TUMORI NEUROENDOCRINI GASTROINTESTINALI

San Vito al Tagliamento (PN) – 30 Gennaio 2009

Trattamento soppressivo dei recettori della somatostatina nella prevenzione delle fistole pancreatiche

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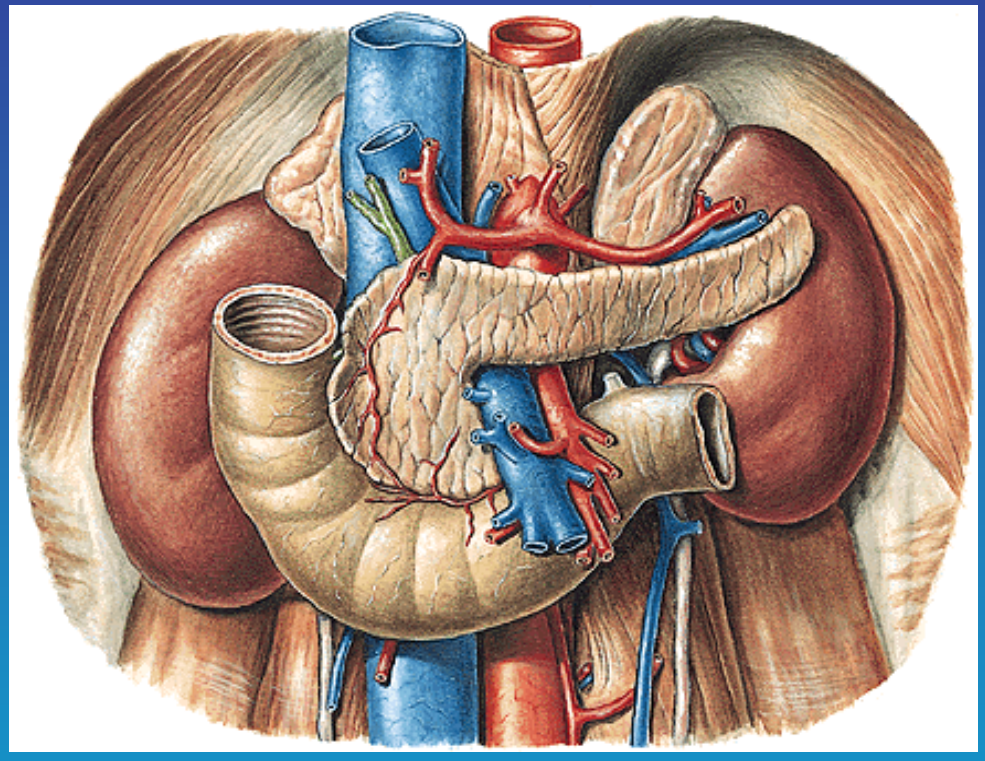
CHIRURGIA PANCREATICA

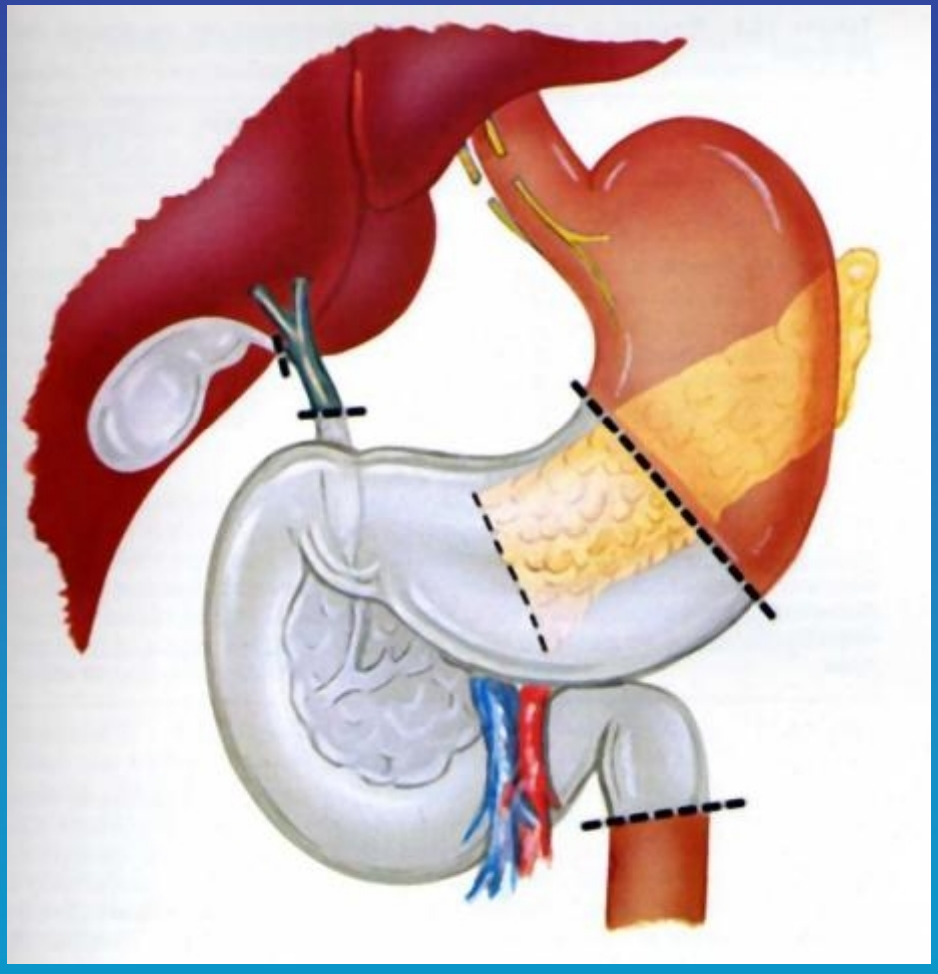


- Enucleoresezione
- Duodenocefalo-pancreasectomia
- Pancreasectomia distale
- Pancreasectomia totale

Mortalità < 5% (2.2-11.0%)

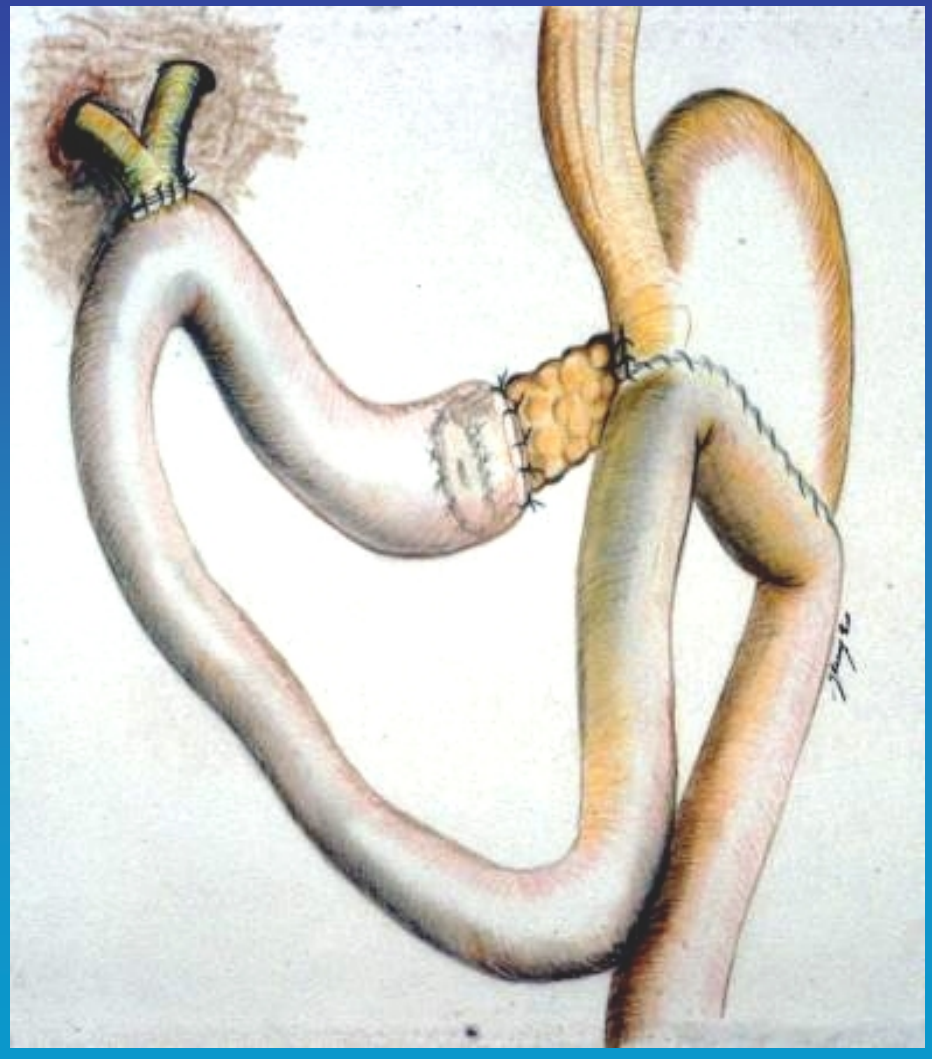
Morbidità = 5-40%

DUODENOCEFALOPANCREASECTOMIA



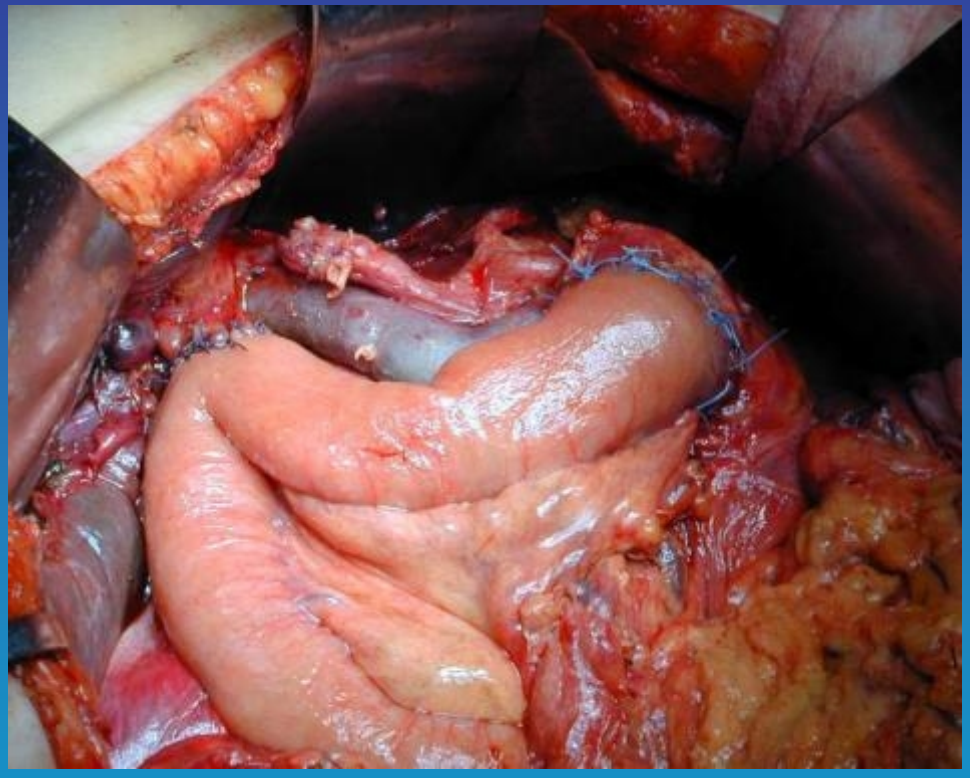
- Adenok pancreatico
- Adenok VB distale
- Tumori ampullari
- Adenok duodenale
- Pancreatite cronica
- Tumori neuroendocrini
- Tumori stromali GI

COMPLICANZE POSTOP. DOPO DCP



- Fistola pancreatica (5-40%)
- Fistola enterica
- Fistola biliare
- Pancreatite acuta
- Emorragia p.o.
- Ascessi intraddominali
- Ritardato vuotamento gastrico

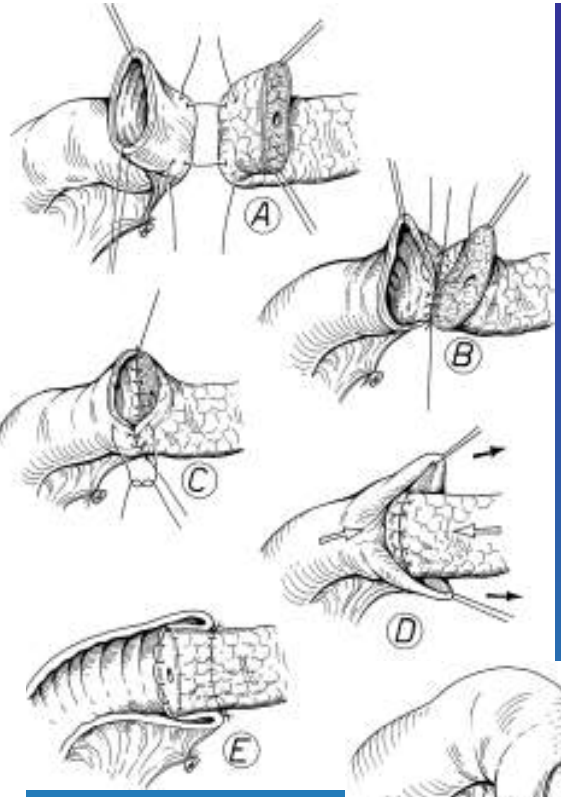
FISTOLA PANCREATICA: FATTORI DI RISCHIO

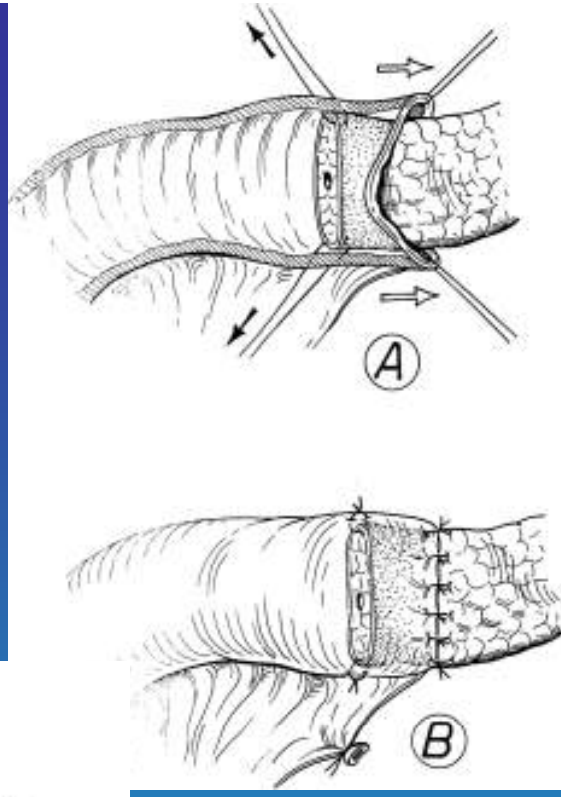


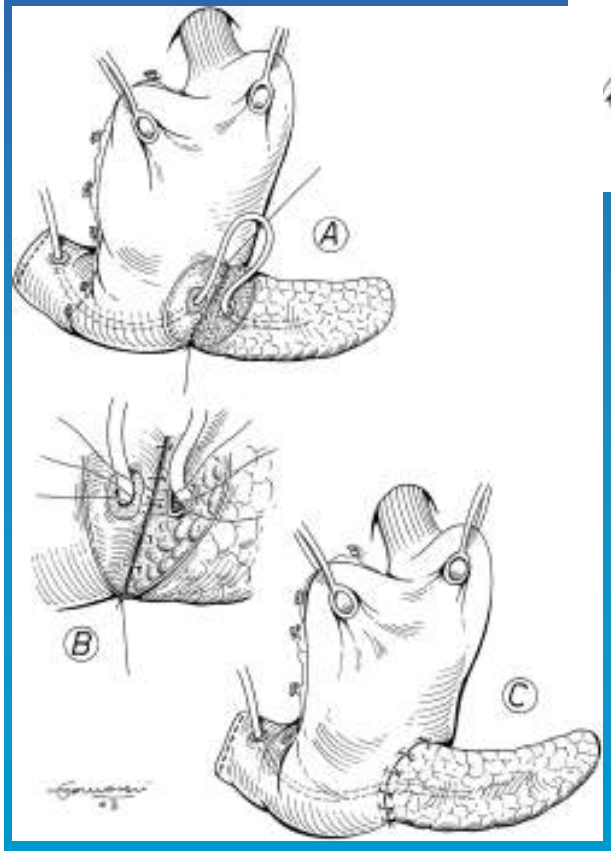
- Legati al paziente
- Legati al chirurgo ed al centro ospedaliero
- Legati alla condizione d'organo

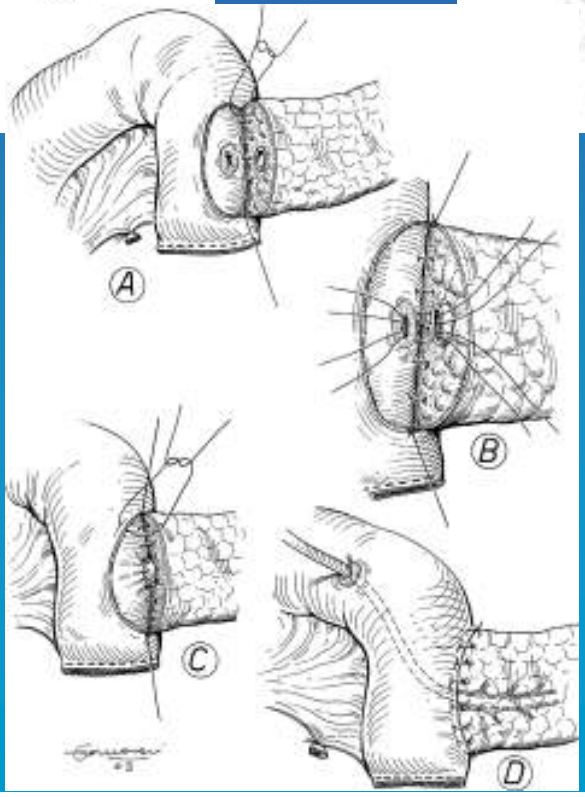
Consistenza del moncone pancreatico (duro/soffice)
Dimensioni del Wirsung (</> 3 mm)
Diagnosi patologica

Trattamento del moncone pancreatico dopo DCP









Management of complications after pancreaticoduodenectomy in a high volume centre: results on 150 consecutive patients

Bassi C et al. Dig Surg 2001; 18: 453-458

The problem of pancreatic fistula after resection of the pancreas is old as pancreatic surgery itself. From the literature and the experience of our group, we conclude that the greatest or lowest risk factor for developing a fistula post-operatively is the definition used!

FISTOLA PANCREATICA DOPO DCP

- Pura / Mista
- Bassa / Alta portata (200 ml/die)
- Precoce / Tardiva (entro 1 settimana)
- Biochimica / Clinica (26 definizioni in Medline)

1. Drenaggio > 10 ml/die di secreto ricco in amilasi (x3) in V°g. post-op o > 5 giorni
2. Drenaggio > 10 ml/die di secreto ricco in amilasi (x3) in VIII°g. post-op. o > 8 giorni
3. Drenaggio tra 25 e 100 ml/die di secreto ricco in amilasi (x3) in VIII°g. post-op. o > 8 giorni
4. Drenaggio > 50 ml/die di secreto ricco in amilasi (x3) in XI°g. post-op. o > 11 giorni

Postoperative pancreatic fistula: an international study group (ISGPF) definition

Bassi C et al. Surgery 2005; 138: 8-13

OUTPUT VIA AN OPERATIVELY PLACED DRAIN OF ANY MEASURABLE VOLUME OF DRAIN FLUID ON OR AFTER POSTOPERATIVE DAY 3, WITH AN AMYLASE CONTENT GREATER THAN 3 TIMES THE UPPER NORMAL SERUM VALUE

Postoperative pancreatic fistula: an international study group (ISGPF) definition

Bassi C et al. Surgery 2005; 138: 8-13

Grade	**A**	**B**	**C**
Clinical conditions	Well	Often well	Ill appearing/bad
Specific teatment	No	Yes/no	Yes
US/CT (if obtained)	Negative	Negative/positive	Positive
Persistent drainage (after 3 wk)	No	Usually yes	Yes
Reoperation	No	No	Yes
Death related to POPF	No	No	Possibly yes
Signs of infections	No	Yes	Yes
Sepsis	No	No	Yes
Readmission	No	Yes/no	Yes/no

SOMATOSTATINA IN CHIRURGIA PANCREATICA: QUALE RAZIONALE?

- Inibizione della secrezione alcalina ed enzimatica pancreatica e della secrezione di bile
- Inibizione della secrezione acida gastrica, della pepsina e del fattore intrinseco
- Inibizione della secrezione ormonale dell'intestino (gastrina, colecistochinina, VIP, GIP, secretina)
- Riduzione del flusso splancnico

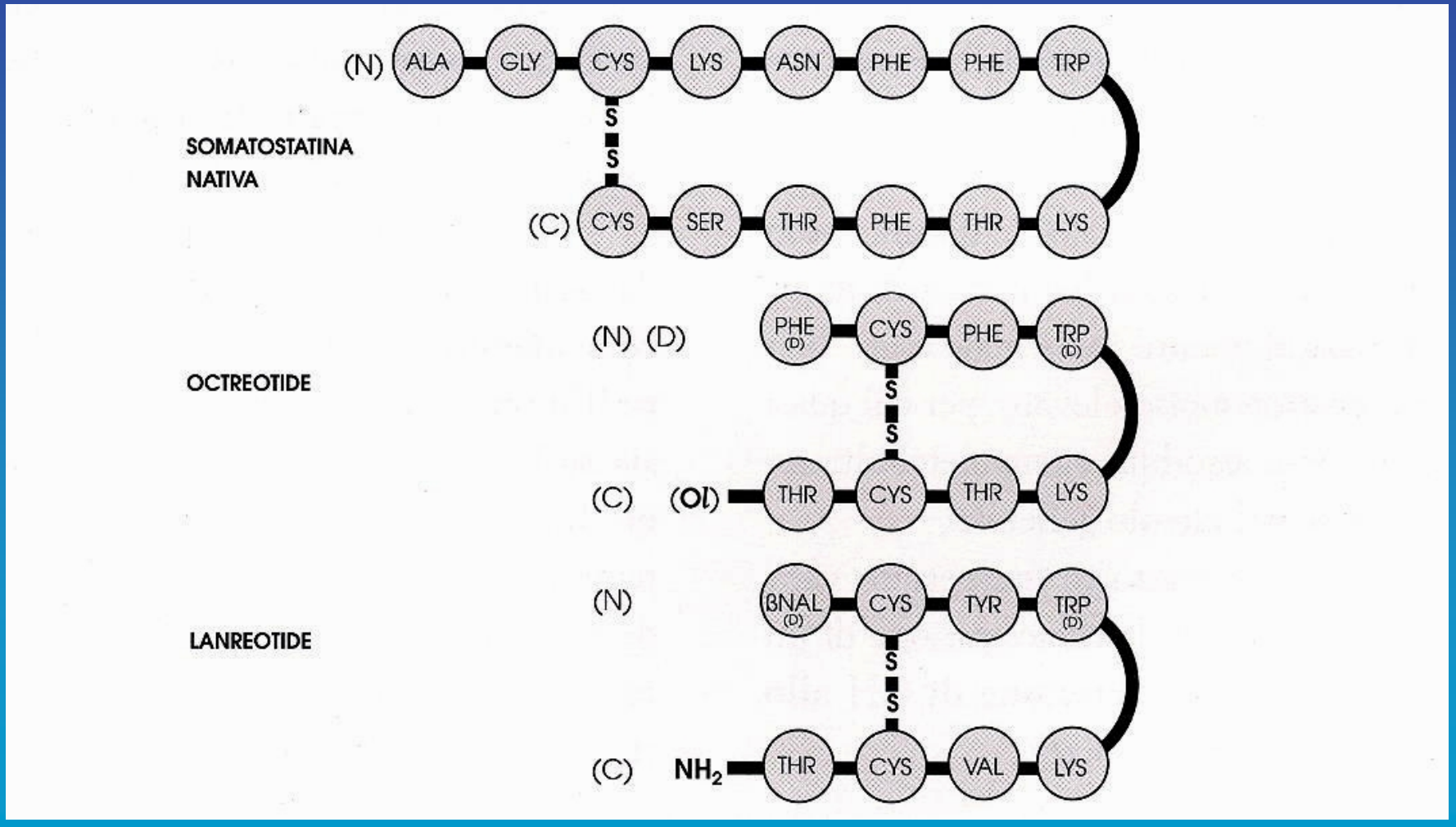
Randomized controlled multicenter trial of somatostatin infusion after pancreaticoduodenectomy

Gouillat C, et al. Lyon Cedex, France

	Somatostatin (n = 38)	Placebo (n = 37)	P
Pancreatic fistula			
Clinical	2†	8†	< 0·05
Biochemical	2	2	
Infected intra-abdominal fluid collection	2‡	4§	0·37
Acute pancreatitis	1	0	0·32
Total pancreatic stump-related complications	5	12	< 0·05
Other complications	3¶	1**	0·37
Overall complications	8	13	0·17
Further surgery	4	1	0·36
Death within 30 days of surgery	2	1	0·61
Hospital stay (days)*	18(1)	26(2)	0·01

Br J Surg 2001;88:1456-62

SOMATOSTATINA ED ANALOGHI



GLI ANALOGHI DELLA SOMATOSTATINA

- OCTAPEPTIDI CICLICI
  - RC 160 (vapreotide); NC 8-12
- OCTAPEPTIDI LINEARI
  - EC 5-21; BIM 23042
- EPTAPEPTIDE CICLICO
  - L 362,855
- ESAPEPTIDI
  - MK 678 (seglitide); BIM 23059

Role of the octreotide in the prevention of postoperative complications following pancreatic resection

Buchler M, et al. University of Ulm, Germany

Number of Patients With One or More Complications in High-Risk and Low-Risk Strata

	Octreotide		Placebo
No. of high-risk* patients (n = 139)	68		71
No. of high-risk patients with one or more complications	26 (38%)	p < 0.01	46 (65%)
No. of low-risk† patients (n = 107)	57		50
No. of low-risk patients with one or more complications	14 (25%)	NS	21 (42%)

*Patients with pancreatic or periampullary tumors.
†Patients with chronic pancreatitis.

Am J Surg 1992;163:125-30

Randomized controlled multicentre study of the prevention of complications by octreotide in patients undergoing surgery for chronic pancreatitis

Friess H, et al. University of Berne, Switzerland

	Octreotide ($n = 122$)	Placebo ($n = 125$)	Total ($n = 247$)
Death	2	1	3
Anastomotic leakage	1	1	2
Pancreatic fistula	12*	28	40
Abscess	5	2	7
Fluid collection	4*	12	16
Shock	2	2	4
Sepsis	2	1	3
Pulmonary insufficiency	8	3	11
Renal insufficiency	2	0	2
Bleeding	7	4	11
Postoperative pancreatitis	2	2	4
No. of patients with complications	20 (16·4)†	37 (29·6)	57

Values in parentheses are percentages. *$P < 0{\cdot}05$, †$P < 0{\cdot}007$ (octreotide *versus* placebo, Fisher's exact test)

Br J Surg 1995;82:1270-3

Efficacy of octreotide in the prevention of pancreatic fistula after elective pancreatic resections: a prospective, controlled, randomized clinical trial

Montorsi M, et al. University of Milan, Italy

	Total (n = 218)		*Octreotide (n = 111)*		*Placebo (n = 107)*	
	No.	*%*	*No.*	*%*	*No.*	*%*
Specific pancreatic complications						
Pancreatic fistula*	31	14.2	10	9.0	21	19.6
Postoperative pancreatitis	7	3.2	2	1.8	5	4.7
Abscess	7	3.2	4	3.6	3	2.8
Fluid collection*	11	5.0	2	1.8	9	8.4
Anastomotic leakage	12	5.5	3	2.7	9	8.4
Bleeding	17	7.8	8	7.2	9	8.4
Respiratory failure	4	1.8	2	1.8	2	1.8
Renal failure	1	0.5	0	0	1	0.9
Other	11	5.0	5	4.5	6	5.6
TOTAL*	101		36		65	

*$p < 0.05$.

Surgery 1995;117:26-31

Efficacy of octreotide in the prevention of complications of elective pancreatic surgery. Italian Study Group.

Pederzoli P, et al. Università di Verona, Italy

	Total ($n = 252$)	Placebo ($n = 130$)	Octreotide ($n = 122$)
Total no. of patients with complications*	57 (22·6)	38 (29·2)	19 (15·6)
Death	7 (2·8)†	5 (3·8)	2 (1·6)
Anastomotic dehiscence	9 (3·6)	5 (3·8)	4 (3·3)
Pancreatic fistula	35 (13·9)	24 (18·5)	11 (9·0)
Abscess	9 (3·6)	6 (4·6)	3 (2·5)
Fluid collection	21 (8·3)	13 (10·0)	8 (6·6)
Pancreatitis	7 (2·8)	6 (4·6)	1 (0·8)
Shock	6 (2·4)	3 (2·3)	3 (2·4)
Sepsis	10 (4·0)	8 (6·1)	2 (1·6)
Respiratory failure	8 (3·2)	6 (4·6)	2 (1·6)
Renal failure	6 (2·4)	4 (3·1)	2 (1·6)
Bleeding	5 (2·0)	2 (1·5)	3 (2·5)

Br J Surg 1994;81:265-9

Does prophylactic octreotide decrease the rates of pancreatic fistulas and other complications after pancreaticoduodenectomy?
Results of a prospective randomized placebo-controlled trial

Yeo CJ, et al. Johns Hopkins Hospital, Baltimore, USA

	Octreotide (n = 104)	Control (n = 107)	P
Death	1 (1%)	0 (0%)	NS
Reoperation	5 (5%)	1 (1%)	.09
Any complication	42 (40%)	36 (34%)	NS
Pancreatic fistula	11 (11%)	10 (9%)	NS
Wound infection	9 (9%)	12 (11%)	NS
Early delayed gastric emptying	7 (7%)	11 (10%)	NS
Intraabdominal abscess	9 (9%)	5 (5%)	NS
Cardiac arrhythmias	4 (4%)	3 (3%)	NS
Bile leak	3 (3%)	3 (3%)	NS
Pancreatitis	3 (3%)	1 (1%)	NS
Cholangitis	1 (1%)	3 (3%)	NS
Hemobilia	1 (1%)	3 (3%)	NS
Postoperative hospital stay (days)			
Mean ± SEM	13.3 ± 1.1	11.9 ± 0.6	NS
Median	9	9	

Ann Surg 2000;232:419-29

Prospective, randomized trial of octreotide to prevent pancreatic fistula after pancreaticoduodenectomy for malignant disease

Lowy AM, et al. Anderson Cancer Center of Houston, Texas, USA

Complication	Octreotide Group (n = 57)	Control Group (n = 53)
Perioperative mortality	1 (2)	0
Anastomotic leaks		
Pancreatic (clinical)	7 (12)	3 (6)
Pancreatic (biochemical)	9 (16)	8 (15)
Pancreatic (total)	16 (28)	11 (21)
Biliary	0	0
Gastric	0	0
Abdominal abscess	3 (5)	2 (4)
Total percutaneous drainage	8 (14)	4 (8)
Reoperation	1 (2)	0
Hospital stay >21 days*	8 (14)	8 (15)
Total patients experiencing 1 or more complications†	17 (30)	13 (25)

Ann Surg 1997;226:632-41

Randomized clinical trials comparing the effect of somatostatin and its analogues with placebo and controls on complication rate after pancreatic surgery

Reference	Type of trial	Number of patients	Drug, dose and type of administration	Treatment provide benefit
Buchler	M, DB, PC	246	O, Pr, 100 μg per 3/day, 7 days	Yes
Pederzoli	M, DB, PC	252	O, Pr, 100 μg per 3/day, 7 days	Yes
Montorsi	M, DB, PC	218	O, Pr, 100 μg per 3/day, 7 days	Yes
Friess	M, DB, PC	247	O, Pr, 100 μg per 3/day, 7 days	Yes
Lowy	S	110	O, I, 100 μg per 3/day, 10 days	No
Yeo	S , DB, PC	211	O, Pr, 250 μg per 3/day, 7 days	No
Gouillat	M, DB, PC	75	S, Po, 6 mg/day infusion, 7 days	Yes
Shan	S	54	S, Po, 250 μg/day infusion, 7 days	Yes
Sarr	M, DB, PC	275	V, P, 0.6 mg per 2/day, 7 days	No
Suc	S	230	O, I, 100 μg per 3/day, 10 days	Yes
Total		1918		

Usage du lanréotide dans la prévention des fistules pancréatiques aprés duodéno-pancréatectomie céphalique. Etude préliminaire

Slim K, et al. Clermont-Ferrand, France

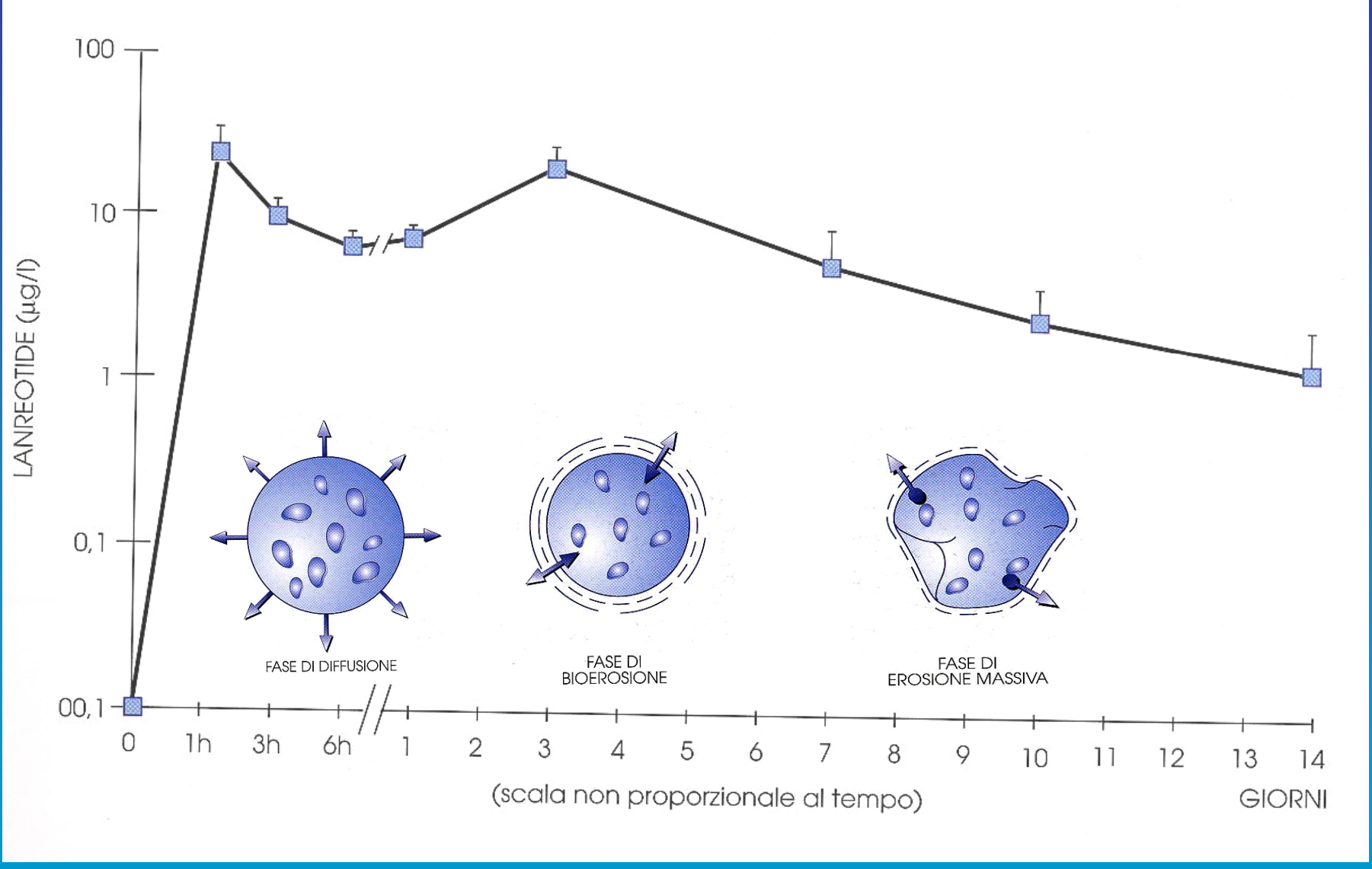
N.ro pz.	N.ro resez.	Metodi	N.ro fistole
40 tumori cefalo-pancreatici	34 DCP (85%)	Lanreotide 30 mg i.m. 12h preop.	6 pazienti (17.6%)

Chirurgie 1999;124:661-5

VANTAGGI DELL'IMPIEGO DEGLI ANALOGHI DELLA SOMATOSTATINA LONG-ACTING

- Potente e specifica azione terapeutica
- Lunga durata di azione (14 giorni)
- Migliore compliance (monodose)
- Buona tollerabilità

FARMACOCINETICA DEL LANREOTIDE



Evaluation of lanreotide effects on human exocrine pancreatic secretion after a single dose: preliminary study

Falconi M, et al. University of Verona, Italy

Secrezione	Lanreotide	Placebo	*P*
1 ora	5.7	8.7	<0.05
6 ore	46.1	76.1	<0.05
9 ore	76.8	115.7	NS
12 ore	104.9	154.4	NS
24 ore	208.6	253.9	NS

Digest Liver Dis 2001; 33:127-32

I° Dipartimento di Chirurgia (Direttore: Dr.Giuseppe Di Falco)
Ospedale Regionale - Treviso

Casistica Gennaio 2004 - Dicembre 2008

- 92 pz.operati: 59 pz. (64%) inoperabili o interventi palliativi

  33 pz.(36%) sottoposti ad intervento resettivo

- 19 F/14 M; Età media 67 aa (33-78)
- Profilassi: Lanreotide 30mg i.m. 12h preoperatorie

I° Dipartimento di Chirurgia (Direttore: Dr.Giuseppe Di Falco)
Ospedale Regionale - Treviso

Casistica Gennaio 2004 - Dicembre 2008

Diagnosi	Intervento	Ricostruzione	Decorso
K.testa 16 pz. K.VBP 4 pz. P.cronica 2 pz. K.papilla 5 pz. K.corpo-coda 6pz.	27 DCP 13 Traverso 14 Whipple 6 P.distale	Pancreatico-digiunostomia 23 TL / 4 TT	Degenza 21 gg (12-73) Complicanze 8 pz. (29.7%)

I° Dipartimento di Chirurgia (Direttore: Dr.Giuseppe Di Falco)
Ospedale Regionale - Treviso

Casistica Gennaio 2004 - Dicembre 2008
Fistola pancreatica postoperatoria

- Grado B: 5 pz. (18.5%); degenza media 35gg
  Trattamento conservativo: II°dose di Lanreotide dopo 15gg

- Grado C: 3 pz. (11%); degenza media 67gg
  Reinterventi: pancreasectomia totale con splenectomia
  Mortalità 0%