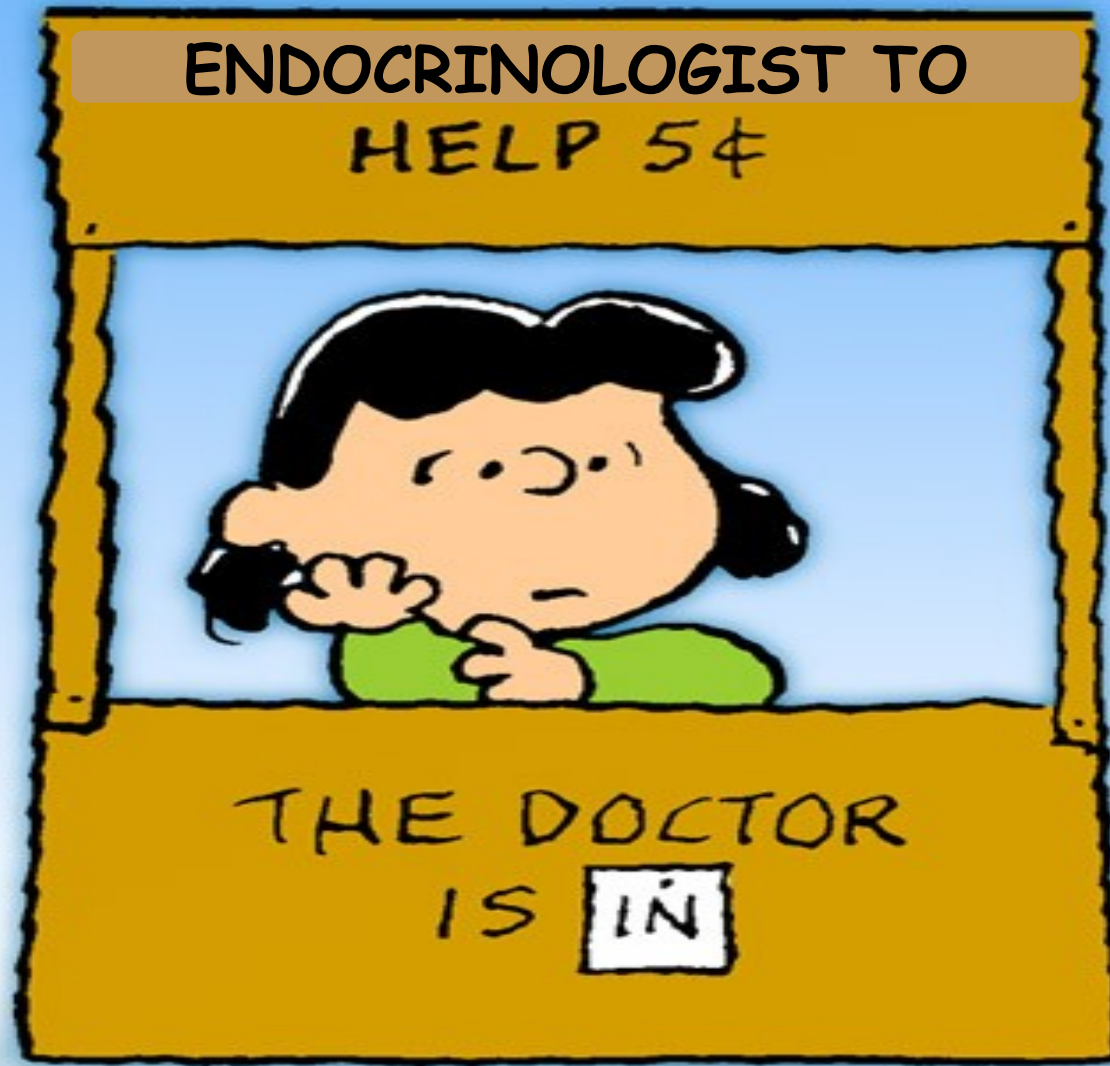
Requisiti della terapia medica

- Riduzione del cortisolo (cut off ?)
- Riduzione del cortisolo (cut off ?)
- Evitare o limitare le complicanze dell'eccesso ormonale
- Evitare o limitare le complicanze dell'eccesso ormonale

Limiti della terapia medica

- Interferenze farmacologiche
- INTERFERENZE FARMACOLOGICHE
- Scarse conoscenze degli effetti a lungo termine
- SCARSE CONOSCENZE DEGLI EFFETTI A LUNGO TERMINE

In quali casi iniziare il trattamento medico ?



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Revisione della letteratura

medical treatment has historically or more recently gained a significant space, in CD, medical treatment is traditionally thought to have a marginal role. Nevertheless, there are numerous circumstances in which medical treatment of CD may be indicated.

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Teresa Porcelli²
Andrea Giustina²

Therapeutics and Clinical Risk Management 2010;6 505–516

Advances in Medical Therapies for Cushing's Syndrome

Tritos NA

Discover Med '12, 13: 171-179

- Fallimento terapia chirurgica
- In attesa dell'effetto della radioterapia
- Modalità palliativa nel carcinoma metastatico
- Prima della chirurgia

Medical Treatment of Cushing's Syndrome: Adrenal-Blocking Drugs and Ketaconazole

Richard A. Felders Leo J. Hofland Wouter W. de Herder

- Controindicazioni alla chirurgia

- Controindicazioni alla chirurgia

REVIEW

THERAPY IN ENDOCRINE DISEASE

Etomidate in the management of hypercortisolaemia in Cushing's syndrome: a review

Veronica A Preda^{1,2}, Jonathan Sen¹, Niki Karavitaki¹ and Ashley B Grossman¹

- Ipercortisolismo severo
- Ipercortisolismo severo
- Compromissione sistemica importante
- Compromissione sistemica importante

Advances in Medical Therapies for Cushing's Syndrome

Tritos NA

Discover Med '12, 13: 171-179

- Ipercortisolismo occulto
- Ipercortisolismo occulto

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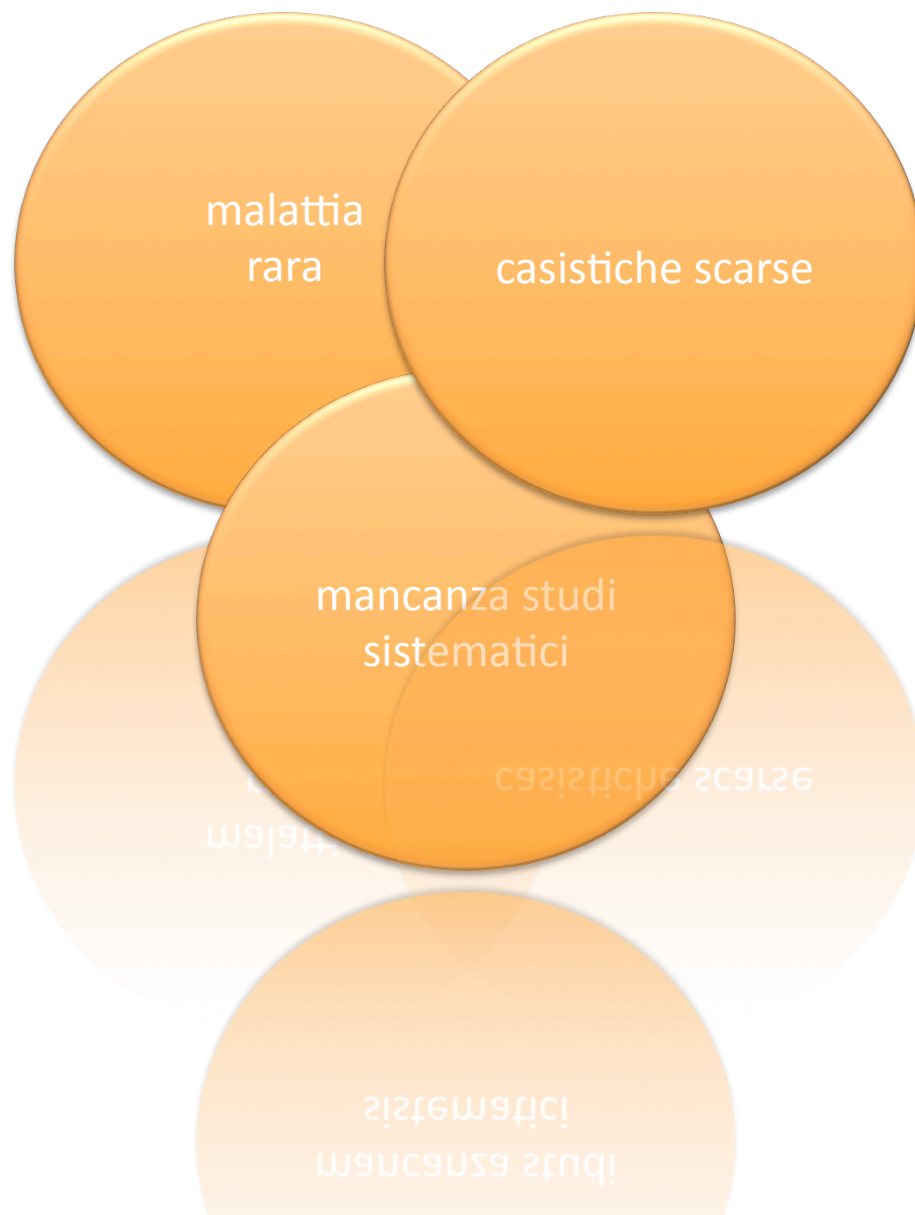
Medical Treatment of Cushing's Syndrome: Glucocorticoid Receptor Antagonists and Mifepristone

Frederic Castinetti Bernard Conte-Devolx Thierry Brue

- Riduzione comorbidità metaboliche e cardiovascolari
- Riduzione comorbidità metaboliche e cardiovascolari

Comportamento terapeutico





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Identificazione di:

- ✧ pz da sottoporre prioritariamente a terapia chirurgica
- ✧ pz da preparare a intervento chirurgico
- ✧ pz da sottoporre a terapia medica temporanea
- ✧ pz da sottoporre a terapia medica definitiva

Problematiche aperte



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- ✓ congruità di iniziare una terapia medica prima di quella chirurgica
- ✓ beneficio della terapia medica in pz con diagnosi incerta di sede
- ✓ indicazione al prosieguo della terapia medica in caso di successo
- ✓ interferenza con le comorbidità indotte dall'eccesso di steroidi circolanti
- ✓ interazione con altri farmaci somministrati per le complicanze

