Tumori ipofisari clinicamente non funzionanti – *Neurochirurgia*

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IRCCS Istituto delle Scienze Neurologiche di Bologna – Ospedale Bellaria

Conflitti di interesse

Ai sensi dell'art. 3.3 sul conflitto di interessi, pag 17 del Regolamento Applicativo Stato-Regioni del 5/11/2009, dichiaro che negli ultimi 2 anni ho avuto rapporti diretti di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

- Novartis (Advisory Board)
- Otsuka (Advisory Board)

Roma, 8-11 novembre 2018

Tumori ipofisari clinicamente non funzionanti - *Neurochirurgia*

ITALIAN CHAPTER

- Indicazioni e work-up *(chi e quando operare?)*
- Approccio chirurgico *(come operare?)*

Disponible en ligne sur ScienceDirect www.sciencedirect.com
Elsevier Masson France EM|consulte www.em-consulte.com
Annales d'Endocrinologie Annals of Endocrinology
Annales d'Endocrinologie 76 (2015) 220–227

Consensus

Non-functioning pituitary adenoma: When and how to operate? What pathologic criteria for typing?☆

Adénomes hypophysaires non fonctionnels : quand et comment opérer ? Quels critères anatomo-pathologiques retenir ?

Frederic Castinetti[a,*], Henry Dufour[b], Stephane Gaillard[c], Emmanuel Jouanneau[d], Alexandre Vasiljevic[e], Chiara Villa[f,g,h], Jacqueline Trouillas[e,f,g,h,i]

Tumori ipofisari clinicamente non funzionanti - *Neurochirurgia*

Indicazioni e work-up *(chi e quando operare?)*

- *Un numero crescente di pazienti giunge alla nostra attenzione per il **riscontro incidentale** di una massa nella regione sellare.*
- *La maggior parte dei casi è costituita da microincidentalomi, generalmente non-secernenti. In questi casi, la chirurgia non ha indicazione, ma è preferibile seguire le linee guida disegnate ad hoc per il follow-up.*
- *Tuttavia, la percentuale di macroincidentalomi può essere rilevante in centri specialistici multidisciplinari con una spiccata vocazione chirurgica. Una volta esclusa la natura secernente, occorre valutare l'**eventuale** opzione chirurgica.*
- *A tale scopo, se la lesione lambisce il chiasma ottico la campimetria visiva è indispensabile, anche se il paziente non riferisce deficit visivo.*

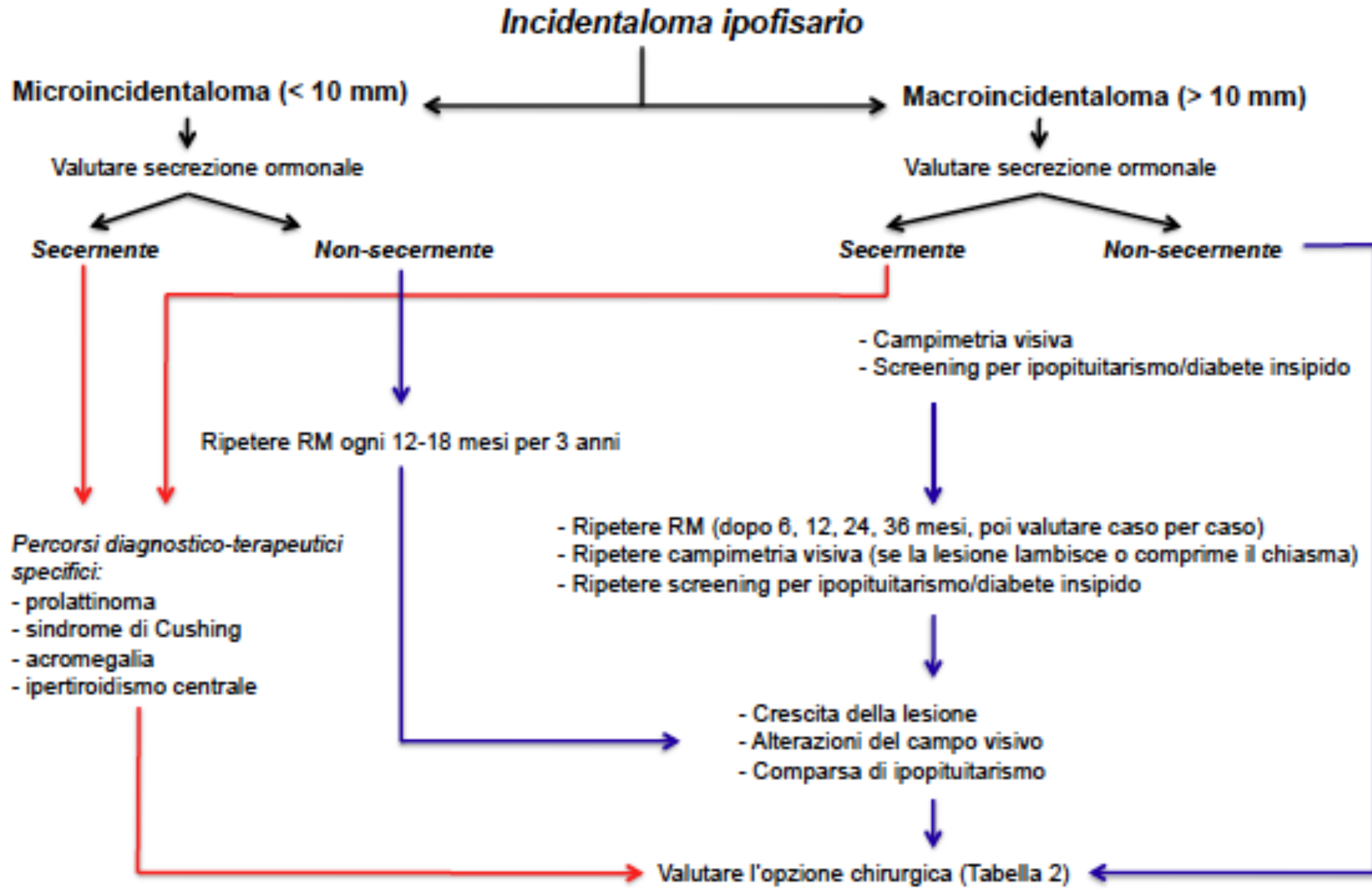

Fig. 1 Percorso diagnostico-terapeutico dell'incidentaloma ipofisario.
Le frecce di colore *rosso* indicano il percorso per le lesioni secernenti.
Le frecce di colore *blu* indicano il percorso per le lesioni clinicamente non-funzionanti

ITALIAN CHAPTER

Faustini-Fustini M, Kara E, Losa M.
L'Endocrinologo 2017 DOI 10-1007/s 40619-017-0286-2

Roma, 8-11 novembre 2018

Indicazioni alla chirurgia nel paziente con incidentaloma ipofisario

- Raccomandazioni forti (evidenze di alta qualità)
  - Deficit visivi campimetrici o altri disturbi visivi o neurologici da compressione
  - Lesione che lambisce o comprime i nervi ottici o il chiasma alla RM
  - Lesione secernente (eccetto il prolattinoma)

- Raccomandazioni deboli (evidenze di bassa qualità)
  - Crescita radiologicamente significativa
  - Ipopituitarismo
  - Donna con lesione in prossimità del chiasma e che intende programmare una gravidanza

Modificato da: Pituitary incidentaloma - An Endocrine Society Clinical Practice Guideline.
J Clin Endocrinol Metab 2011; 96: 894

Indicazioni e work-up *(chi e quando operare?)*

- *Una porzione variabile di pazienti giunge alla nostra attenzione già con sintomi/segni di malattia (deficit visivo, ipopituitarismo, …) per l'effetto "massa" esercitato dalla neoplasia, che può avere un diverso grado di estensione extrasellare.*

- *È indispensabile fare riferimento alle **classificazioni sull'estensione del tumore ipofisario**!*

Hardy-Wilson classification:

Sella Turcica radiological classification	Extrasellar extensions				
	Suprasellar			Parasellar	
Grado 0 (normal)	A	B	C	D	E
Grado I					
Grade II					
Grade III					
Grade IV					
	Symmetrical			Asymmetrical	

Knosp classification:

Grade 0

Grade 1

Grade 2

Grade 3A

Grade 3B

Grade 4

Tumori ipofisari clinicamente non funzionanti - *Neurochirurgia*

- Indicazioni e work-up *(chi e quando operare?)*
- Approccio chirurgico *(come operare?)*

A strong voice of pituitary patients worldwide

Robert Knutzen,
Newbury Park, California
Patient, patient educator and advocate through the Pituitary Network Association

'… *we need to agree that pituitary tumors/disorders are not in fact a primarily surgical problem to overcome*. The problems and therefore the solutions are so multifaceted and difficult to enumerate that *a wise surgeon knows when his/her skills and professional care are not needed*, and uppermost in his/her mind is:

Whom should see this patient next?

Both surgical and medical outcomes in patient treatment are closely linked to training and numerical surgical experiences in the facility where the patient is being treated'

Neurosurgery, 2014; 74: E143

A strong voice of pituitary patients worldwide

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Patient, patient educator and advocate through the ***Pituitary Network Association***

'… I was first acquainted with the concept of pituitary centers of excellence through Dr Charles Wilson, the "near pioneer'' in pituitary surgery at University of California, San Francisco, nearly 22 years ago.
I well remember his frustration over the numerous "re-do's" he was called on to handle and the damage that was done by medical/surgical colleagues with very little experience in this area of medicine.'

Neurosurgery, 2014; 74: E143

The management of regrowth of residual tumour

The challenge of re-do's

Roma, 8-11 novembre 2018

Beyond gross total and subtotal: does volumetric resection matter in NF pituitary macroadenomas?

ITALIAN CHAPTER

World Neurosurg 2018; 116: e733-37

A

% Recurrence

1.0
0.8
0.6
0.4
0.2
0.0

○ ≥ 86% EOR
+ < 86% EOR

P = 0.001

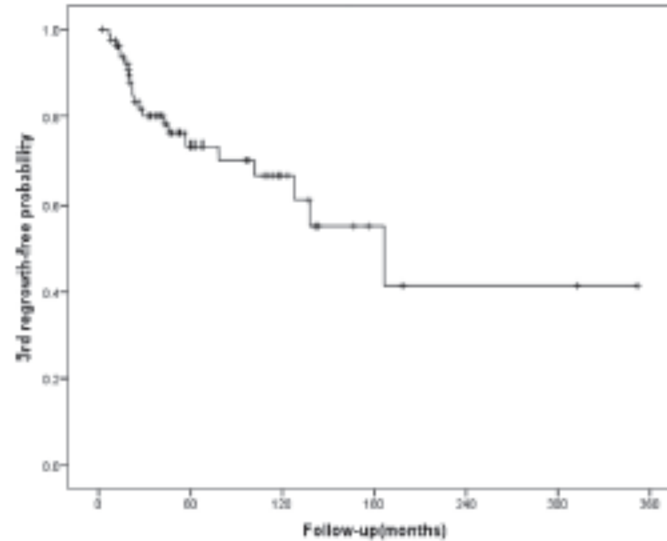
0 50 100 150 200

Months of follow-up

'… We found that increasing age and extent of resection were associated with a smaller risk of regrowth and retreatment. However, other studies have shown that subtotal resection combined with postoperative radiotherapy also achieves recurrence rates on par with gross total resection.'

Treatment and Follow-Up of Clinically Nonfunctioning Pituitary Macroadenomas

J Clin Endocrinol Metab 2008; 93: 3717



Kaplan-Meier regrowth free-survival curves for total group of patients with a first (left) and second (right) regrowth

Roma, 8-11 novembre 2018

MRI texture analysis as a predictor of tumor recurrence or progression in patients with clinically non-functioning pituitary adenomas

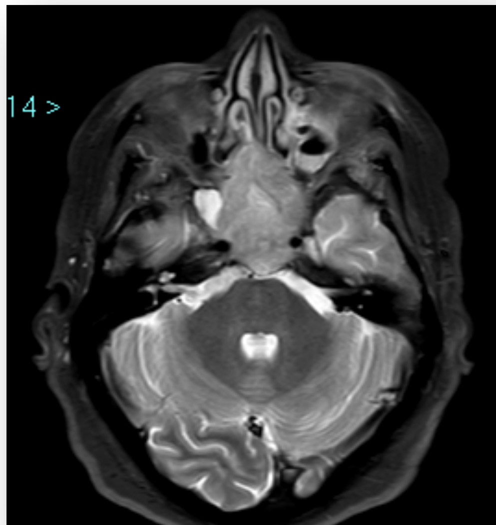
ITALIAN CHAPTER

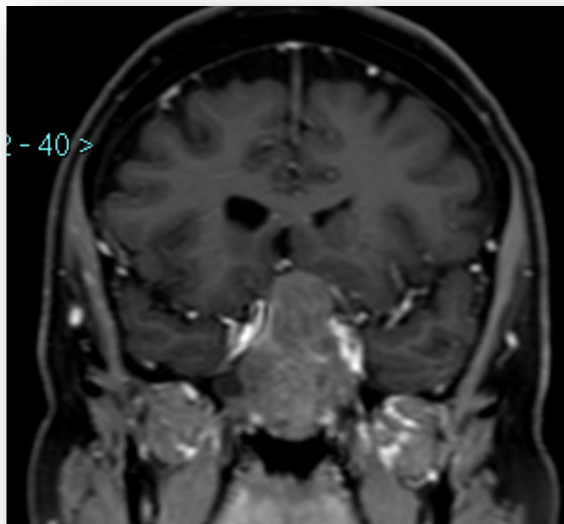
Below median
Above median
Hazard ratio, 0.44 (95% CI, 0.21-0.94)
Recurrence or progression
1.00
0.75
0.50
0.25
0.00
0
20
40
60
80
Time (months)

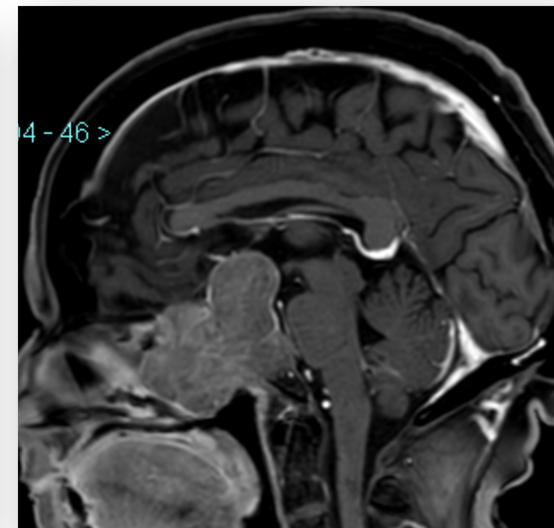
Eur J Endocrinol 2018; 179: 191

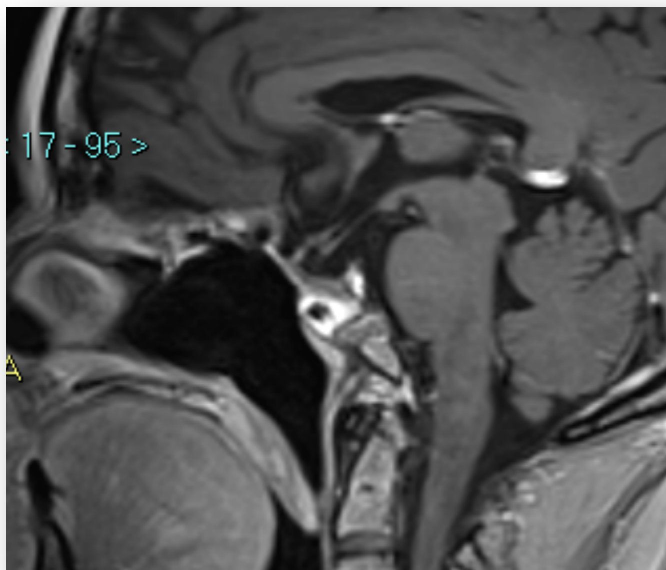
The challenge of giant pituitary tumours

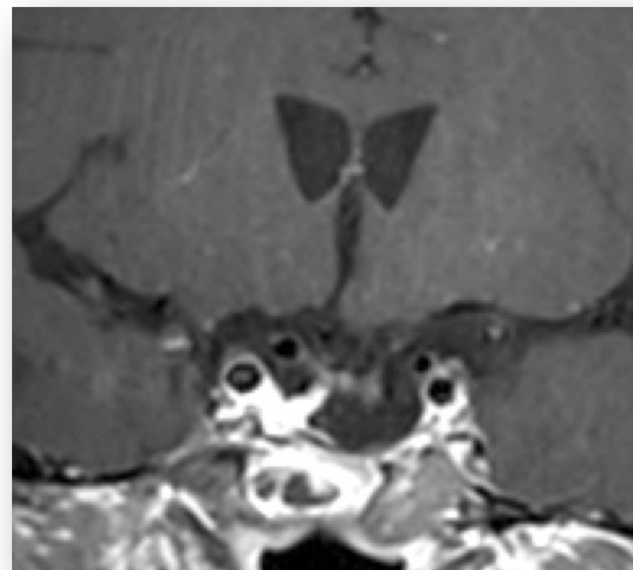
P. MI, f. 70 aa
RM del 8-05-2017





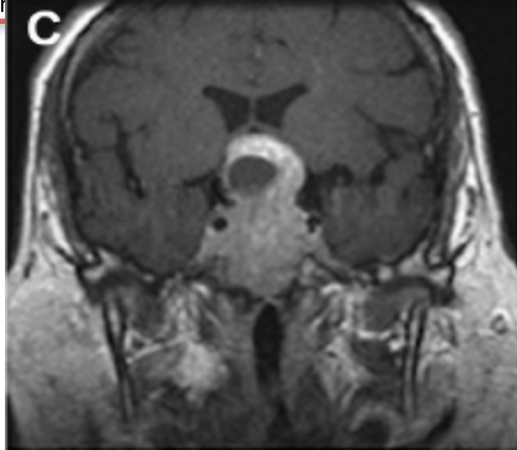


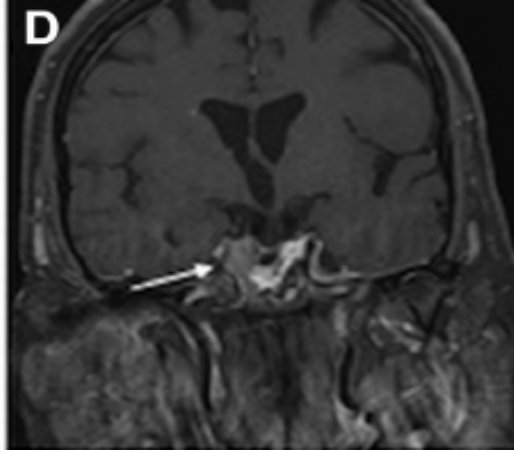


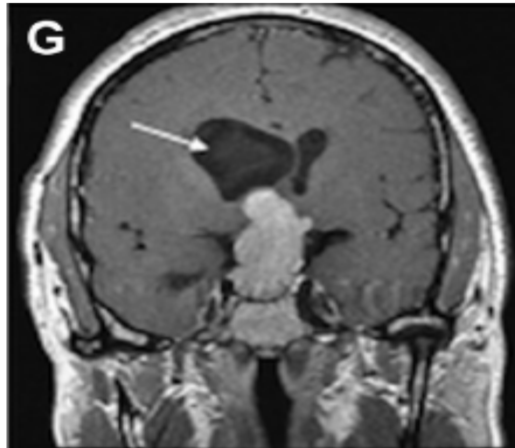


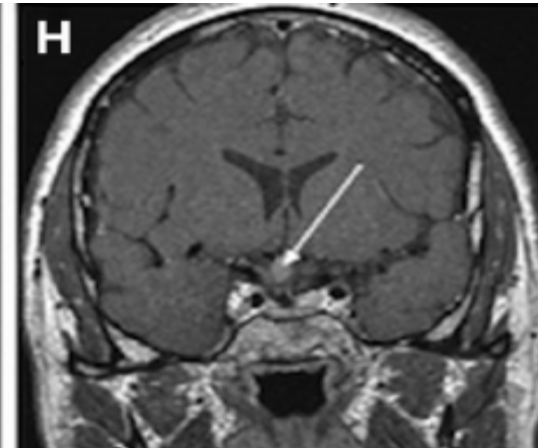
P.MI, controllo RM dopo 6 mesi

Clinical outcomes after endoscopic endonasal resection of giant pituitary adenomas









World Neurosurg 2018; 114: e 447-456

Endoscopic endonasal surgery for giant pituitary tumours

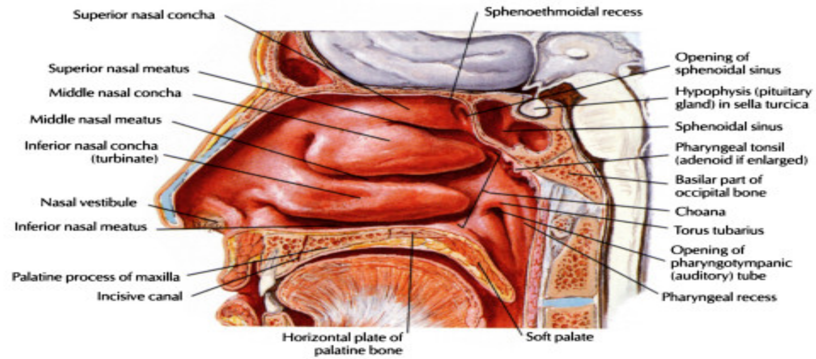
World Neurosurg 2018; 114: e 447-456

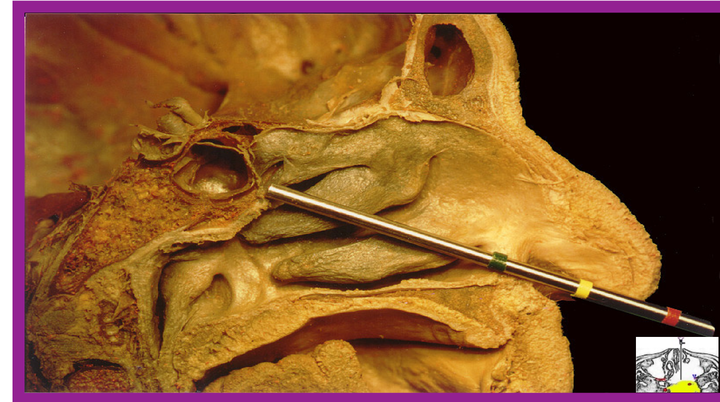
- *Giant adenomas* (*n=55*)
  - *Non secretory* (*N=51*)
    - EEA
      - GTR [N=24 (44%)]
      - Residual (N=27)
        - OBSERVATION [N=21]
        - Initial radiotherapy (FSRT) [N=6]
    - Follow up period 41 (9-95) months (in all the non-secretory patients)
      - Stable [N=45 (88%)]
      - Late recurrence/ progression (N=6) [12%]
        - Continued observation (N=2)
        - FSRT (N=3)
        - Surgery followed by FSRT (N=1)
  - *Secretory* (*N=4*)
    - EEA + (adjuvant medical treatment in all, FSRT in 3, GKRS in one)
    - follow up time 28 (4-58) months
    - Chemical remission in all

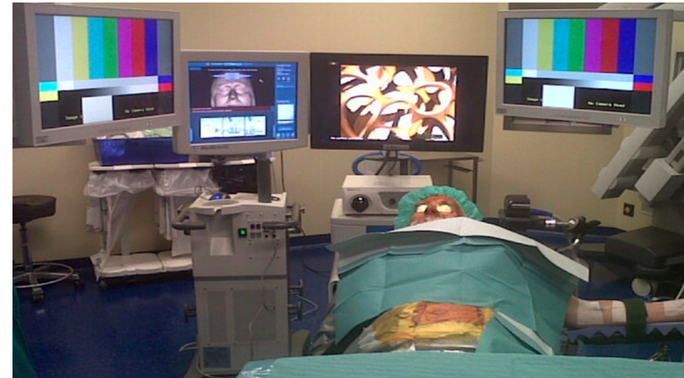
Roma, 8-11 novembre 2018

Endoscopic Endonasal Transsphenoidal Approach (EETA)

ITALIAN CHAPTER







NFPA – A single centre experience over the last six years (Pituitary Unit, Bologna)

291 patients (159 males – 132 females)

Diagnosis	Number of patients
Incidental *	112 (38.5%)
Visual symptoms	72 (24.7%)
Endocrinological symptoms	43 (14.7%)
Recurrence/residual/progression	41 (14.1%)
Apoplexy	14 (4.8%)
Neurological symptoms	9 (3.1%)

Neuroradiological evaluation

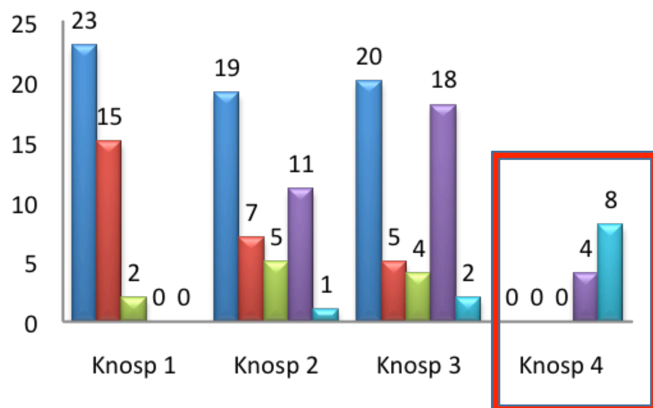
Hardy grade	Number of patients (%)
1	14 (5%)
2	220 (76%)
3	48 (17%)
4	2 (1%)

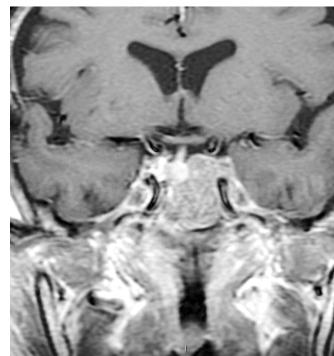
Wilson grade	Number of patients (%)
A	135 (46%)
B	85 (29%)
C	6 (2%)
D	6 (2%)
E	41 (14%)

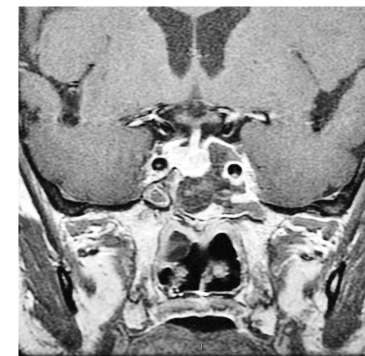
Knosp grade	Number of patients (%)
0	146 (50%)
1	40 (14%)
2	43 (15%)
3	49 (17%)
4	13 (11%)

Knosp grade 1 - 4: 50%

Real invasion of the cavernous sinus





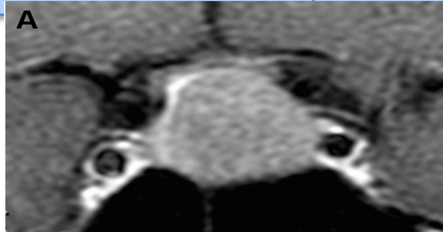


Pre-op

Post-op

Surgical outcome

Resection	RM a tre mesi	RM a distanza (M=46 mesi)
GTR	83%	82%
Residual	17%	14%
Regrowth	/	3%
Recurrence	/	1%

A


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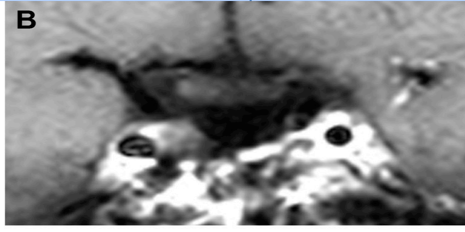

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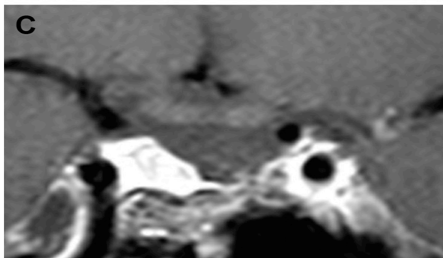

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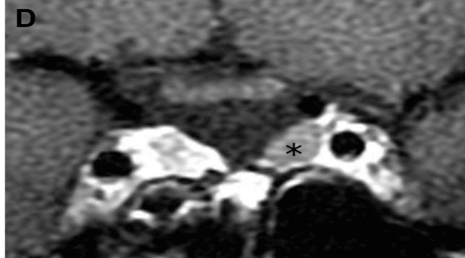

A: Preoperative MRI

B: 3-month postoperative MRI without residual

C: 24-month postoperative MRI

D: 55-month postoperative with recurrence in left cavernous sinus

Surgical outcome

Symptoms	Improved	Unchanged	Worsened
Visual	82%	14%	3%
Endocrinological	46%	43%	11%
Neurological	67%	32%	1%

Complications

Medical complications	Number of patients
Transient diabetes insipidus	11 (3.8%)
Permanent diabetes insipidus	7 (2.4%)
SIADH	4 (1.4%)
Uro-genital	3 (1.0%)
Pulmonary	3 (1.0%)
Cardiovascular	1 (0.3%)
Meningitis	1 (0.3%)

Surgical complications	Number of patients
CSF leak	12 (4.1%)
Epistaxis	5 (1.7%)
Cranial nerves palsy	4 (1.4%)
Postoperative haematomas	3 (1.0%)

Roma, 8-11 novembre 2018

Review of the medical literature

Author	Patients	Histology	GTR	Visual improvement	Endocrinolgic. improvement	Recurrence
Losa et al. (2008)	491	49% null; 45%gonad	64%	87%	35%	19%
Zhan et al. (2015)	313	NA	77%	80%	NA	11%
Hosp. Bellaria (2018)	291	74% null; 13% gonadotrop; 2% ACTH	83%	82%	46%	1%
Lee et al. (2016)	289	31% null; 10% ACTH; 39%gonad	67%	NA	29%	8%
Hwang et al. (2016)	275	NA	67%	NA	NA	17%
Yildirim et al. (2016)	160	NA	90%	44%	35%	17%
Iglesias et al. (2017)	131	NA	38%	34%	0%	NA
Robenshtok et al. (2014)	105	NA	NA	84%	62%	33%
de Aguiar et al. (2009)	104	43% null; 14%gonad	38%	61%	20%	NA
Berkmann et al. (2012)	92	NA	79%	NA	10%	NA
de Mello et al. (2012)	87	NA	<80%	NA	5%	19%
Messerer et al. (2013)	76	NA	67%	41%	15%	NA
Anagnostis et al. (2011)	57	NA	19%	59%	4%	0%
Karppinen et al. (2015)	41	NA	56%	90%	9%	12%
Langlois et al. (2017)	39	39 silent corticotr	42%	NA	NA	36%
Marenco et al. (2015)	25	44% gonad; 33% null; 4% ACTH	31%	70%	22%	21%
Alahmadi et al. (2012)	20	20 silent corticotr	60%	NA	0%	13%

Mind!

Surgeon practice volume!

Expertise of other specialists of the team!

Oversight of the verification process!

Spectrum of pituitary tumors!

Grazie dell'attenzione

Pituitary Unit
IRCCS Istituto delle Scienze Neurologiche di Bologna
Azienda USL Bologna – Ospedale Bellaria

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ALMA MATER STUDIORUM UNIVERSITÀ DI BOLOGNA

13° UP TO DATE

GESTIONE CLINICA INTEGRATA DEL PAZIENTE CON TUMORE IPOFISARIO

5 e 6 aprile 2019

RELAIS BELLARIA
Hotel & Congressi
Via Altura, 11/bis Bologna

IL RESPONSABILE SCIENTIFICO
Marco Faustini Fustini
Pituitary Unit
IRCCS Istituto delle Scienze Neurologiche di Bologna

PRESIDENTE ONORARIO
Giorgio Frank

SAVE THE DATE

Sono stati richiesti i patrocini di: **AME, SIE, Regione Emilia-Romagna**

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Antonella Bacci
Maria Elena Ciocchini
Luigi Cirillo
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Maria Pia Foschini
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