SURGICAL OPTIONS FOR FAMILIAL ADENOMATOUS POLYPOSIS

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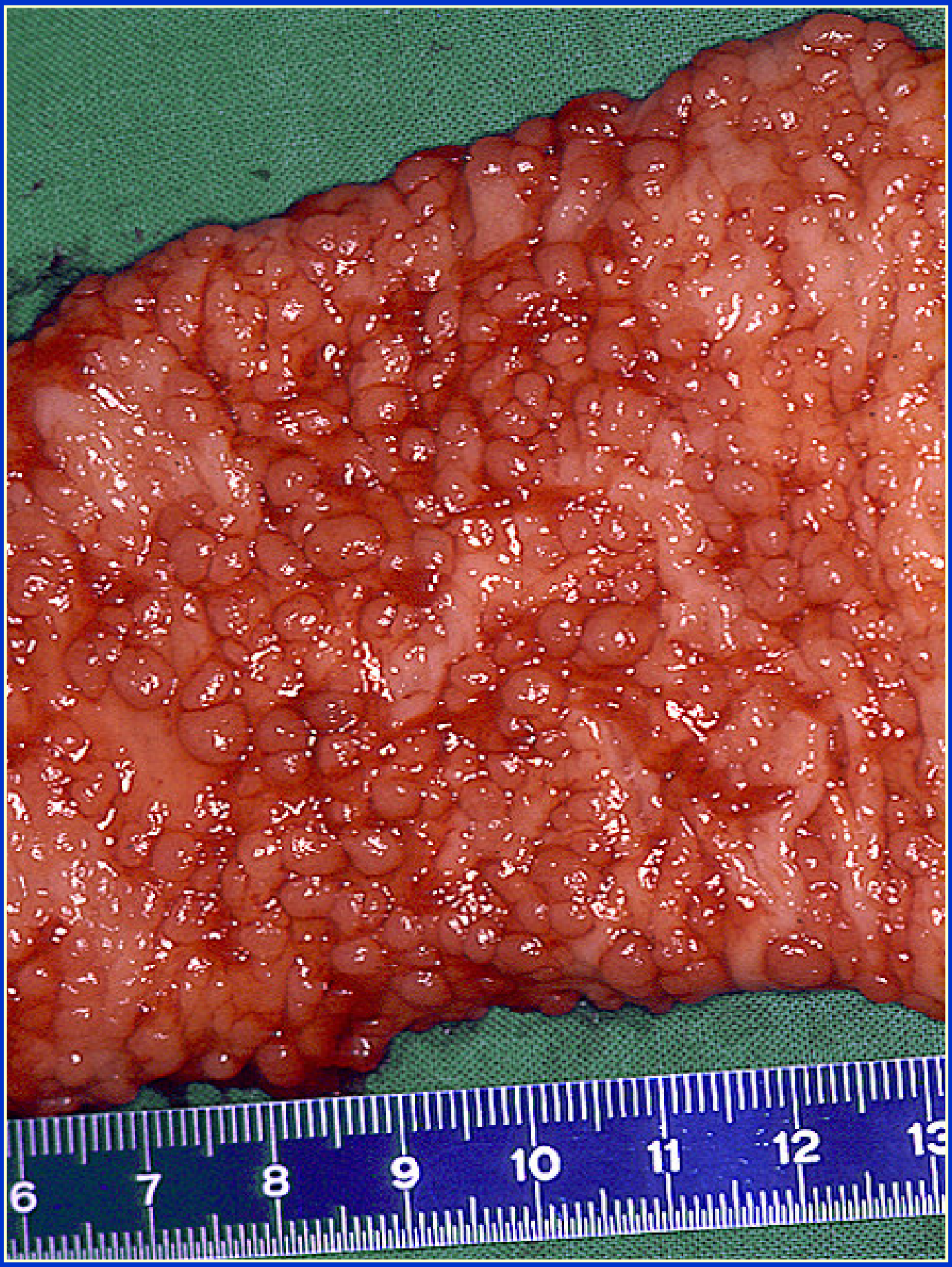
FAMILIAL ADENOMATOUS POLYPOSIS

TYPE		GENE		COLONIC POLYPS
FAP	profuse (severe)	APC	1250-1464	>5000
FAP	sparse (mild)	APC	157-1250 1464-1578	+/- 1000
AFAP		APC	3' 5' - exon 9	< 50-100
MAP		MYH		<50 ➡ 100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F A P
SURGICAL OPTIONS

- TOTAL COLECTOMY WITH ILEORECTAL ANASTOMOSIS
- PROCTO-COLECTOMY WITH ILEO ANAL POUCH ANASTOMOSIS

F.A.P.
ILEO RECTAL ANASTOMOSIS

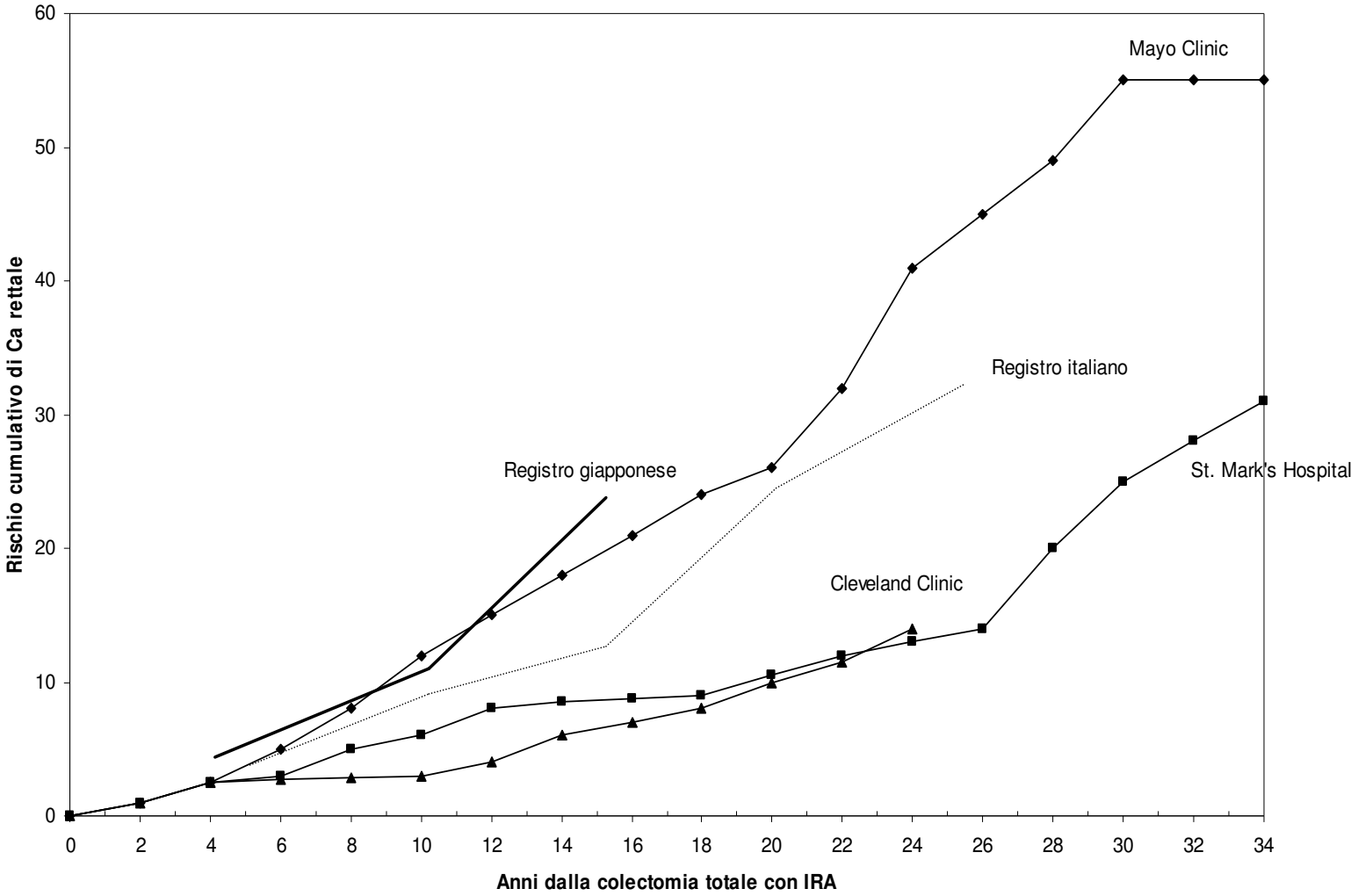
PROS

- SIMPLE PROCEDURE
- GOOD FUNCTIONAL RESULT

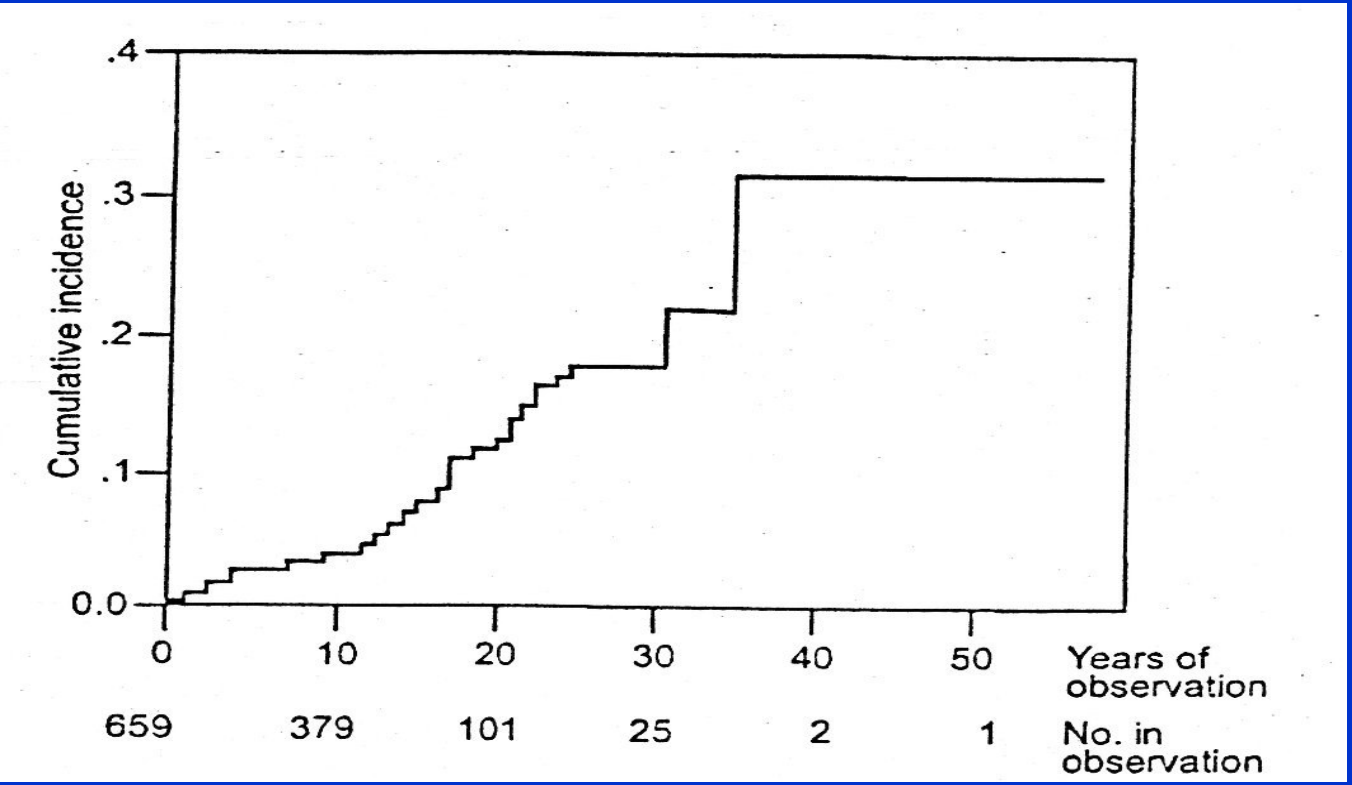
CONS

- RECTAL CANCER RISK
- FREQUENT ENDOSC. EXAM.

Incidence of rectal cancer after IRA vs. time from colectomy

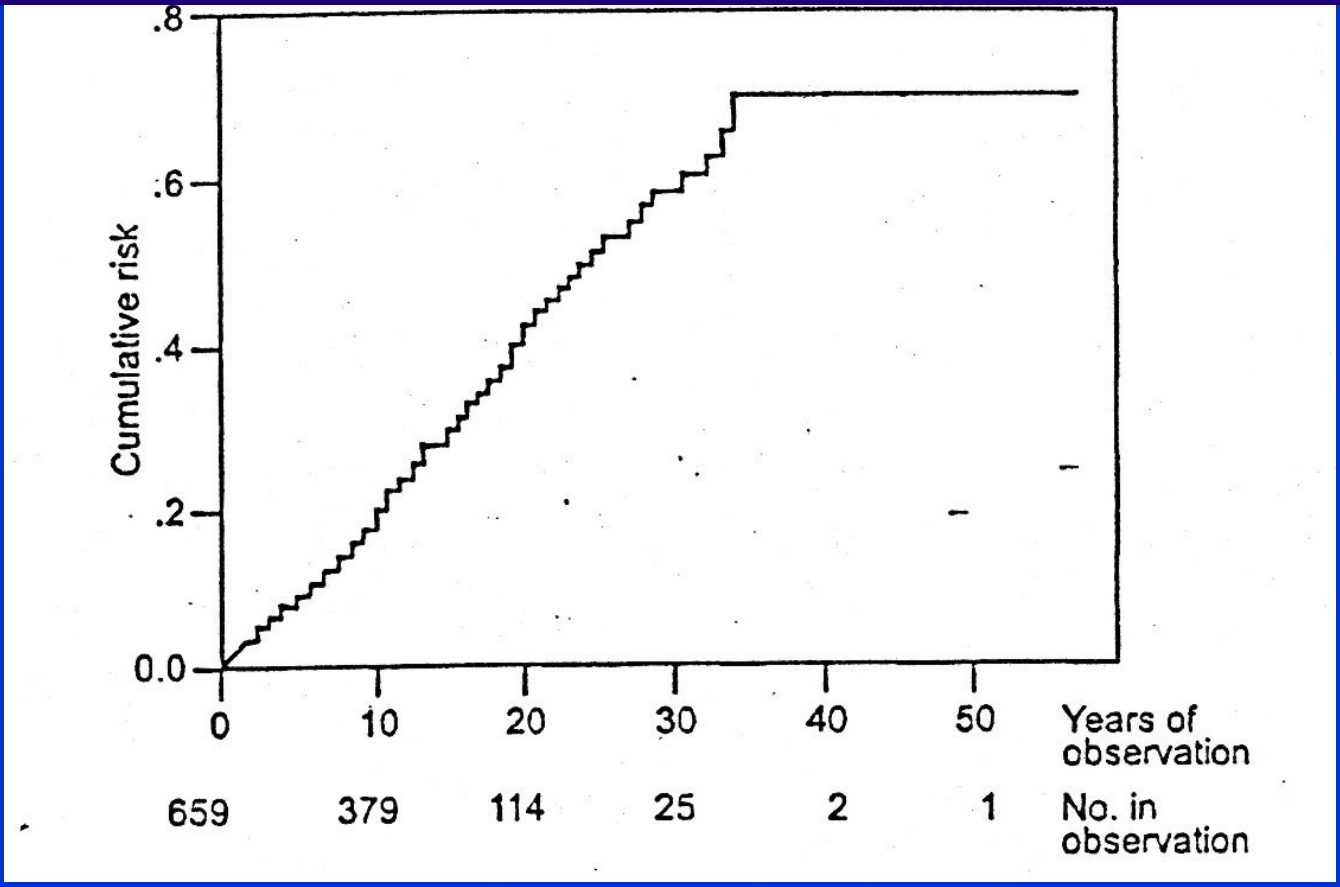


Cumulative incidence rate of rectal cancer after IRA by time



Bülow C. et al. Gastroenterology 2000

Cumulative incidence rate of proctectomy after IRA by time

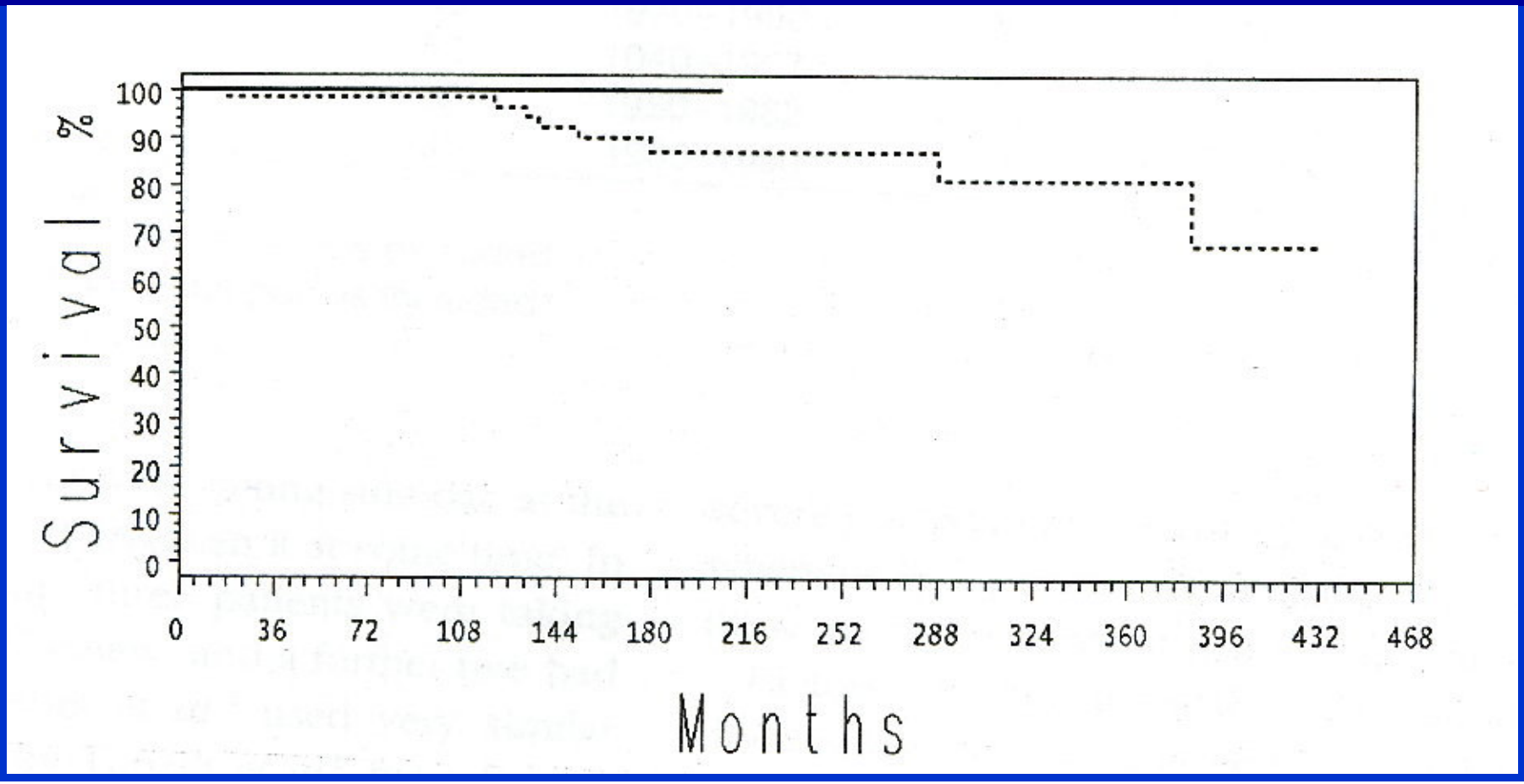


Bülow C. et al. Gastroenterology 2000

FAP
CUMULATIVE SURVIVAL FROM RECTAL CANCER AFTER IRA

(J.Church et al. Dis Colon Rectum, 2003)

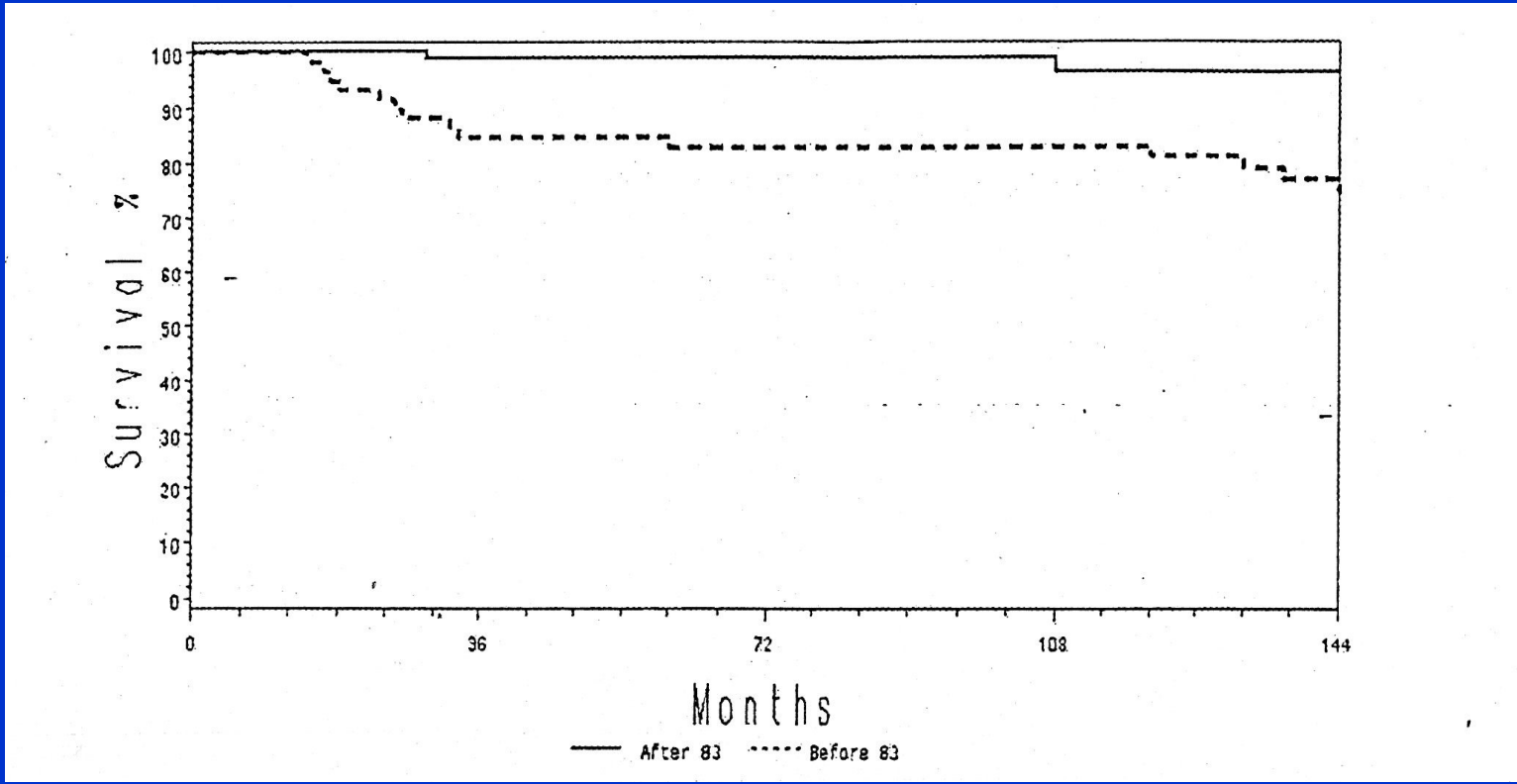
Cleveland Clinic___ **after 83** **----- before 83**



CUMULATIVE SURVIVAL FROM SECONDARY PROCTECTOMY AFTER IRA

(J.Church et al. Dis Colon Rectum, 2003)

Cleveland Clinic___ **after 83** **----- before 83**



FAP - Open issue

Which is the indication for preserving the rectum ?

1. Number of rectal polyps
2. APC mutation
3. Colonic cancer
4. Mesenteric desmoids
5. Age of the patient
6. Agreement for surveillance

FAP – Indications for IRA
(Slors et al. - Amsterdam Univ.)

< 10 flat, small polyps

< 5 protruding polyps

no severe dysplasia

RESULTS of IRA
(1950-1986 – 44 pts)
(Slors et al. - Amsterdam Univ.)

- **Rectal cancer 3/44 ► 6.8 %**
- **Proctectomy 9/44 ► 20 %**

FAP - Open issue

Which is the indication for preserving the rectum ?

1. Number of rectal polyps
2. APC mutation
3. Colonic cancer
4. Mesenteric desmoids
5. Age of the patient
6. Agreement for surveillance

APC mutation risk and IRA

• Vasen (1996)	>1250	• high rish of secondary proctectomy
• Bertario et al (2000)	1250-1464	• increased risk rectal cancer
Bülow et al (2000)	1250 - 1500	high risk of secondary proctectomy
	<200 - >1500	no risk of secondary proctectomy

FAP

INDICATION IN PRESERVING THE RECTUM

Personal guide-lines

- Less than 10 polyps (< 1cm) in the last 10 cm of the rectum (anal verge)
- Absence of sessile polyps bigger than 5 mm
- Lifelong endoscopic surveillance

Tonelli F. et al Word J Surg 21:653-9; 1997

PRIMARY SURGERY FOR FAP
personal experience 1986-2008

IRA	39 pts (44%)
RTPC	48 pts
TPC	1 pt

CLINICAL DATA OF FAP Pts.

	IRA	IAA	
N. pazienti	39	48	
Age(yrs) (range)	29.5±12.48 (10-62)	27.3+10 (9 - 59)	
N colonic polyps (media ± DS)	851 ± 320	2550 ± 1270	P<0.01
N rectal polyps (media ± DS)	9.10 ± 12.6*	534± 38 ^	P<0.05
Colonic cancer	3	4	
Rectal cancer	0	2	

IRA for FAP – Personal experience on 25 patients(1986-2002)

n. of rectal polyps at surgery	rectal polyps/year/patient mean
0-5	0.67
6-9	1.52
>10	9.29 *

*p<0.001

*Valanzano R, Tonelli F. et al: Balance between endoscopic and genetic information in the choice of ileorectal anastomosis for familial adenomatous polyposis. J Surg Oncol. 2007

Correlation between rectal polyps and *APC* and *MYH* mutation in 25 patients with IRA (personal experience)

Codon number	Type of polyposis	N° rectal polyps at surgery (range)	Recurrent rectal polyps/year/pts mean value
APC 144,208, 232,367	AFAP	0-6	0.57
APC 437,1061, 1114,1237,1324	Classic FAP	0-10	3.35
APC 1309	Severe FAP	10-30^	4.54 p<0.01
Unknown	Unknown	0-8	1.28
APC 165,231,368,374 MYH	MAP	0	0

^diminutive polyps - MAP: *MYH*- Associated Polyposis

IRA for FAP Rectal Stump Cancer- Proctectomy Personal Experience (follow- up: 11.8 ± 6.5 years)

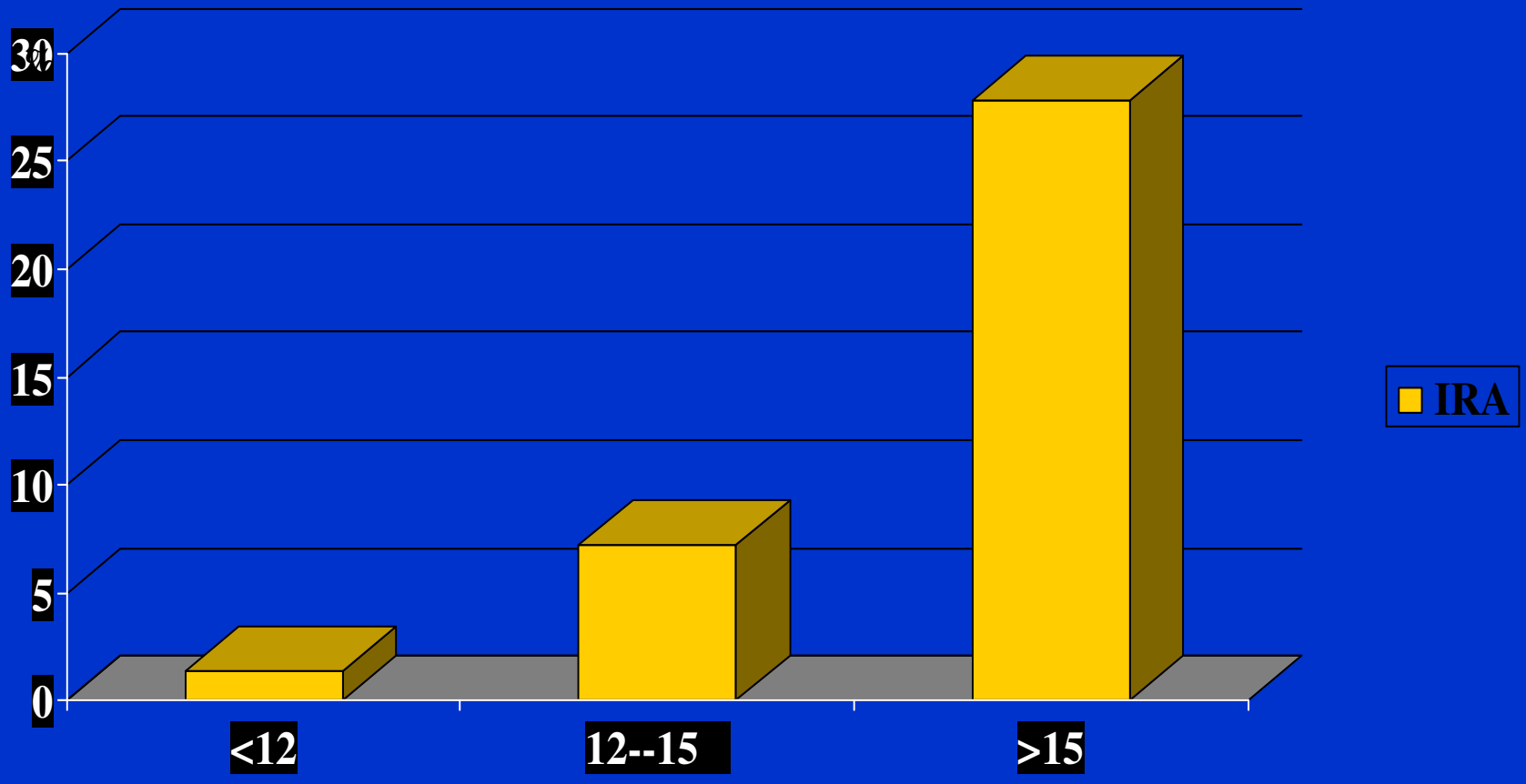
- RECTAL CANCER 0
- SECONDARY PROCTECTOMY /IPAA 2 (8%)

FATE OF THE RECTUM AFTER IRA IN RELATIONSHIP TO RECTAL POLYPS

N° Rectal Polyps at surgery	N° Patients	Rectal stump Cancer	secondary proctectomy
0 - 5	74	0 %	6 %
6 - 19	54	3.6 %	5 %
> 19	37	10.8 %	35 %

Church et al. DCR 2001 - Cleveland Clinic

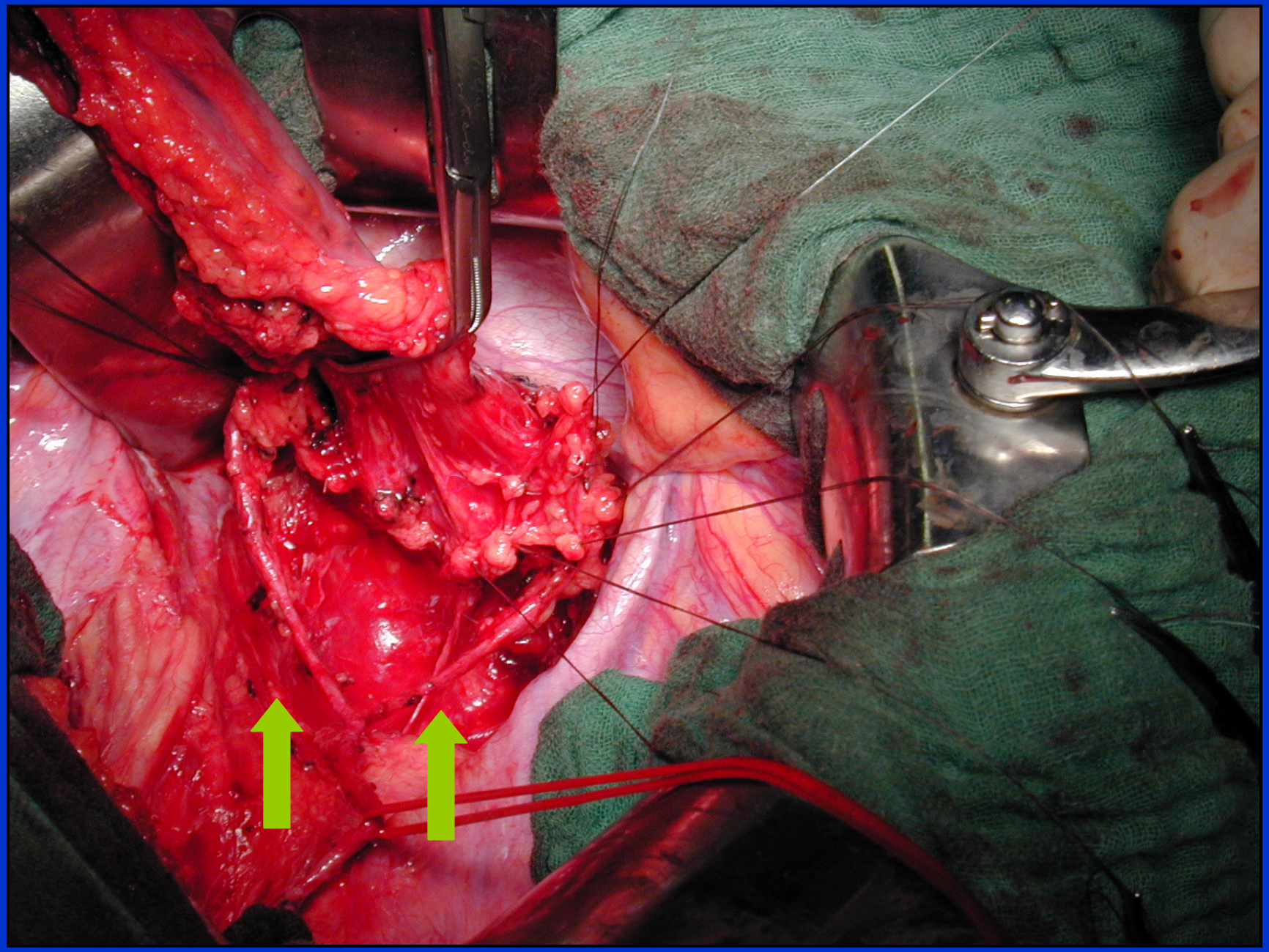
FAP RECTAL CARCINOMA AFTER I.R.A vs. LEVEL OF ANASTOMOSIS

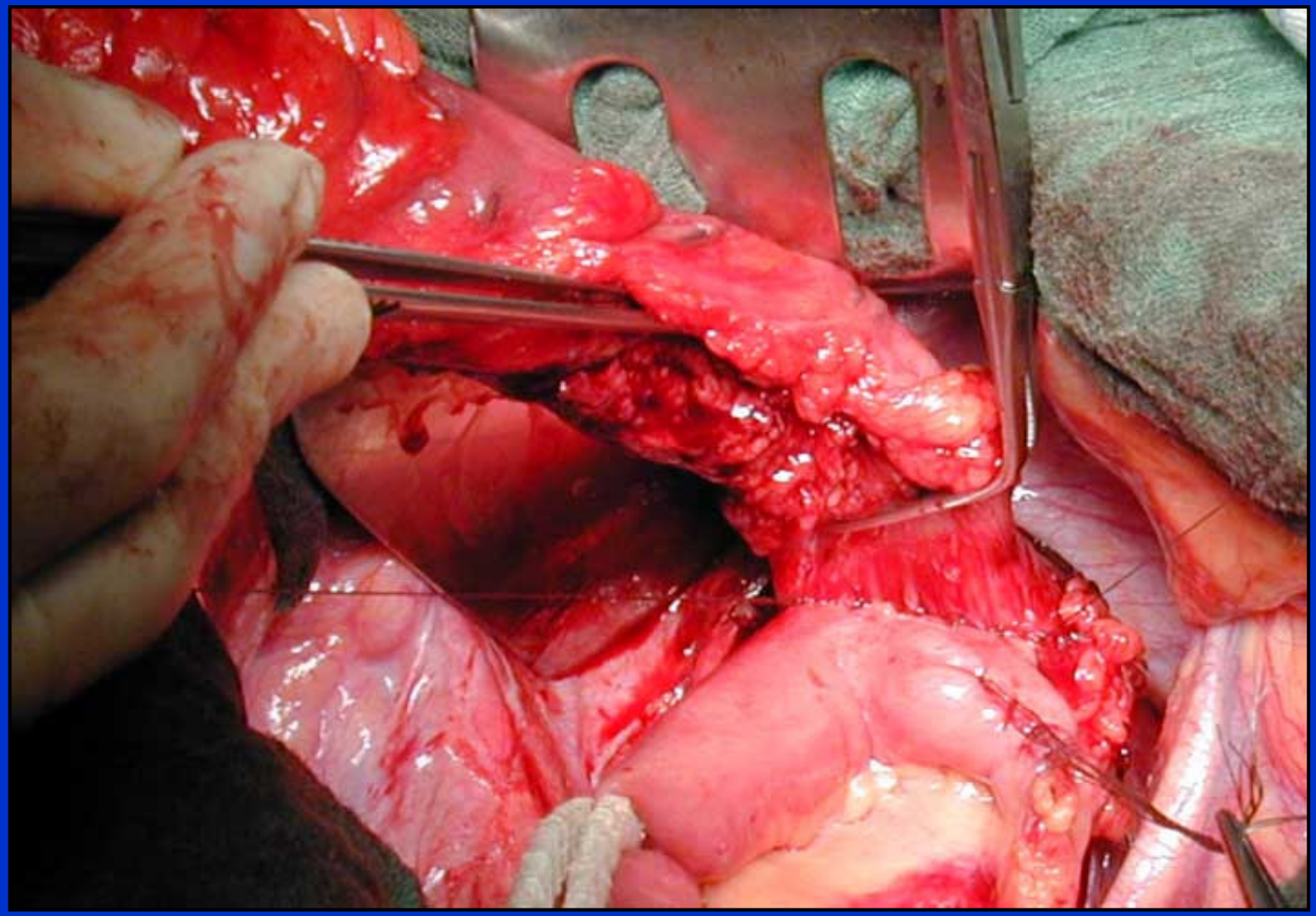


Tonelli F SIC 2000

cm. from anal edge

Literature data





Functional Results of IRA

Anastomosis below peritoneal reflection

Stool Frequency	
- 24 / hr	3.4 (1.2)
- nocturnal	0.5 (0.7)
Perfect Continence	88 %
Occasional Urgency	12 %
Soiling	/

mean (sd)

CONCLUSIONS (1)

- Low risk of rectal stump cancer after IRA when performed with less than 10 polyps in the last rectal 10 cm
- Anastomosis at the middle rectum should be performed
- Germ-line mutation can be of value only in selected cases

ILEO ANAL POUCH ANASTOMOSIS

PROS

- COMPLETE REMOVAL OF RECTAL MUCOSA

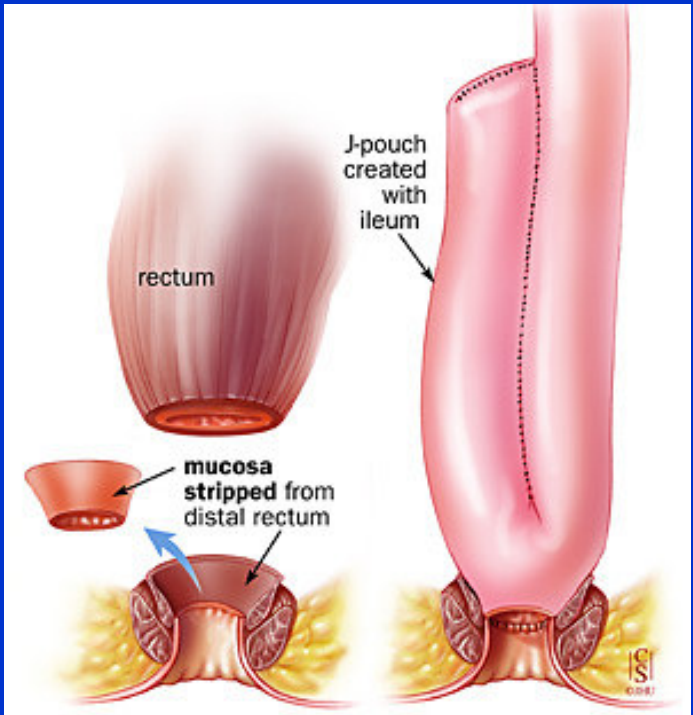
CONS

- COMPLEX PROCEDURE
- POSSIBILE INCONTINENCE
- POST-OP COMPLICATIONS (SEPSIS, NERVE INJURY)
- POUCH COMPLICATIONS (ADENOMA, CARCINOMA)

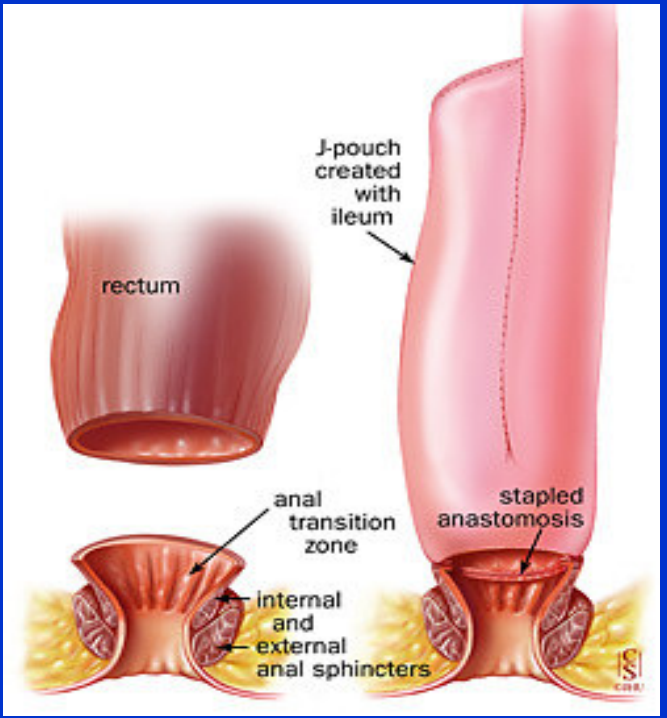
RTPC
WHICH PROCEDURE ?

POUCH	ANASTOMOSIS
J	HAND-SEWN
S	STAPLED
OTHER	
STRAIGHT	

When one of the two anastomosis techniques is used to construct IPPA :



MUCOSECTOMY



STAPLED ANASTOMOSIS


9
8
7
6
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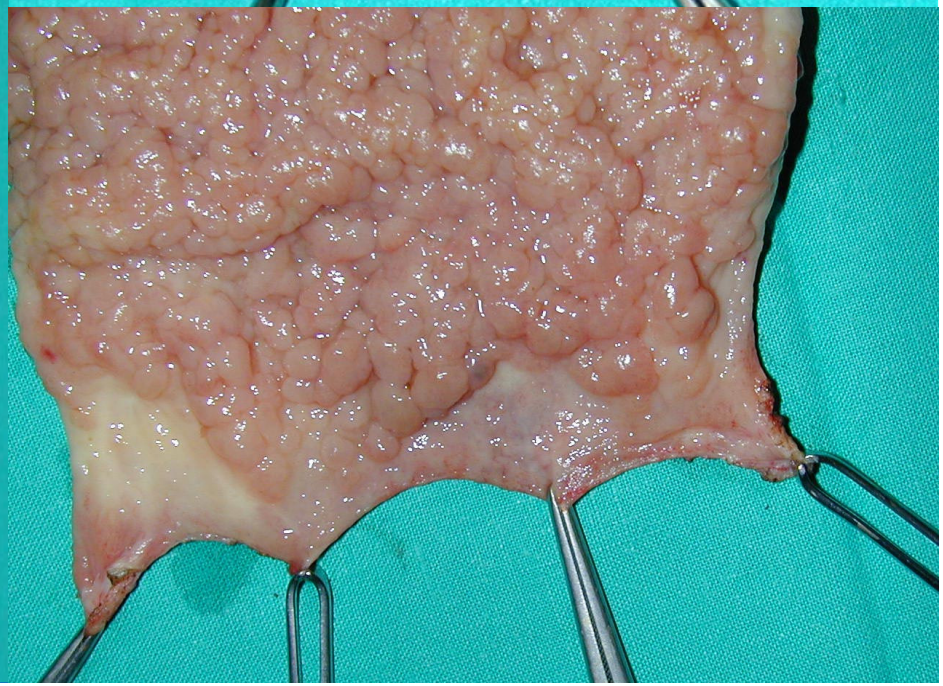
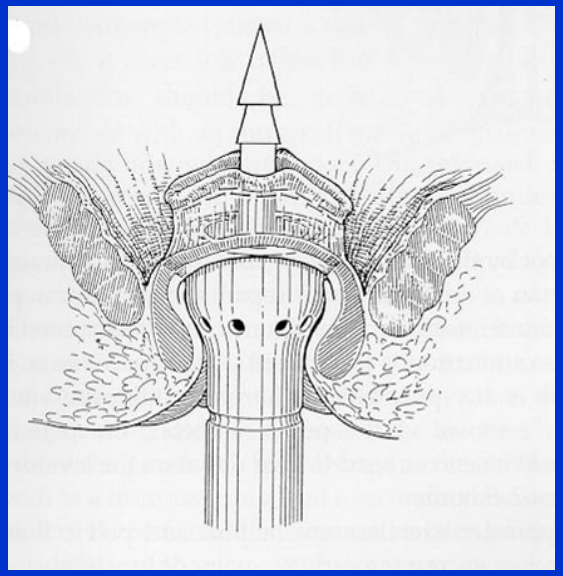
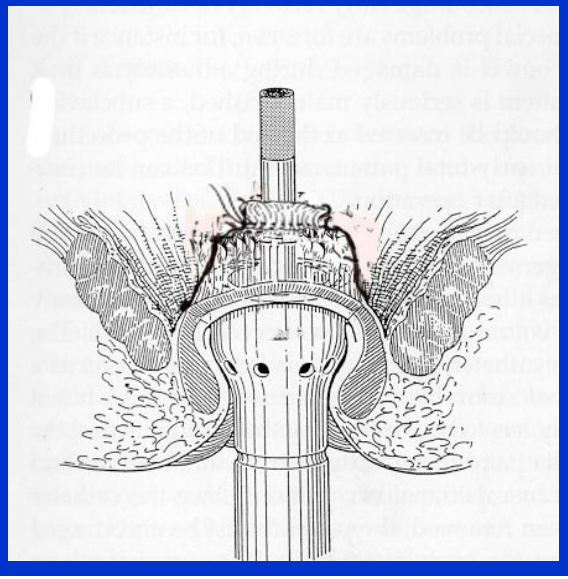
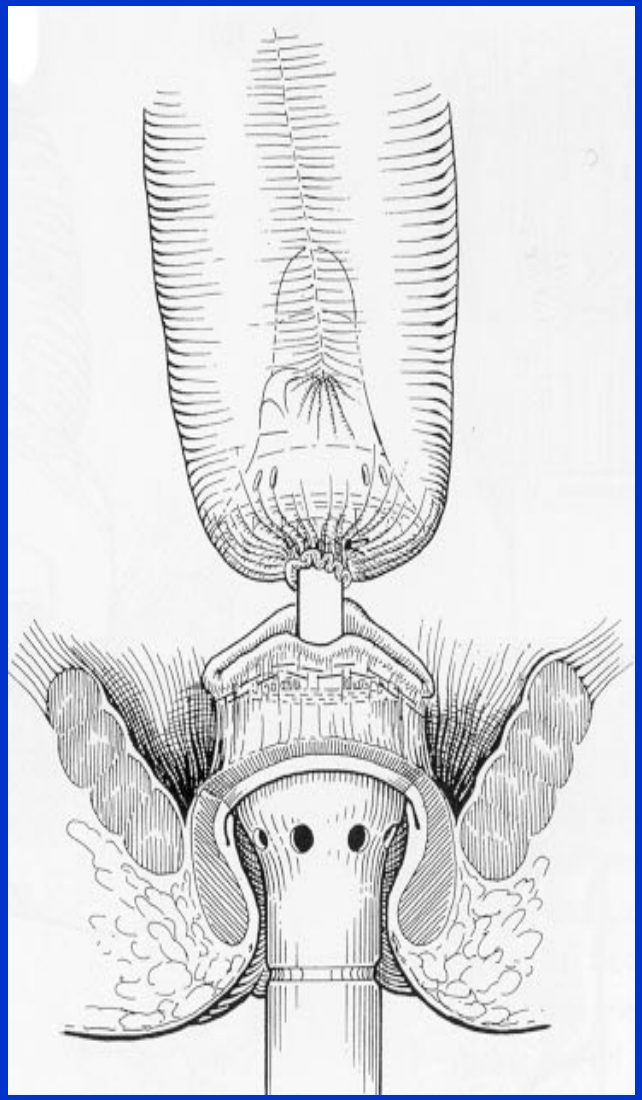
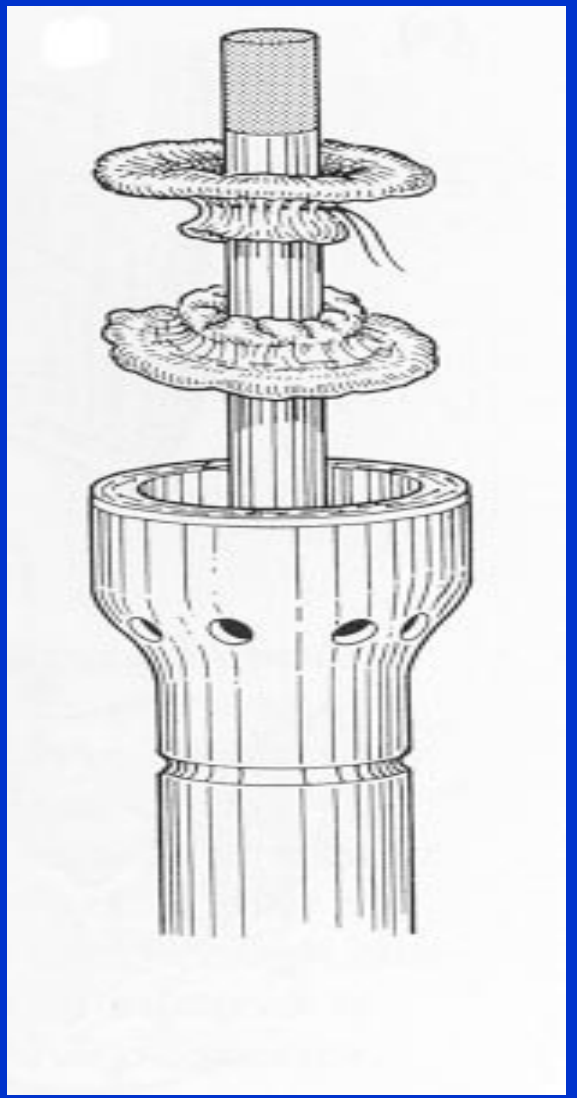


DOUBLE STAPLING TECHNIQUE









Why stapling the ileoanal anstomosis?

- **To have a better function**
- **To reach easily the anal canal**
- **To perform the operation in troublesome situation**

SURGERY FOR FAP and MAP

Personal experience (1986-2008): 104 pts

PRIMARY			SECONDARY
IRA	**IAA**	**ILEOSTOMY**	**IAA**
39*	**48**	**1**	**18(2*)**

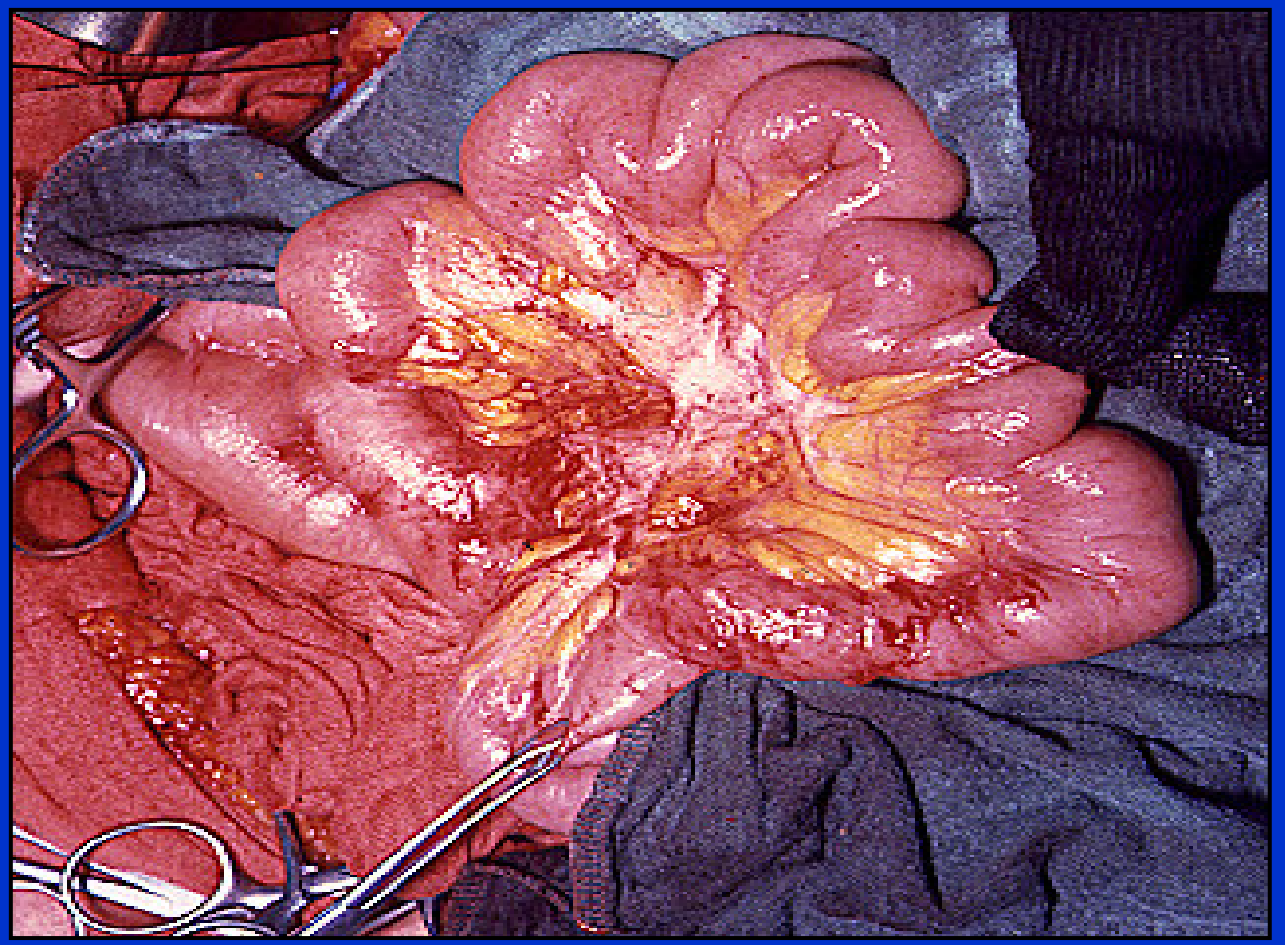
IAA: 63%

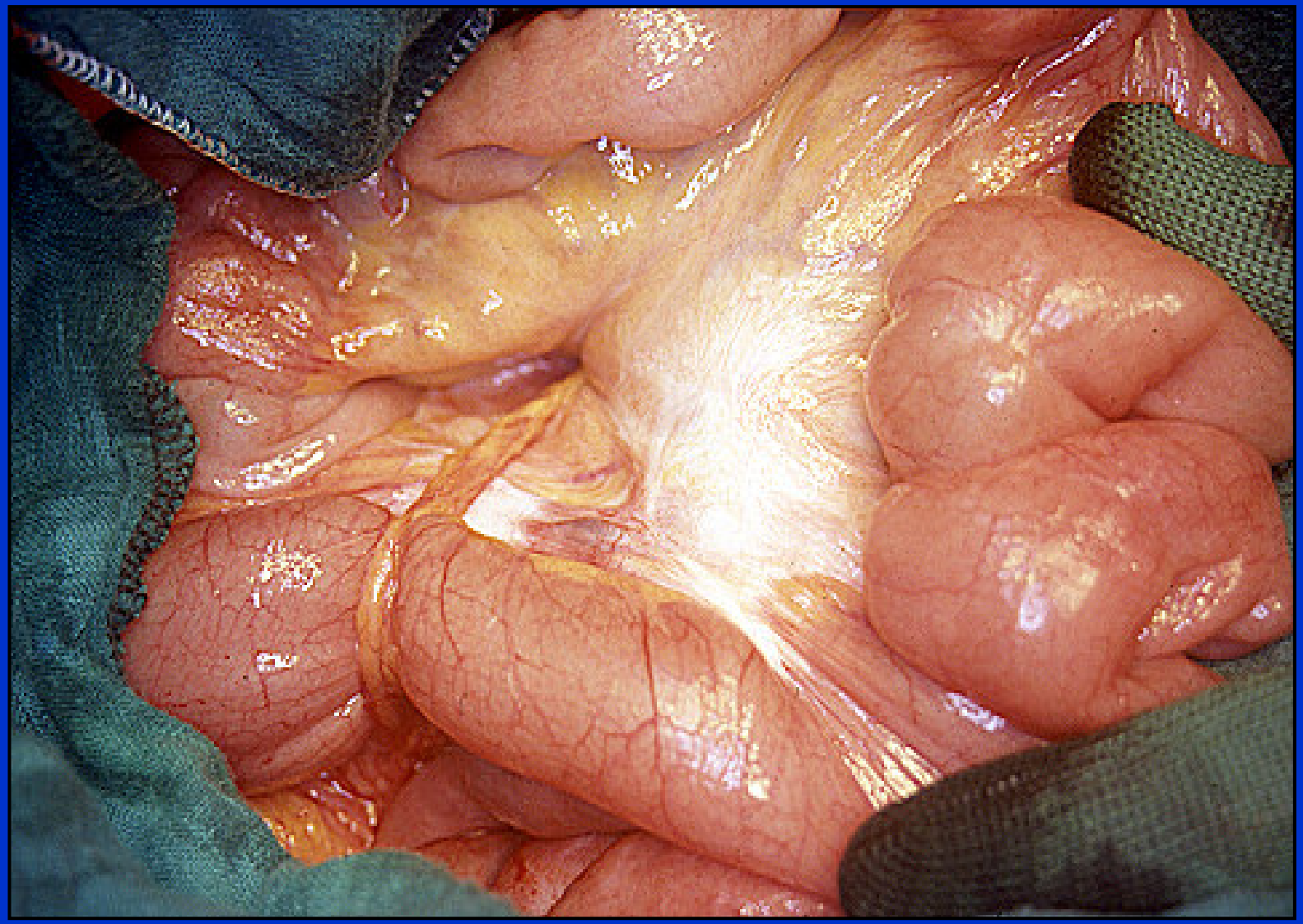
IRA: 36%

TYPE OF ILEO-ANAL ANASTOMOSIS

	PRIMARY	SECONDARY
MUCOSECTOMY HANDSEWN AN	**48** (97%)	**16** (84%)
STAPLED ANASTOMOSIS	**1** (3%)	**3** (16%)

P<0,01



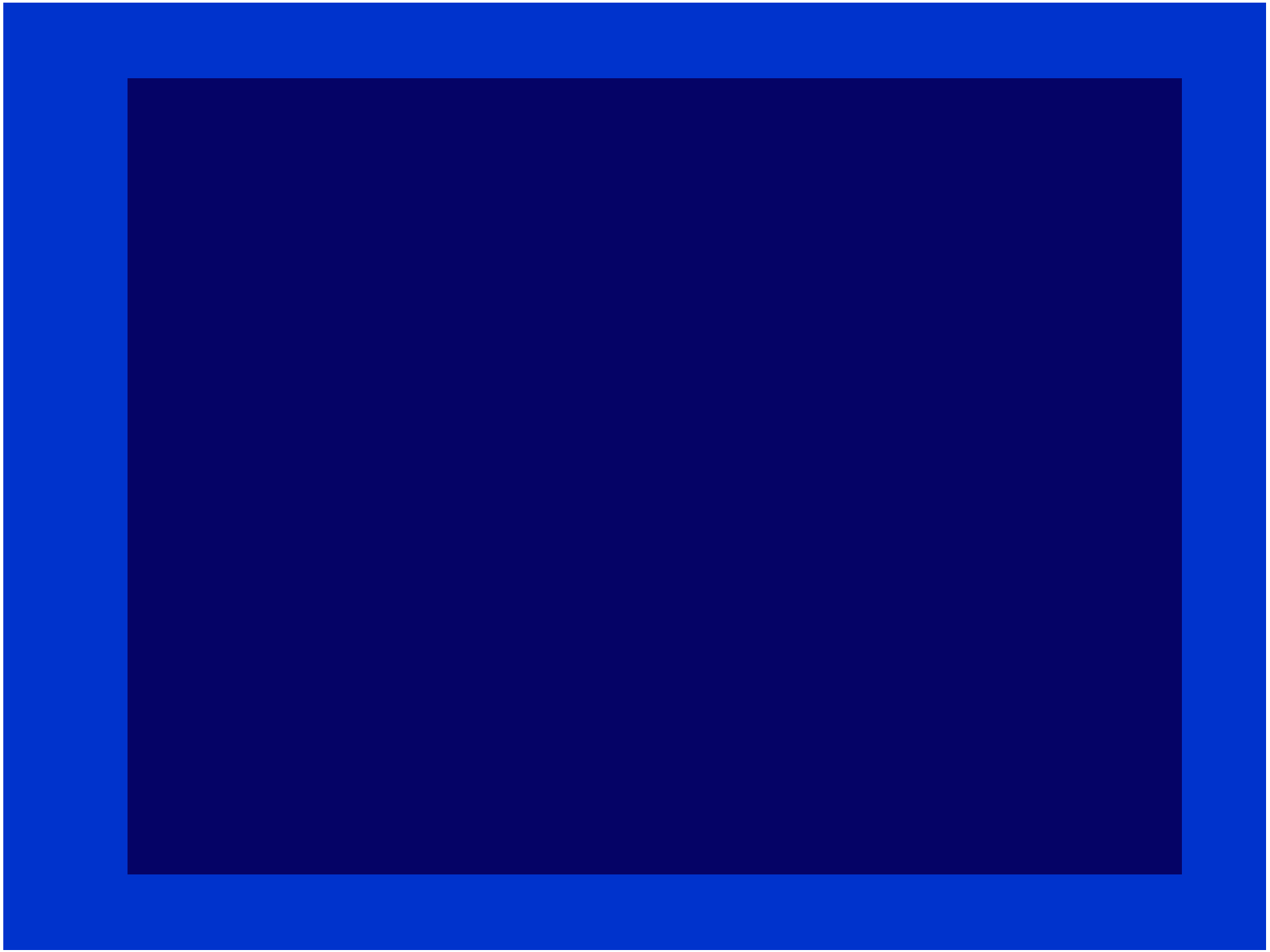


Tonelli F, Batignani G, Ficari F, Mazzoni P, Garcea A, Monaci I.

Straight ileoanal anastomosis with multiple ileal myotomies as an alternative to pelvic pouch.
Int J Colorectal Dis. 1997;12(5):261-6.

Type of pouch for RTPC
(61 pts)

	Primary	Secondary
J	**21**	**7**
S	**18**	**6**
Straight with multiple myotomies	**7 (16%)**	**6 (40%)** P<0.0l



RTPCT and FAP

Functional results – Personal experience

Pouch	S	J	Straight miot.
Stool Frequency (n.)			
• 24 / hr	3.3	3.8	4.1
• nocturnal	0.7	0.2	1
Soiling (%)			
• Nocturnal	18	26	45
• Diurnal	6	13	27

FAP - Open issue

Which is with time
the fate
of ileal pouch ?

ILEAL POUCH ADENOMAS

Author / yr	No. pts	Pouch Adenomas (%)
Nugent ’93	38	18
Wu ‘98	26	42
Renzi ‘01	118	17
Thompson 01	33	42
Park ‘01	85	35
Polese ’03	30	7
Groves ‘05	72	57
Tonelli ‘08	69	28

Polipi della pouch

- N. pz. 25/69 (27.63%)
- Età media 32.6±11.9
  (range 17-63)
- Primary IPAA: n. 19/41
- Secondary IPAA: n. 6/18

Polyps features

- Total n. of adenomas 201 (range 1-47 per pts)
- Single 32% Sporadic 40%; Multiple 18%
- Mean size 3 (range 1-40) mm
- Site:
  - Pouch 22
  - Anastomotic site 3

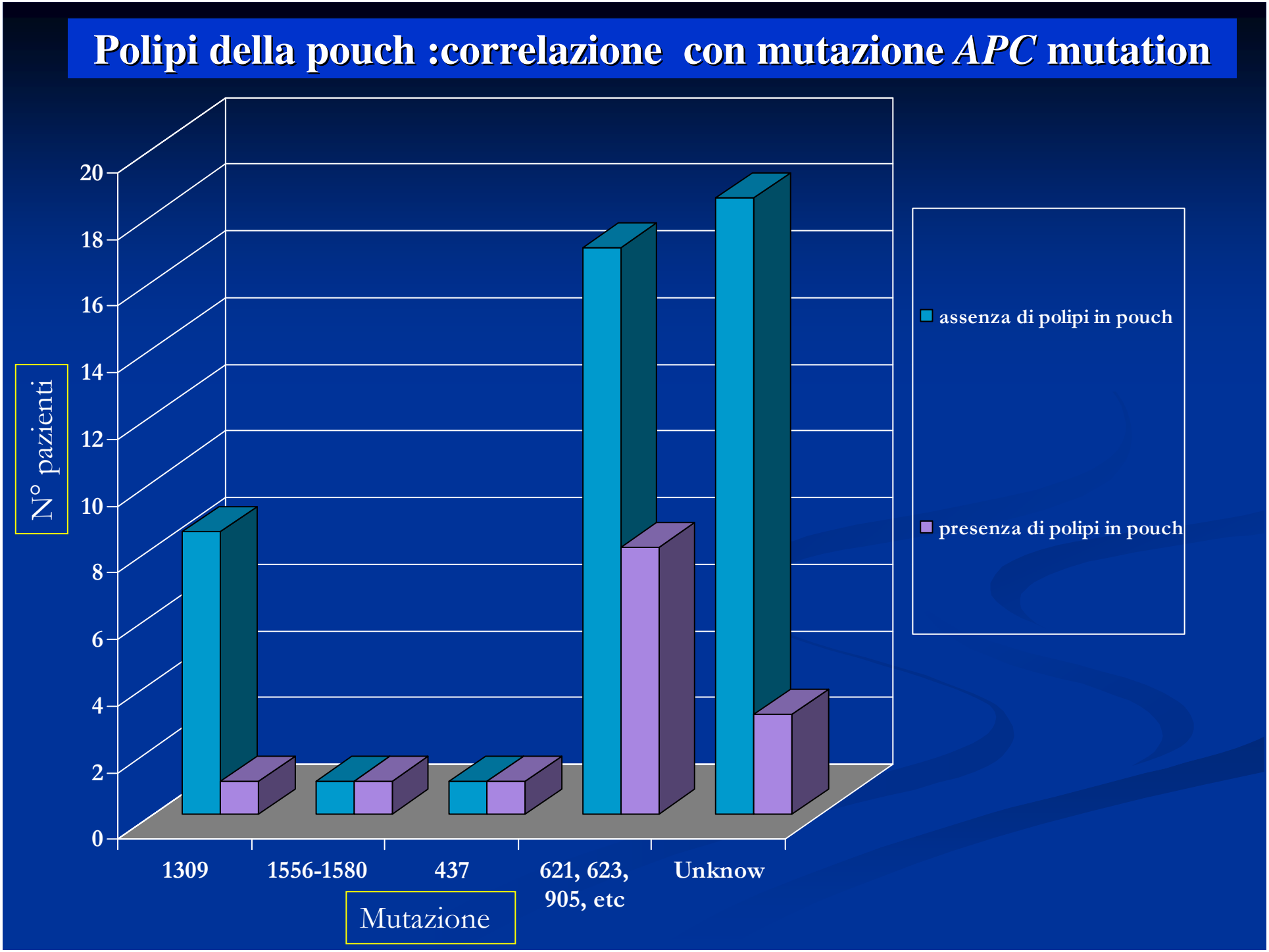
Histologic findings of pouch adenomas

• Tubular adenomas	20 pts
• Tubulo-villous adenomas	5 pt
• Low grade dysplasia	24 pts
• High grade dysplasia	1 pt

Factors that could influence the risk of pouch adenomas after IPAA

1. Age
2. Lenght of follow-up
3. Severity of colonic and duodenal disease
4. Type of APC mutation
5. Type of anastomosis

Polipi della pouch :correlazione con mutazione *APC* mutation



ILEAL POUCH-ANAL ANASTOMOSIS ADENOMAS

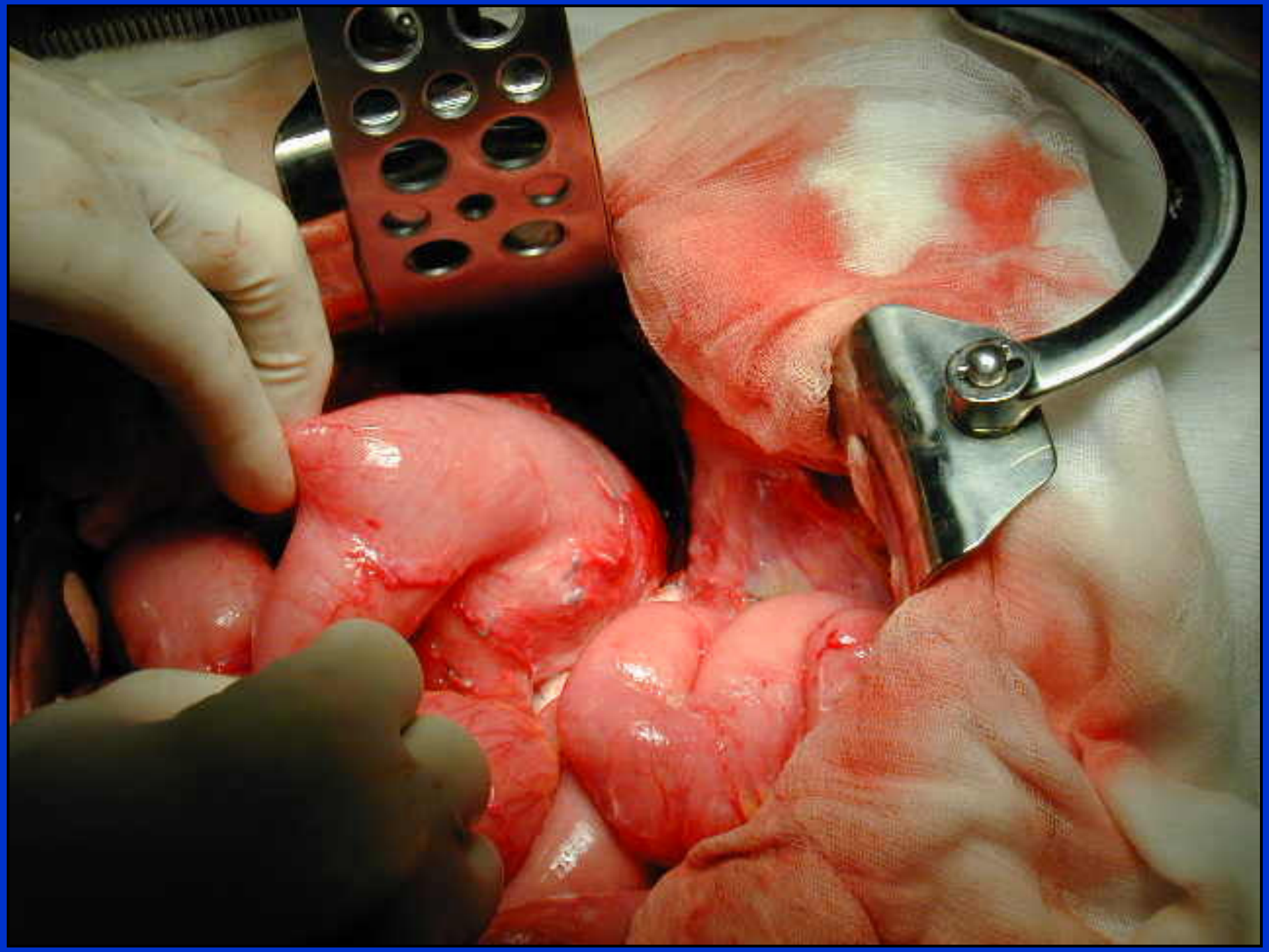
Author / yr	Adenomas (%)	
	Hand-sewn	Stapled
Van Duijvendjk ’99	9	20
Renzi ’01	14	28

Ileal-pouch polyps: treatment

- Fulguration n.9 pts
- Endoscopic polypectomy n.4 pts
- Surgical polypectomy n.5 pts
- Surveillance n.10 pts

Cancers at the ileo-anal anastomosis after IPAA

Author/year	n. cases	site	Type of anastomosis
Hoehner 94	1	anastomosis	Hand-sewn
Von Herbay 96	1	anastomosis	Hand-sewn
Vuilleumier ‘00	1	anastomosis	Double-stapled
Brown ’01	1	anastomosis	Hand-sewn
Ooi ’03	2	anastomosis	1 Double-stapled 1 Hand-sewn
Vrouenraets ‘04	2	anastomosis	2 Double-stapled




Metric
1
2
3

Possible causes of ileal pouch carcinoma

- Tumor cells of primary colorectal cancer at time of pouch surgery may implant into the ileal pouch and present as a new tumor (Ravitch 1984: unlikely)
- Island of rectal mucosa retained in the rectal cuff or at anastomosis
- The ileal pouch itself as a source of carcinoma

Pouch carcinoma after IPAA for FAP

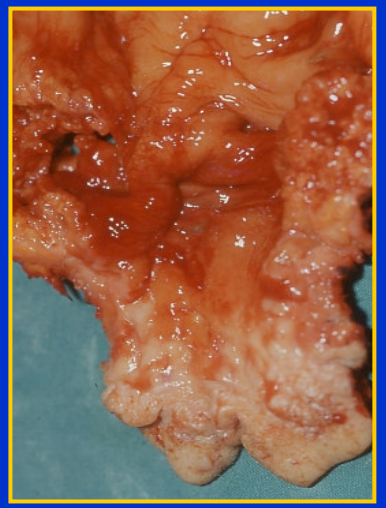
Autor/yr	No. cases	Site of cancer	Type of IPAA
Hoehner ‘94	1	anastomosis	Hand-sewn
Bassuini ‘96	1	pouch	Hand-sewn
Von Herbay ’96	1	pouch	Hand-sewn
Palkar ’97	1	pouch	Hand- sewn
Vulleumier ’00	1	anastomosis	Stapled
Brown ’01	1	anastomosis	Hand-sewn
Ooi ’03	2	anastomosis anastomosis	1 Stapled 1 Hand-sewn
Tonelli ’05	2	Pouch (2)	2 Hand –sewn

Ileal pouch cancer: case 1

- Man 29 years old
- 1982: colectomy with IRA
- 1989 Proctectomy with IPAA (S pouch with hand-sewn anastomosis) for rectal diffuse polyposis, severe dysplasia,but not signs of invasive carcinoma

Ileal pouch cancer: case 1

- August 1992 no ileal pouch polyps
- August 1993 mild proctorragy
- September 1993 evidence of ileal pouch carcinoma (excision of the pouch)

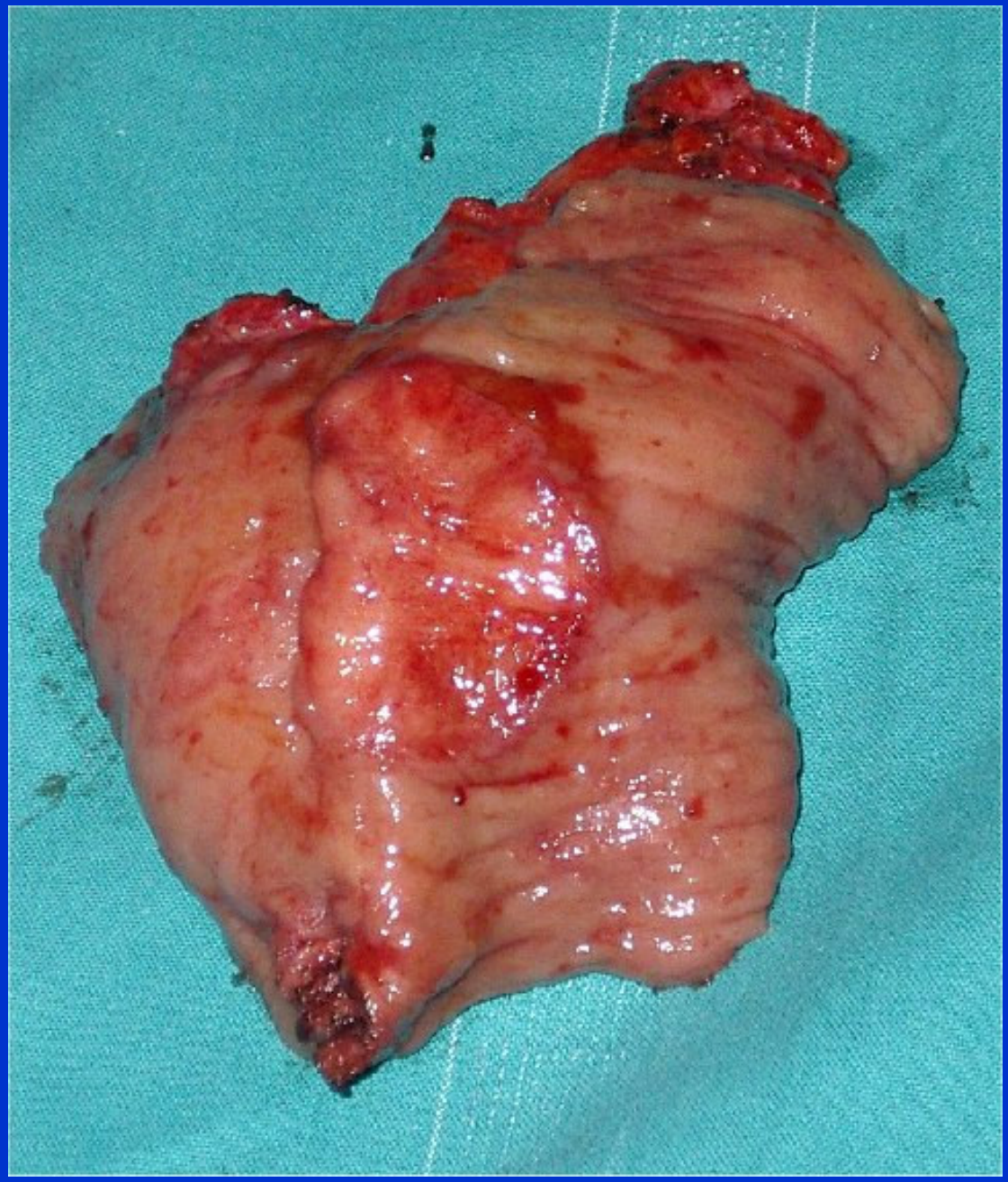


Histology

Invasive colloidal carcinoma
(stage T3N0)

Ileal pouch cancer: case 2

- Female 58 years old
- 1978 IRA
- 1993 IPAA (S pouch, with hand-sewn anastomosis) for rectal cancer (T1N0)
- April 2004 no ileal pouch polyps
- November 2004 evidence of large flat, centrally depressed lesion of the ileal pouch
- Excision of the pouch.



Histology

Moderately differentiated adenocarcinoma with colloidal expressions (stage T2N0)

CONCLUSIONS (2)

- IPAA remains the treatment of choice in the majority of FAP patients.
- Double stapled anastomosis could be particularly at risk for adenomas and carcinoma growth.
- The ileal pouch is at risk for carcinoma onset
- Life-long strict endoscopic surveillance is mandatory after RTPC.

Si ringraziano

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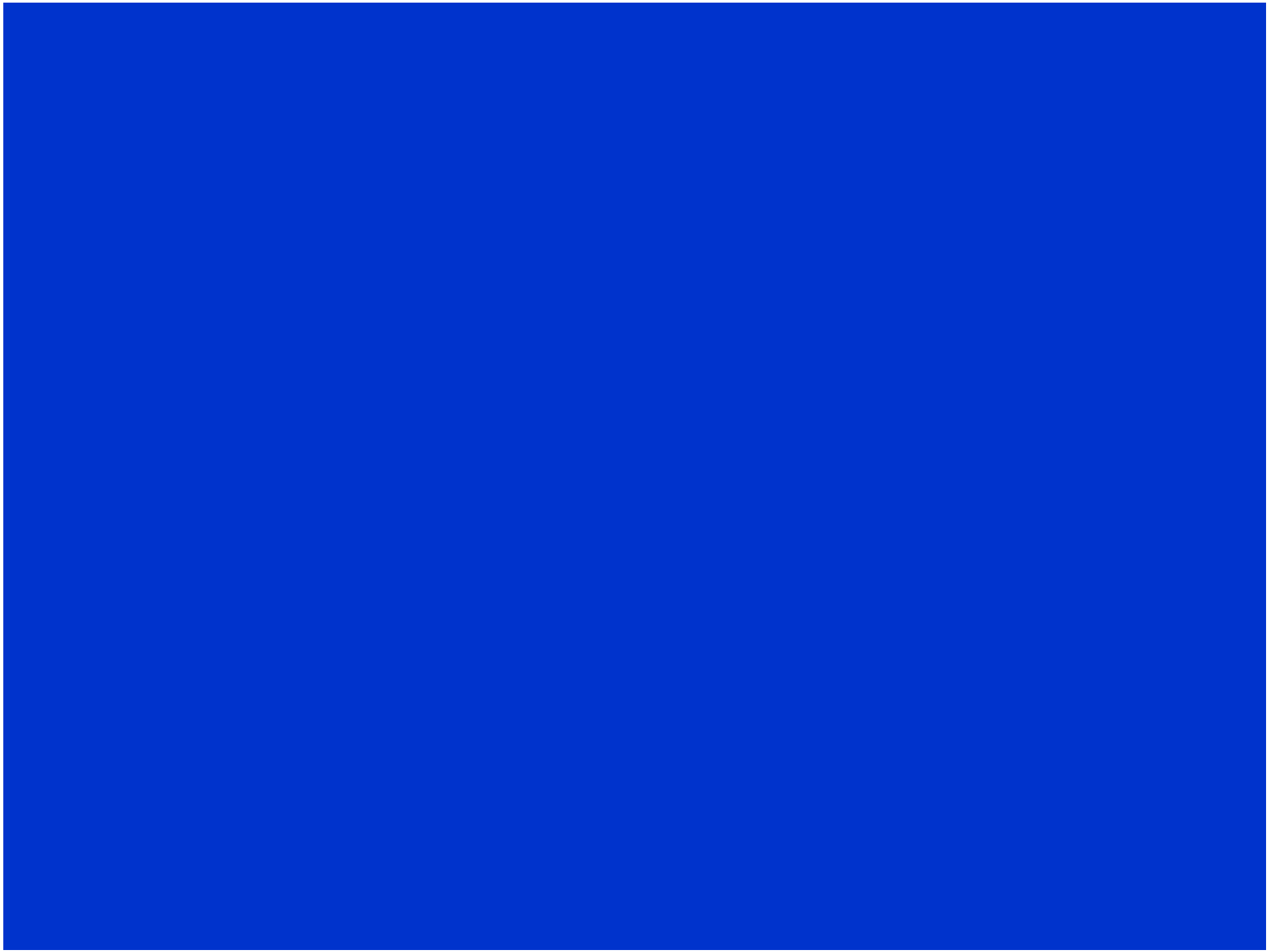
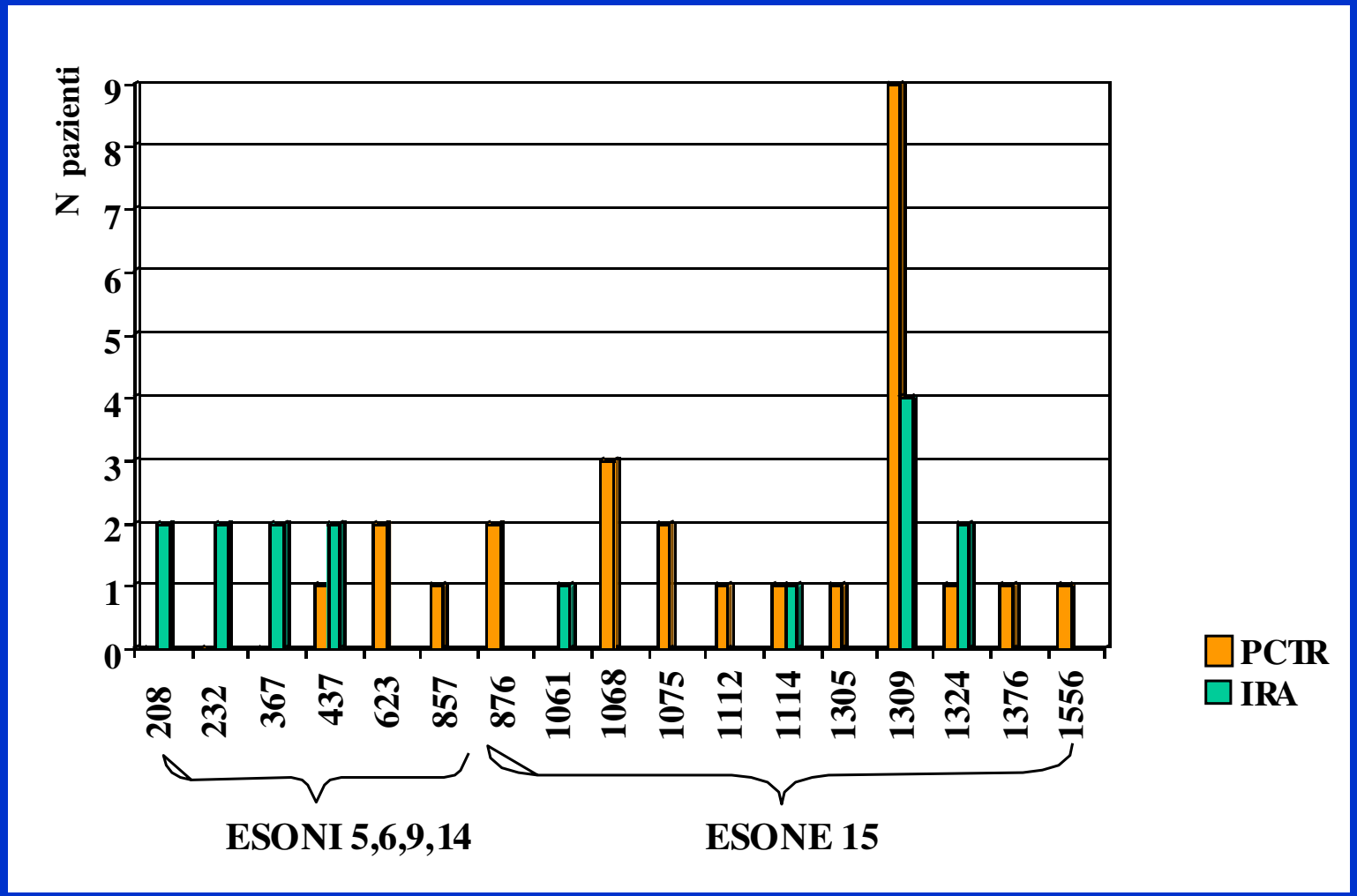


MUTAZIONI DEL GENE APC
TIPO DI INTERVENTO CHIRUGICO
ESPERIENZA PERSONALE



Rischio di cancro dopo IPAA

Author/year	n. cases	site	Type of anastomosis
Hoehner 94	1	anastomosis	Hand-sewn
Bassuini 96	1	pouch	Hand-sewn
Von Herbay 96	1	anastomosis	Hand-sewn
Palkar 97	1	pouch	
Vuilleumier ‘00	1	anastomosis	Double-stapled
Brown ’01	1	anastomosis	Hand-sewn
Ooi ’03	2	anastomosis	1 Double-stapled 1 Hand-sewn
Vrouenraets ‘04	2	anastomosis	Double-stapled

Polipi della pouch Tempo dalla IPAA

Anni	assenti	sporadici	multipli	cancro	Totale (%)
0-5	15	3	2	1	6/21 (28.5)
6-15	22	4	7	1	12/33 (36.3)

Polipi della pouch all'ultimo follow-up

Età	Assenti	Sporadici	Multipli	Cancro	Totale (%)
< 30	19	3	1	1	5/24 (20.8)
31-50	15	2	3	/	5/20 (25)
> 50	8	2	3	1	6/14 (42.8)

Polipi della pouch: correlazione con il tipo di pouch

Tipo di pouch	Assenti	Sporadici	Multipli	Cancro
S	16	3	3	2
J	17	6	5	/
Diretta	8	3	2	/
Double stapled IAA	1	2	1	/

Polipi della pouch: correlazione con i polipi duodenali

Adenomi della pouch	Adenomi duodenali	Papillary adenomas	Totale %
NO (46 pts)	11	5	34 %
YES (15 pts)	9	/	60 %

- **1 carcinoma**

TIPO DI INTERVENTO CHIRURGICO

	IRA	IAA
FAP	22	34
AFAP	8	0
AMAP	4	1
NO APC/ MYH	5	13

Cancers at the ileo-anal anastomosis after IPAA

Author/year	n. cases	site	Type of anastomosis
Hoehner 94	1	anastomosis	Hand-sewn
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Ooi ’03	2	anastomosis	1 Double-stapled 1 Hand-sewn
Vrouenraets ‘04	2	anastomosis	2 Double-stapled

POLIPI DEL DUODENO: SPIGELMAN'S SCORE

- 58/135 pz affetti da FAP presentano polipi del duodeno
- 29 M; 29 F
- Età media all'ultima endoscopia: 39 aa (range 21-63)
- Tempo medio di follow-up: 124 mesi

	SPIGELMAN'S SCORE		
	I stadio	II stadio	III stadio
N. pz	25 (43%)	22 (38%)	11 (19%)

POLIPI DEL DUODENO: TRATTAMENTO

- Numero cumulativo di polipi: 489 (media 7,3/pz)
- I o II stadio: rimozione endoscopica con ansa diatermica; YAG laser; polipectomia.
- III stadio trattato con chirurgia:
  - 3 duodenotomie con polipectomie (media 12 polipi/pz)
  - 5 duodenotomie con ampullectomia
  - 3 duodenopancreatectomie in casi di cancro duodenale (2 pz) o carpeting polyposis (1pz)

Pouch carcinoma after IPAA for FAP

Autor/yr	No. cases	Site of cancer	Type of IPAA
Hoehner '94	1	anastomosis	Hand-sewn
Bassuini '96	1	pouch	Hand-sewn
Von Herbay '96	1	pouch	Hand-sewn
Palkar '97	1	pouch	Hand- sewn
Vulleumier '00	1	anastomosis	Stapled
Brown '01	1	anastomosis	Hand-sewn
Ooi '03	2	anastomosis anastomosis	1 Stapled 1 Hand-sewn
Vrouenraets '04	2	anastomosis	2 Double-stapled
Tonelli '05	2	Pouch (2)	2 Hand –sewn

FAP: SURGICAL OPTIONS

TOTAL COLECTOMY WITH ILEO RECTAL ANASTOMOSIS (IRA)

- NO RECTAL POLYS OR VERY FEW (A.F.A.P.)
- PALLIATIVE SURGERY

PROCTOCOLECTOMY WITH ILEO ANAL POUCH ANASTOMOSIS (IPAA)

- RECTAL CARCINOMA
- *Severe* FAP 1309 mutation

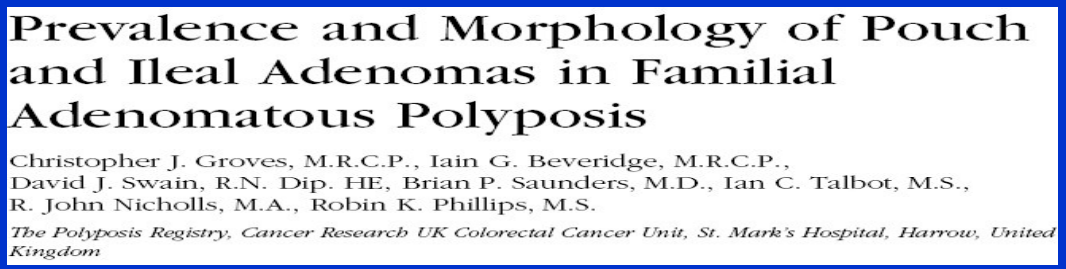
INCIDENZA DEI DESMOIDI IN RELAZIONE AL TIPO DI INTERVENTO

SEDE	IRA	IAA
Parete	5	6
Mesentere	8	8
Retroperitoneo	1	1
Sedi multiple	1	3
DESMOIDI TOTALE	15(34.5%)	18(30.4%)

No correlation between pouch adenomas and *APC* mutation

Correlation with age

Polyps:43.1 vs No polyps:36.2 (p=0.017)



Prevalence and Morphology of Pouch and Ileal Adenomas in Familial Adenomatous Polyposis

Christopher J. Groves, M.R.C.P., Iain G. Beveridge, M.R.C.P., David J. Swain, R.N. Dip. HE, Brian P. Saunders, M.D., Ian C. Talbot, M.S., R. John Nicholls, M.A., Robin K. Phillips, M.S.

The Polyposis Registry, Cancer Research UK Colorectal Cancer Unit, St. Mark's Hospital, Harrow, United Kingdom

Correlation with length of follow-up

Pearson's correlation P<0.01

Nontruncating *APC* Germ-line Mutations and Mismatch Repair Deficiency Play a Minor Role in *APC* Mutation-negative Polyposis[1]

Karl Heinimann,[2,3] Annick Thompson,[4] Andreas Locher,[4] Tamara Furlanetto,[4] Eva Bader, Angela Wolf, Remy Meier, Klaus Walter, Peter Bauerfeind, Giancarlo Marra, Hansjakob Müller, Dorothee Foernzler, and Zuzana Dobbie

7 years vs 4 years (P=0.015)

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Correlation with duodenal polyps

Parc YR et al. Ann Surg 2001

Pouch adenomas	Duodenal adenomas	Papillary adenomas
NO	41%	8%
YES	77%	50%
	P =0.002	P= 0.001

Polipi della pouch: correlazione con i polipi del colon

Polipi del Colon	Assenti	Sporadici	Multipli	Cancro
< 200	4	/	/	/
200-1000	18	3	3	/
>1000	12	4	6	2