09:30-10:30 SIMPOSIO 5
UN ASPETTO PECULIARE DELLE COMPLICANZE:
LA GESTIONE DELLE COMPLICANZE PSICO-SOCIALI E SESSUALI
Moderatori: Salvatore Maria Corsello, Emmanuele A. Jannini

09:30-09:45 **QUALITA' DELLA VITA**
Monica De Leo

09:45-10:00 **DISORDINI PSICOSOCIALI:**
IMPATTO DELL'IMMAGINE CORPOREA
Giacomo Ciocca

10:00-10:15 **DISTURBI DELLA SESSUALITA':**
FATTORI PSICOLOGICI ED ORMONALI
Alessandra Delli Veneri

10:15-10:30 Discussione

Quality of life

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Impairment of quality of life in patients with Cushing's syndrome

- Cushing's syndrome is known to be associated with several complications that induce significantly impaired health-related quality of life (HRQoL) which persist even after resolution of cortisol excess
- The mechanisms through which Cushing's syndrome determines HRQoL impairment are probably multifactorial involving physical and psychological features
- Patients mainly complain of fatigue or weakness, changes in physical appearance, emotional instability, cognitive problems, depression and also sleeping difficulties; the majority of patients report interference with family life and relations with their partner and half of them with school or work performance

Impairment of quality of life is variably associated with several clinical parameters:

- Age, male gender, age at diagnosis
- Urinary free cortisol levels
- Hypopituitarism

Colao A et al, Clinical Endocrinology 2012,;76;776-777; Heald AH et al ,Clin Endocrinol 2004;61:458-465; Van Aken et al, J Clin Endocrinol Metab,;2005, 90:3279-3286; Lindsay JR et al ,J Clin Endocrinol Metab, 2006, 91;447-453; Pivonello R et al Arq Bras Endocrinol Metab 2007

The high impact of CS on patient's HRQoL led to develop a specific questionnaire for CS

- **5 Countries: Spain, France, Germany, Italy, Netherlands**
- **125 patients with CS (107 CD, 18 Adrenal CS)**

39 hypercortisolemic
28 pharmacological treatment for CS
47 adrenal insufficiency

- **Clinical and hormonal data were correlated with:**
  - **SF-36**
  - **A question on self-perceived general health status**
  - **CushingQoL**

SF-36
36 items
8 domains

Vitality
Physical functioning
Social functioning
Functional performance
Emotional performance
Pain
Effect on work
Mental health

Health status

Very bad
Fairly bad
Slightly bad
Neither good nor bad
Slightly good
Fairly good
Very good

Webb SM et al Eur J Endocrinology 2008; 158:623-630

To evaluate the psychometric properties (validity and reliability) of CushingQoL and its correlation with clinical parameters relevants for patients

CushingQoL

- Time frame referred to the preceding 4 weeks
- 12 item
- The score is the sum of all the item responses a ranges from 12 (worst HRQoL) and 60 points (best HRQoL)
- The lower the score, the greater the impact on HRQol
- The score can be interpreted if the number of unanswered items does not exceed 3 (25% of questions)

Webb SM et al Eur J Endocrinology 2008; 158:623-630

CushingsQol is feasible, reliable and valid instrument. Scores correlate with relevant clinical parameters

- CushingQoL scores decreased as self-perceived health status worsened
- CushingsQol scores were moderately correlated with all dimensions of the SF-36 questionnaire.

- CushingQoL scored worse in patients:
  - With recent hospital admission
  - Diagnosed in the prior 2 years
  - With hypercortisolemic state
- Female gender and elevated UFC levels are main contributors to impaired HRQoL

Relationship between CushingQoL scores and clinical variables.

		CushingQoL score	*P* value
Time elapsed since diagnosis	Recent diagnosis (≤24 months; *n*=50)	44±22	<0.001
	Old diagnosis (>24 months; *n*=74)	59±20	
Clinically, active and concomitant high free urinary cortisol	No (*n*=60)	56±21	0.004
	Yes (*n*=26)	44±22	
Hospital admissions	No admissions (*n*=63)	59±21	0.002
	With admissions (*n*=61)	47±22	

Webb SM et al Eur J Endocrinology 2008; 158:623-630

CushingsQol is feasible, reliable and valid instrument. Scores correlate with relevant clinical parameters

No relation was identified between the CushinsQol score and the presence or not of adrenal insufficiency, but time elapsed since diagnosis of adrenal insufficiency was positively related with CushingsQol score

In CD the presence or not of hypopituitarism did not determine differences in CushingsQol score

Webb SM et al Eur J Endocrinology 2008; 158:623-630

CushingQoL global score does not capture all aspects of QoL

WHO recommends that QoL be treated as a multidimensional construct:
- Physical issues
- Pycological issues
- Social issues

- 341 patients in remission from CS (238 CD)
- Mean time of remission:6,9 years
- 131 patients (38%) with hypopituitarsim

- ➢ Single global score
- ➢ 2-subscale solution
- Subscale 1: psychosocial issues
- Subscale 2: physical problems

WHO: World Health Organization

Tiemensma J et al, Eur J Endocrinology 2016 174;33-40

The global score collapses QoL across all dimensions, which makes it impossible to disentagle physical problems and psycosocial issues

- Patients with hypopituitarism scored lower on the global CushingQol, on physical problems subscale and psycosocial issues than patients without hypopituitarism
- There was a positive association between duration of remission and global CushingQol and psycosocial issues
- There was a positive association between duration of follow-up and psycosocial issues

Example global CushingQoL and subscale scores.

Participants	Psychosocial issues	Physical problems	Global CushingQoL score
Entire sample ($n=341$)	43.89 (S.D. = 23.7)	50.66 (S.D. = 24.2)	45.54 (S.D. = 21.9)
Participant no. 51	**0.00**	**25.00**	**6.25**
Participant no. 52	**69.44**	**33.33**	**60.42**
Participant no. 63	36.11	33.33	35.42
Participant no. 144	**11.11**	**50.00**	**20.83**
Participant no. 146	**0.00**	**50.00**	**12.50**
Participant no. 148	**91.67**	**58.33**	**83.33**
Participant no. 167	55.56	58.33	56.25
Participant no. 284	**33.33**	**91.67**	**47.92**
Participant no. 285	97.22	100.00	97.92

2-subscale scoring solution was a significantly better fit than the global scores

Tiemensma J et al, Eur J Endocrinology 2016 174;33-40

To develop a disease-specific questionnaire for Cushing's disease, the Tuebingen Cushing's disease quality of life inventory (Tuebingen CD-25)

- Preliminary inventory comprising 64 HRQoL item
- 63 patients with CD, 6 age groups similar in size, 28 pre-operatively, 35 retrospectively
- Final version comprising 25 HRQoL item

WHOQoL-BREF

26 items
4 domains

Physical health
Psychological health
Social relationships
Environment

Tuebingen CD-25

25 items
6 domains

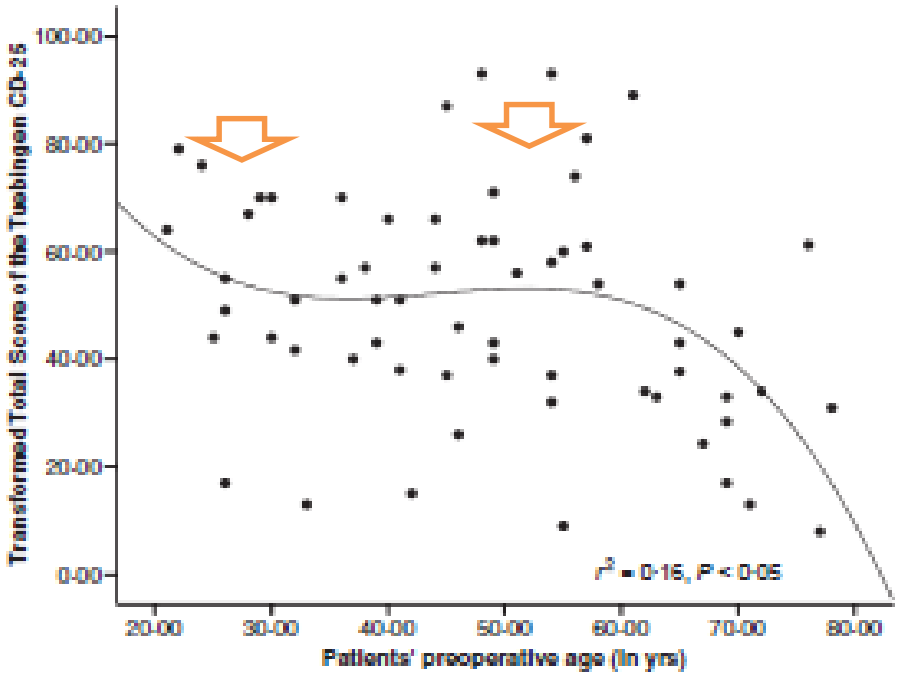
Depression
Sexual activity
Environment
Eating behaviour
Bodily restriction
Cognition

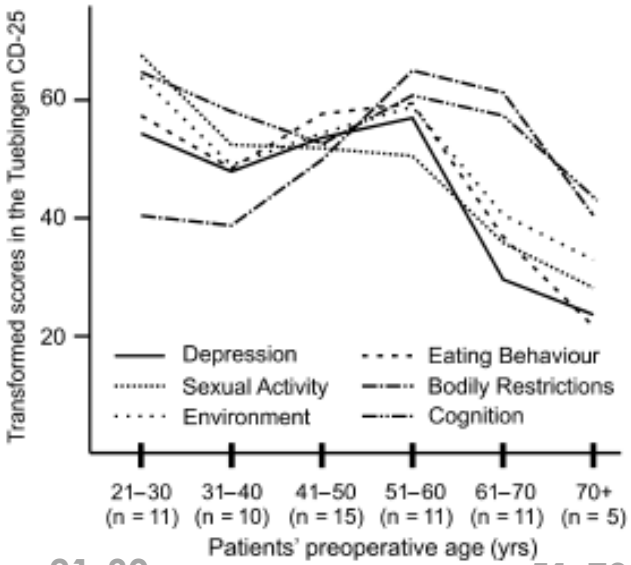
Score range: 0-100

Milian M et al Clinical Endocrinology 2011; 76:851-860

The Tuebingen CD-25 is a valid and reliable instrument to evaluate HRQoL in CD.

- The retrospective rating of the Tuebingen CD-25 showed similar results compared to the pretreatment group
- Non-linear correlation between the Tuebingen CD-25 scores and patients' age, younger (21-30 years) and middle-aged (51-60 years) patients having inferior HRQoL than patients between 31 and 50 years and older than 61 years
- Preoperative 24 h urinary free cortisol levels correlated significantly with the subscale Cognition and Eating Behaviour





21-30 yrs

Sexual activity
Cognition
Social environment
Eating behaviour

51-70 yrs

Bodily restriction
Cognition

Milian M et al Clinical Endocrinology 2011; 76:851-860

To better understand how hypercortisolism affects the QoL in CD patients

- 63 patients with CD
- 1784 healthy controls, 7 age groups
- Recruited via a German online internet version of the questionnaire
- Tuebingen CD-25

70% of CD patients shows impaired HRQoL

- 28.6% slight impairment
- 41.3% severe impairment

Female patients are more depressed and impaired in their social environment than male patients when compared with HC

Milian M et al Clin Endocrinol 2012;76:861-867

To analyze factors associated with self-reported QoL

- 269 patients with CS (184 CD, 67 adrenal CS, 12 other CS)
- 193 remission state
- 67 hypercortisolemic state
- CushingQoL questionnaire

- The association between QoL scores and the number of symptomatic years without a diagnosis showed a statistically significant negative correlation coefficient
- Negative correlation between number of physicians seen and Qol score

At multiple regression analysis were significant predictors of QoL

- Remission status
- Radiation therapy
- Time to diagnosis
- Hypopituitarism

A delay in diagnosis continued to negatively impact QoL even after biochemical cure of the disease. Education of health care providers may lead to earlier recognition of CS and perhaps could improve the QoL of those affected by this disorder. Obtaining control of cortisol excess improves QoL and remains an important goal in the care of CS patients

Papoian V et al, Endocr Pract 2016;22:51-67

To explore illness perpections, as potentially modifiable psychological factors, in relation to QoL

- **Illness perception: The way patients make sense of, and respond to, their illness**
- 52 patients in remission from CS
- 35 patients with acute pain
- 63 patients with cronic pain
- 171 patients with COPD
- 80 patients with vestibular schwannoma

- IPQ
- Physical symptom checklist
- EuroQoL-5D
- CushingQoL

Patients with CS scored distinctively more negative on the IPQ compared with patients with vestibular schwannoma and patients with acute pain, and also reported more illness-related complaints.
Illness perpections showed a strong correlation with QoL.

Tiemensma J et al, Eur J Endocrinology 2011;156:527-535

Conclusions:

CS is associated with impaired quality of life and negative illness perception

This impairment partially resolves after successful treatment
At long-term follow-up, despite apparent clinical remission, there is evidence of reidual impaired HRQoL

Irreversible effects of hypercortisolism on neurological function and cognition and the persistance of high cardiovascular risk even after cure could contribute to long-term impairment in HRQoL

QoL assessment is an essential outcome in the postoperative period and subsequent follow-up

Early diagnosis and treatment remain important goals in the care of CS patients to improve the HRQoL

The management of CS requires a multidisciplinary and individualized approach including strategies to control hypercortisolemic state and to improve patients HRQoL, as cognitive behavioral therapy, self-menagement training and information on the negative effects of the disease .

Thanks