

Altogether
to Beat
Cushing's
Syndrome



Viaggio alla
(ri)scoperta
della Sindrome
di Cushing

Quarta Edizione

Napoli, 5-7 maggio 2015
Hotel S. Lucia

11:00-12:00

**SESSION 6: THE THERAPEUTIC ALGORITHM OF CUSHING'S
DISEASE: AN UPDATE**

Chairs: Paolo Cappabianca, Salvatore Corsello

11:00-11:15

THE THERAPEUTIC ALGORITHM: PAST, PRESENT AND FUTURE

Alessia Cozzolino

11:15-11:30

THE ROLE OF PITUITARY SURGERY

Luigi Maria Cavallo

11:30-11:45

THE ROLE OF RADIOTHERAPY

Giuseppe Minniti

The therapeutic algorithm: past, present and future

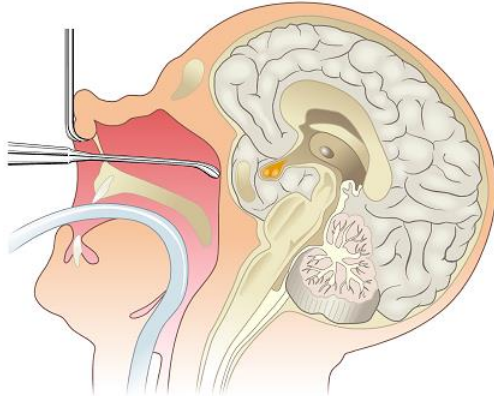
Alessia Cozzolino

**Dipartimento di Medicina Clinica e Chirurgia,
Sezione di Endocrinologia
Università Federico II di Napoli**

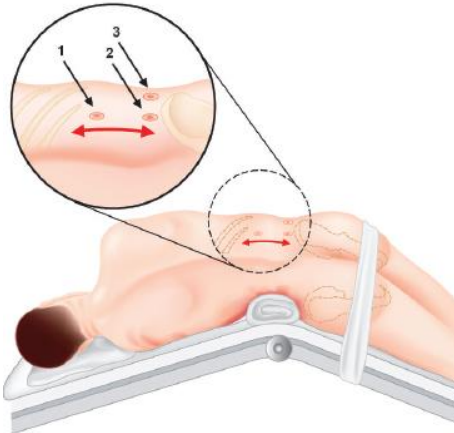
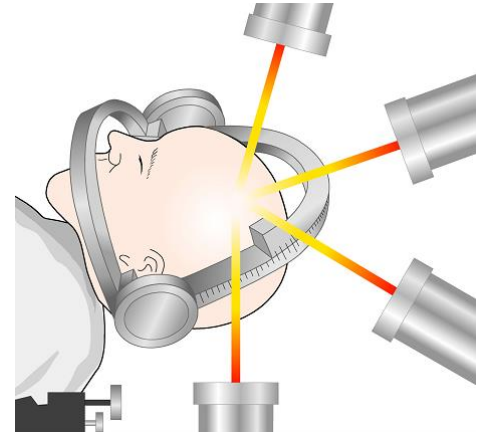


Treatment options for Cushing's disease

Neurosurgery



Radiotherapy



Adrenalectomy



Medical therapy

Past...

The New England Journal of Medicine

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Number 5

RESULTS OF TREATMENT IN 108 PATIENTS WITH CUSHING'S SYNDROME

DAVID N. ORTH, M.D., AND GRANT W. LIDDLE, M.D.

108 CS

64 CD

Past...

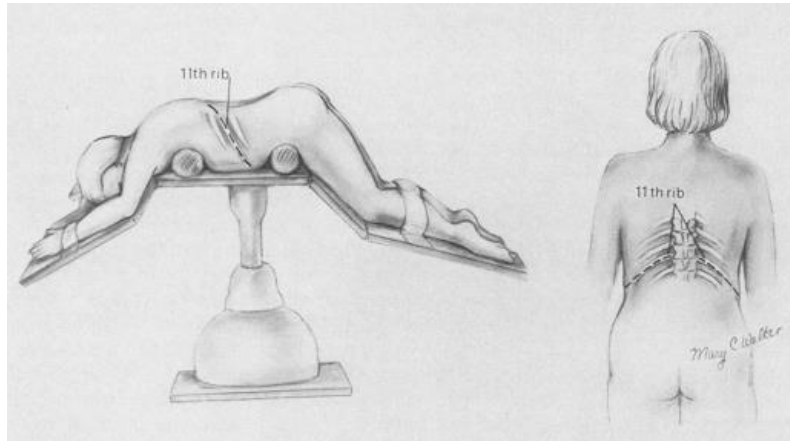
Table 1. Results of Treatment in 108 Patients with Cushing's Syndrome.

CAUSE OF CUSHING'S SYNDROME	TREATMENT	PATIENTS'		AGE (YR)		RESULTS OF TREATMENT'	FOLLOW-UP PERIOD		COMPLICATIONS'	
		TOTAL	MALES	FEMALES	RANGE		MEAN	RANGE		MEAN
Cushing's disease	Pituitary irradiation	51	15	36	7-68	35	10 patients cured	1-14 yr	9 yr	0
							13 patients improved	1-13 yr	9 yr	
							21 patients unimproved			
							7 patients followed for < 1 yr			
	Adrenalectomy	28	8	20	14-63	33	1 unrelated death	2 yr		
							21 patients cured			1 death from post-operative hemorrhage
							19 total bilateral	1-13 yr	8 yr	
							2 subtotal	1,5 yr		1 death from possible adrenal insufficiency after 1 yr
							1 patient improved (subtotal)	10 yr		
							8 patients unimproved			
							2 subtotal			
							6 unilateral			
							1 unrelated death	3 yr		
	o,p'DDD	8	1	7	22-68	42	8 patients cured	1-5 yr	3 yr	4 nausea
							1 unrelated death	3 yr		
	Hypophysectomy	3	0	3	30,35,41		1 patient cured	11 yr		
							2 patients unimproved			
							1 trans-sphenoidal			1 recurrent meningitis
							1 stalk section			1 major visual loss

Past...

Surgical Experience with Cushing's Disease

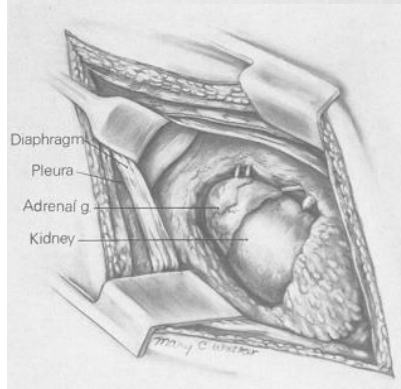
H. WILLIAM SCOTT, JR., M.D., GRANT W. LIDDLE, M.D., J. L. MULHERIN, JR., M.D., T. J. MCKENNA, M.D.,
S. L. STROUP, M.D. AND R. K. RHAMY, M.D.



1952-1976

119 CD

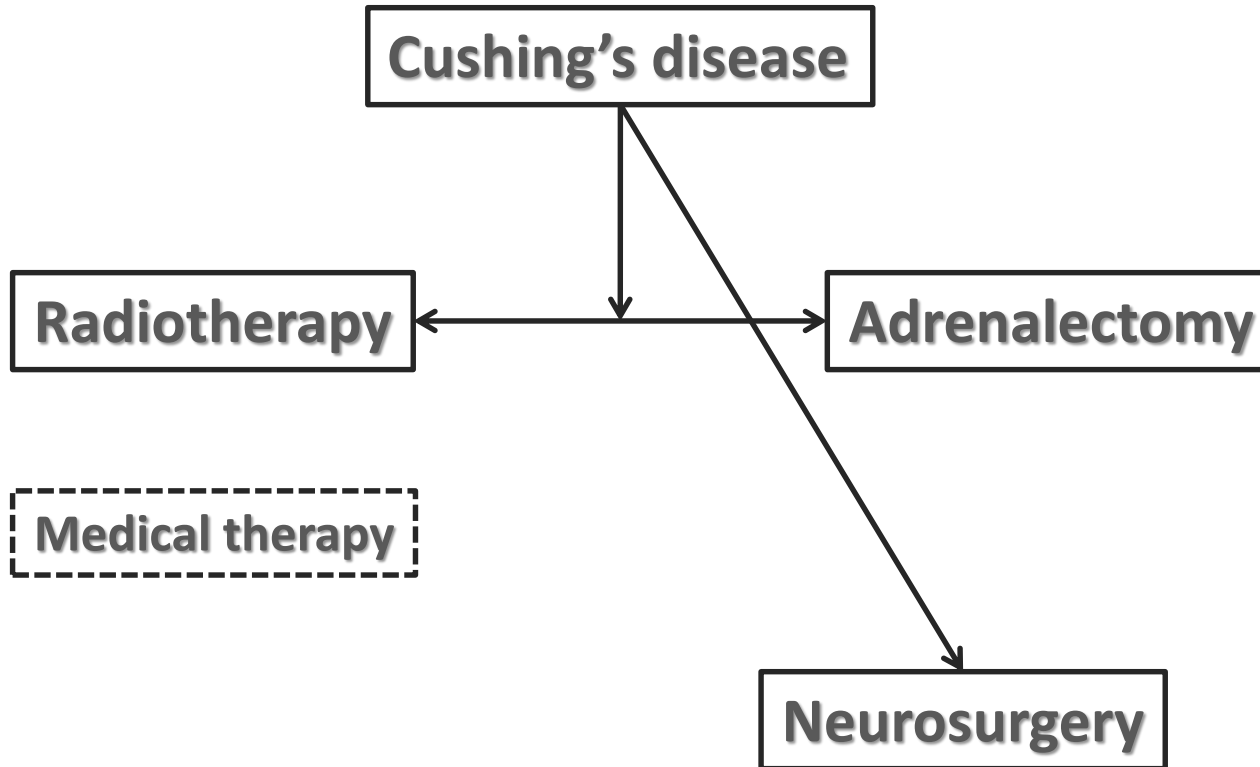
29 BLA



Summary

During the period 1952 to 1976 at Vanderbilt University Hospital 119 patients with pituitary-dependent hypercortisolism or Cushing's disease were studied. The less severe cases, which constitute a majority, were treated by pituitary irradiation with endocrinologic cure or improvement in two-thirds of the treated patients. Bilateral total adrenalectomy was reserved for the most severe cases and for failures of pituitary irradiation. In 29 patients with total bilateral adrenalectomy

Past...



The Medical Treatment of Cushing's Syndrome

JEFFREY W. MILLER AND LAWRENCE CRAPO

I. Introduction

WITH the advent of synthetic glucocorticoids in the late 1940s, adrenalectomy ushered in the modern era of treatment for Cushing's syndrome. Nearly two decades later, the development of transsphenoidal microsurgical techniques allowed the treatment of Cushing's disease with preservation of anterior pituitary function. Medical treatment for

TABLE 6. Transsphenoidal surgery in Cushing's disease

Ref	n	Postop remission	Late relapse	Mean follow-up
136	216	169/216	10/169	3.9 yr
137	102	72/102	5/72	3.4 yr
212	100	86/100	8/86	3.1 yr
213	75	70/75	2/70	
138	34	25/34		1 wk
215	23	19/23	2/18	
214	18	16/18		1.5 yr
139	15	14/15	1/14	
216	13	13/13		7 yr
217	14	9/14	1/9	
218	7	7/7		1-4 yr
Totals	610	81%	7%	

The Medical Treatment of Cushing's Syndrome

JEFFREY W. MILLER AND LAWRENCE CRAPO

TABLE 9. The potential role of medical therapy in Cushing's syndrome (CS)

Etiology	% of CS	Surgical outcome	Indication for med Rx	Potential med Rx
Cushing's disease	69%			
Pituitary microadenoma	50%	Cure (89%) Failed (11%)	None Definitive	6%
Pituitary macroadenoma	8%	Cure (66%) Failed (44%)	None Definitive	4%
Negative sella exploration	8%	Cure (59%) Failed (41%)	None Definitive	3%
Late postoperative relapse ^a		Relapse (7%)	Definitive	3%

IX. Indications for Medical Therapy in Cushing's Syndrome

Hypercortisolism may be treated medically for one of three reasons: 1) to correct metabolic abnormalities before attempted surgical cure, 2) to palliate surgically noncurable disease, and 3) to achieve remission pharmacologically in patients for whom surgery is unlikely to achieve satisfactory long-term results. Preoperative treatment for adrenal tumors

Present...

Cushing's Syndrome

Rosario Pivonello, MD, PhD*,
Maria Cristina De Martino, MD, Monica De Leo, MD,
Gaetano Lombardi, MD, Annamaria Colao, MD, PhD

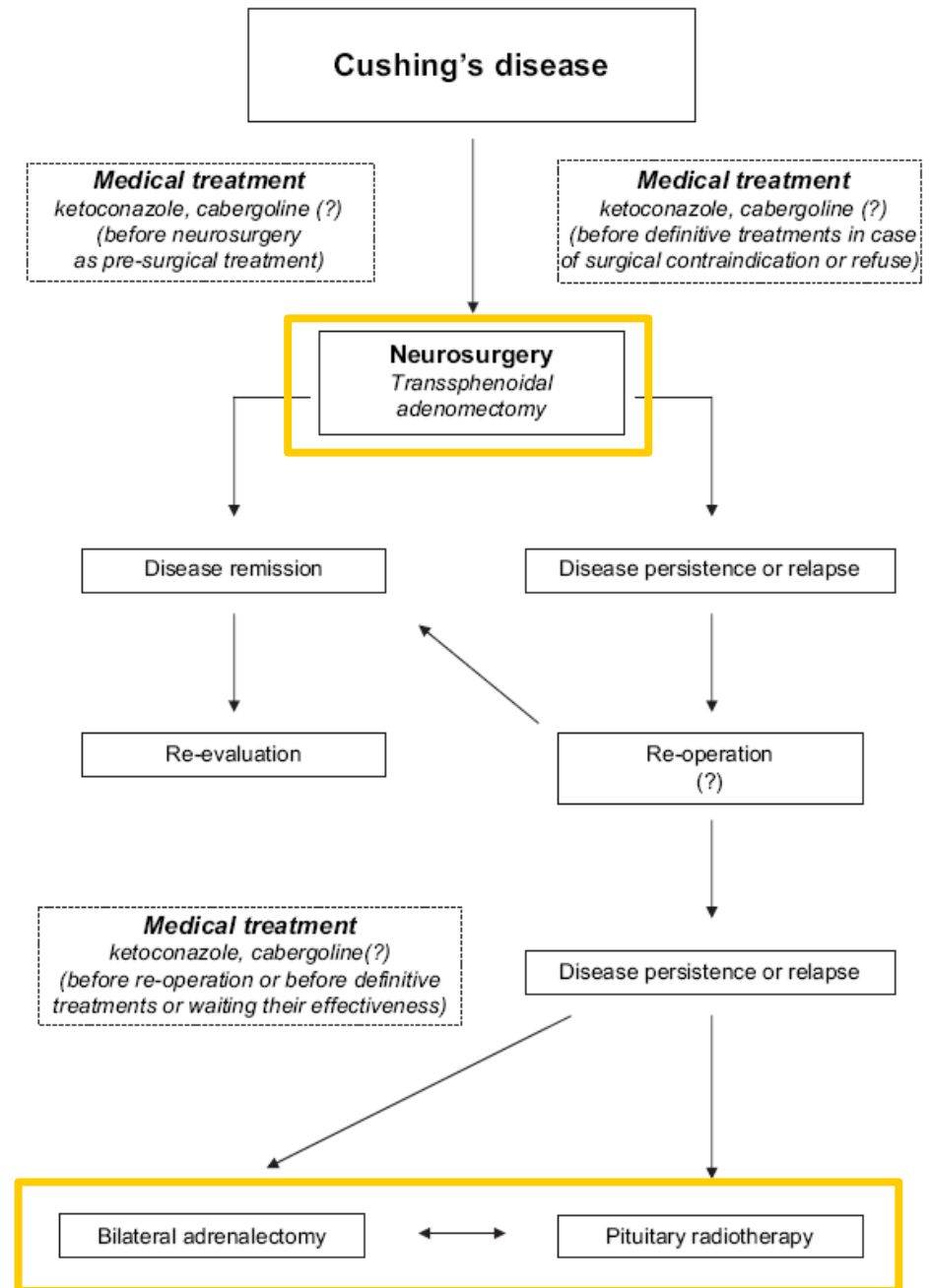
Medical therapy

Before surgery

Pre-surgical treatment
Contra-indication for surgery
Refusal of surgery

After surgery

Adjuvant treatment
Failure of alternative treatments
Contra-indications for alternative treatments
Refusal of alternative treatments

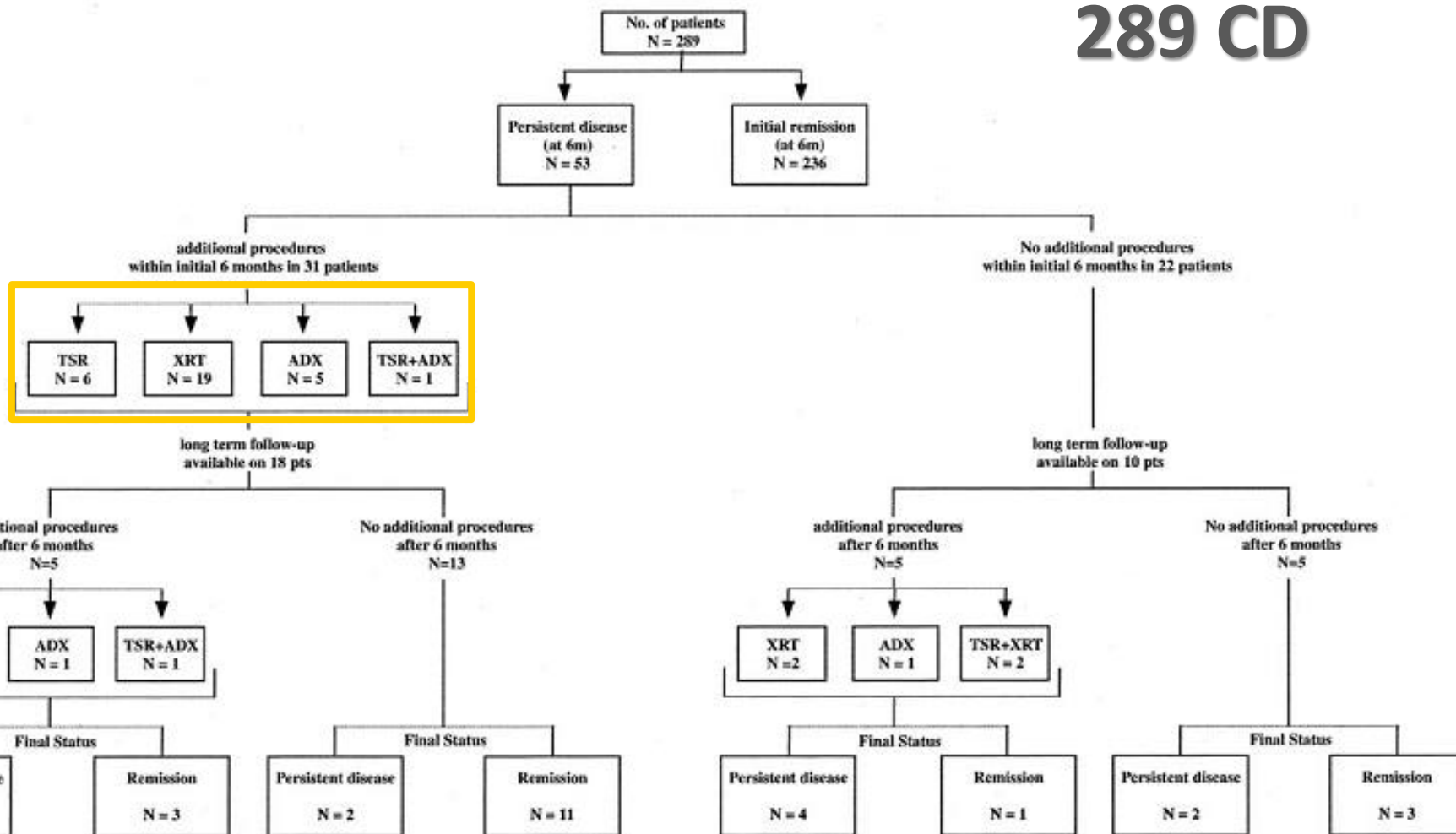


Present...

Transsphenoidal Microsurgery for Cushing's Disease: Initial Outcome and Long-Term Results

GARY D. HAMMER, J. BLAKE TYRRELL, KATHLEEN R. LAMBORN, CAROL B. APPLEBURY,
ELIZABETH T. HANNEGAN, SCOTT BELL, RIVA RAHL, AMY LU, AND CHARLES B. WILSON

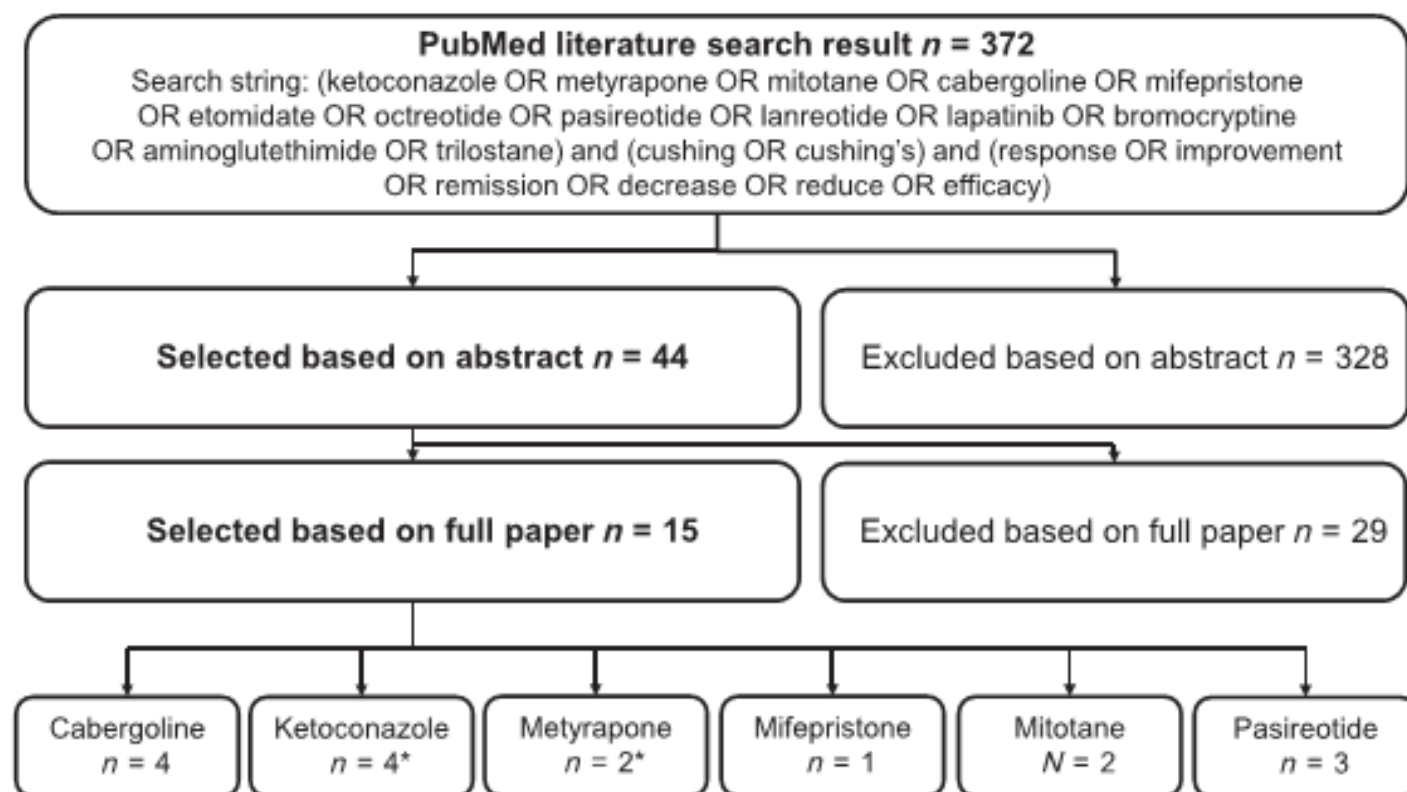
289 CD



Present...

Efficacy of medical treatment in Cushing's disease: a systematic review

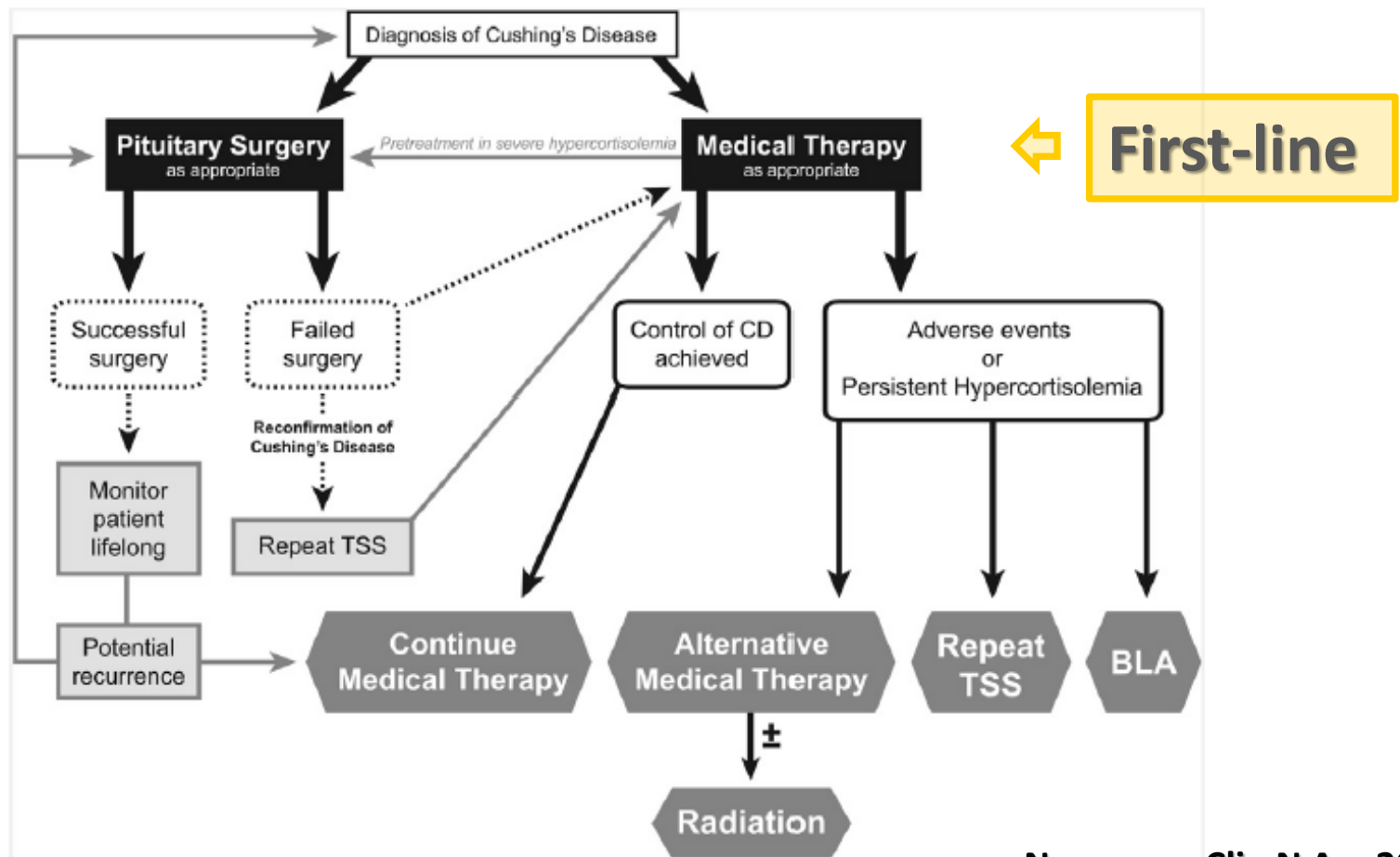
Mônica R. Gadelha* and Leonardo Vieira Neto*†



Present/Future...

Medical Management of Persistent and Recurrent Cushing Disease

Maria Fleseriu, MD^{a,b,*}



Treatment of Cushing's disease: a mechanistic update

Daniel Cuevas-Ramos^{1,2} and Maria Fleseriu³

Table 2 Use of medical therapy in Cushing's disease –
indications and needs

Before or after pituitary surgery
Preparation for surgery
Patients with contraindications for surgery
High operation risk
Patients unwilling to undergo surgery
After unsuccessful surgery
Amelioration or control of the metabolic effects of
hypercortisolemia
Potentially life-threatening complications
Patients awaiting effects of pituitary radiation
Whenever a definitive treatment is delayed

Primary medical therapy
Low probability of surgical cure
Unfavorable localization
Invisible adenomas
Adenoma without optic chiasm compression

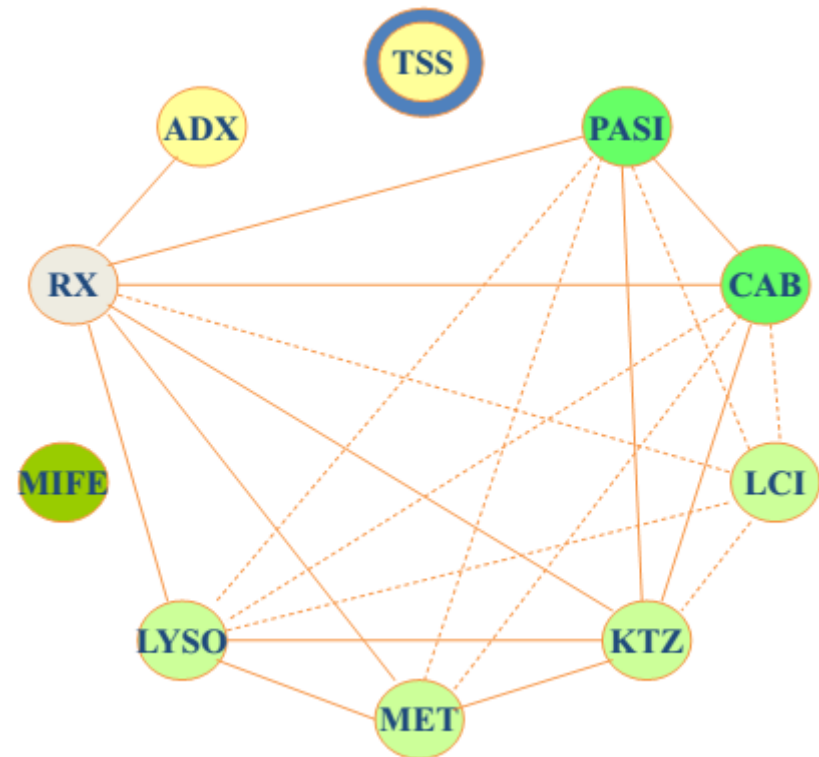
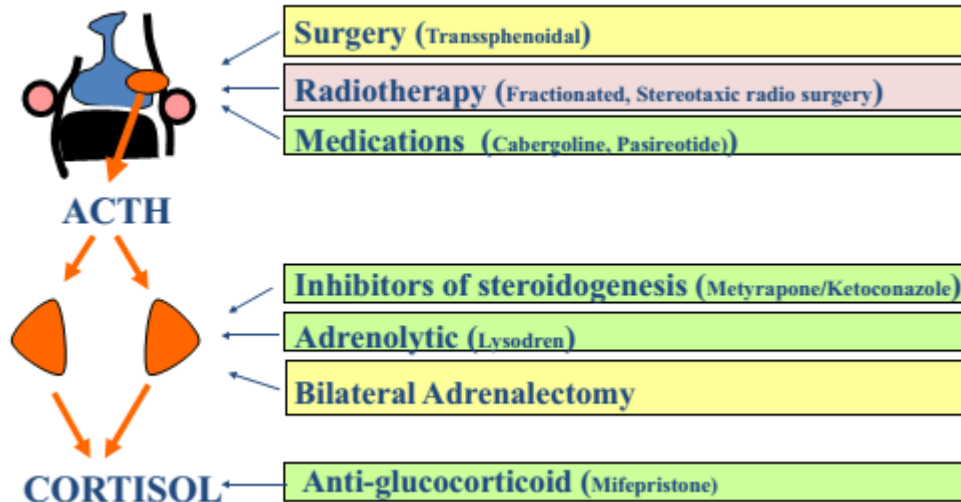
Future: which is the best treatment?

- ✓ **Effective**
- ✓ **Tailored according to patient characteristics**
- ✓ **Low incidence of complications/adverse effects**
- ✓ **Improving comorbidities and QoL**

Future...

Approach to the Cushing's Disease Patient With Persistent/Recurrent Hypercortisolism After Pituitary Surgery

Xavier Bertagna and Laurence Guignat



Thank you for the attention!



Maria Cristina De Martino
Monica De Leo
Chiara Simeoli
Davide Iacuaniero
Francesco Carlomagno
Gaetano Piccolo

Rosario Pivonello
Annamaria Colao