

췌장암의 고식적 치료의 선택

-외과 의사의 입장에서 Surgical Palliation of Pancreas Cancer

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* Palliative treatment in pancreas cancer

Significance of palliative treatment in pancreas cancer

1. pancreas cancer의 80%는 진단 시 advanced, unresectable disease 상태이므로 상당수의 pancreas cancer 환자에서 life quality를 향상시킬 목적으로 시행하는 palliative treatment가 중요한 의미를 갖는다.
2. pancreas cancer 의 경우 술 전 검사에 의한 resectability 판정의 정확도에 한계가 있어 개복술 시행 후 unresectability가 확인되어 palliative treatment를 시행하게 되는 경우가 있다.

Objects of palliative treatment in pancreas cancer

- : 1. to relieve obstructive jaundice
- 2. to treat duodenal (gastric outlet) obstruction
- 3. to relieve pain

Palliative procedure 선택의 기본 조건

- : obstructive jaundice, duodenal obstruction, pain의 증상을 호전시켜 life quality를 향상시켜야 하며 morbidity와 mortality는 낮아야 한다
- 환자 개개인에 따라 적절한 palliation method를 선택해야 한다.

* Surgical palliation의 대상

- : patient with unresectable disease discovered at the time of potentially curative laparotomy
- unresectable disease로 진단이 된 환자 중 operation risk가 낮고 non-operative method로 tumor-related symptom이 잘 해결되지 않는 경우

Surgical Palliation of Obstructive Jaundice

*** Jaundice in pancreas cancer**

: most common (about 70%) symptom at the time of diagnosis

clinical problem: progressive liver dysfunction, hepatic failure, early death

pruritus - unbearable, seldom responsive to medication

associated with anorexia, nausea, progressive malnutrition

relief of jaundice는 환자의 overall well-being에 dramatic improvement 효과

obstructive jaundice가 있는 경우 거의 모든 환자가 palliation의 indication됨

*** Main issues**

: surgical or non-operative

optimal surgical approach: bile duct or gallbladder

jejunum or duodenum

1. Surgical vs non-operative palliation of obstructive jaundice

: successful relief of jaundice in more than 90% of patients by either surgical bypass or non-operative techniques

non-operative technique; endoscopic or percutaneous

- amenable to almost all patients

low morbidity and mortality, short hospital stay after procedure

surgical - reserved for selected patient

; better operative candidate, longer projected survival case unresectable disease diagnosed at the time of laparotomy

*** Various studies for comparison of the results of surgical or non-operative palliation of obstructive jaundice**

Watanapa and Williamson, 1992, meta analysis

: short-term morbidity, mortality, and hospital stay

- similiar, but generally greater in surgical series

major advantage of surgical bypass - lower rate of late complications

Comparative results between percutaneous and endoscopic stent placement and surgical bypass in patients with malignant obstruction of common bile duct

	Percutaneous stent (n=490)		Endoscopic stent (n=689)		Surgical bypass (n=1,807)	
	Range	Mean	Range	Mean	Range	Mean
30-day mortality (%)	6 ~ 33	9	0 ~ 20	14	0 ~ 31	12
Hospital stay (days)	13 ~ 18	14	3 ~ 26	7	9 ~ 30	17
Success rate (%)	76 ~ 100	92	82 ~ 100	90	75 ~ 100	93
Early complications (%)	4 ~ 67	16	8 ~ 34	21	6 ~ 56	31
Late complications (%)	7 ~ 38	28	13 ~ 45	28	5 ~ 47	16

prospective, randomized clinical trials, 1986 ~ 1989

: short-term relief of jaundice - equally effective

endoscopic stenting - lower procedure-related complication rate

shorter overall period of hospitalization

30-day mortality rate - 11% in non-operative stenting

18% in surgical bypass

cf) recent report (1990 ~ 1993) - less than 5%

long-term recurrent jaundice - lower incidence in surgical bypass

surgical bypass의 경우 동반되어 있거나 향후 발생할 가능성이 있는 duodenal obstruction을 동시에 해결하기에 용이함.

- development of late duodenal obstruction in stenting group: 9 ~ 14%

*** Summary**

Unresectable pancreas cancer diagnosed by preoperative diagnostic modalities (including diagnostic laparoscopy)

→ non-operative palliation

Equivocal or potentially resectable pancreas cancer by preoperative diagnostic modalities or unresectable disease diagnosed at the time of laparotomy

→ surgical biliary bypass

cf) prophylactic surgical biliary bypass -- controversial

Results of prospective, randomized trials of nonoperative versus surgical palliation for malignant biliary obstruction

	South Africa ⁴		United Kingdom ³⁴		Denmark ¹		United Kingdom ¹³	
	Stent	Surgery	Stent	Surgery	Stent	Surgery	Stent	Surgery
Number	25	25	23	25	25	25 [§]	65	62
% success	84%	76%	82%	92%	96%	88%	94%	94%
Complications	28%	32%	30%	56%	36%	20%	23%	50%
30-day mortality	8%	20%	9%	20%	20%	24%	6%	15%
Hospital stay (day)	18	24*	5	13 [†]	26	27	11	15
Late complications								
Jaundice/cholangitis	38%	16%	30% [‡]	0%	0%	0%	17%	3%
Gastric outlet obstruction	14%	0%	9%	4%	0%	0%	14%	3%
Survival (weeks)	19	15	22	18	12	14	22	16

*Median postprocedural hospital stay was significantly shorter in stented patients; however, when readmissions for late complications were considered, there was no longer a significant difference, [†] Both initial and total hospital days were less in the stented group, [‡] 13% required two admissions for late biliary complications, [§] Six patients randomized to surgical arm did not undergo surgical palliation. In one patient extensive tumor precluded palliative bypass. Five other patients underwent endoscopic stent placement. Data presented based on randomization.

2) Methods of surgical palliation of obstructive jaundice (Surgical options)**Hepaticojejunostomy (choledochojejunostomy)**

: preferred method in most patients

intestinal conduit

- defunctionalized Roux-en-Y limb vs simple jejunal loop

: advantage of Roux-en-Y limb

- lower rate of cholangitis

easier management of biliary-anastomotic leak

improved mobility of Roux-en-Y limb to reach the hepatic hilum

Cholecystojejunostomy

: merit - performed quickly, no dissection of extrahepatic biliary tree

caution - notify at least 2~3 cm of free margin between the junction of cystic duct with

CBD and tumor mass to prevent future obstruction

cancer가 진행함에 따라 cystic duct obstruction으로 인한 recurrent jaundice의 발생 가능성이 있음

Choledochoduodenostomy

: concern - proximity of the anastomosis to the tumor → recurrent jaundice anastomotic leak
→ leakage of bile and gastroduodenal secretion

Potts JR et al.(Cleveland Clinic), 1990

- choledochoduodenostomy routinely with overall good results
; low complication rate (3%), short postoperative hospital stay (10 days) recurrent jaundice - 1/61 patients

Singh SM et al.(UCLA), 1990

- recurrent jaundice in 1/3 of patients, remained elevation of serum bilirubin in more than 80% of patients
high perioperative morbidity - 58%

현재 대부분의 surgical groups은 recurrent jaundice 발생 문제 때문에 periampullary cancer로 인한 obstructive jaundice의 surgical palliation 방법으로 choledochoduodenostomy를 권장하지 않음.

cf) choledochotomy and T-tube drainage

: jaundice relief는 효과적이거나 많은 양의 bile loss로 severe fluid and electrolyte imbalance를 초래하므로 palliation procedure로 적합하지 않음.

cholecystogastrostomy

: bile gastritis, gastric acid hypersecretion secondary to gastrin release, food entry into biliary tree 등의 문제점 때문에 palliation procedure로 적합하지 않음.

*** Various studies for the comparison of hepaticojejunostomy (HJ) and cholecystojejunostomy (CJ) for surgical palliation of obstructive jaundice**

Retrospective study

Sarr and Cameron, 1983

operation mortality: 20% in HJ, 16% in CJ
mean survival time: 6.5 ms in HJ, 5.3 ms in CJ
recurrent jaundice: 0% in HJ, 8% in CJ

Watanapa and Williamson, 1992, meta analysis

success rate: 97% in HJ, 89% in CJ

operation mortality: similar

recurrent jaundice and cholangitis: 8% in HJ, 20% in CJ

Prospective randomized study

Sarfeh et al., 1988

significantly less operation time, blood loss in CJ

significantly more major postoperative complications in CJ

significantly more late bypass failure in CJ

*** Summary**

: Hepaticojejunostomy is better!

← less late bypass failure and recurrent jaundice

less postoperative major complication

early cholecystectomy and division of bile duct

→ facilitate dissection and determination of resectability

Surgical Palliation of Duodenal (Gastric outlet) Obstruction (DO)

*** Main issues**

: prevalence of DO requiring gastroenteric bypass

surgical bypass or non-operative stent

optimal surgical approach

need for prophylactic gastrojejunostomy in laparotomy case

1. Prevalence of DO requiring gastroenteric bypass in pancreas cancer

-- controversial

: pancreas cancer 환자의 30~50%에서 진단 시 nausea, vomiting 증상을 보이거나, 실제로 radiologic or endoscopic examination으로 확인되는 actual duodenal mechanical obstruction은 훨씬 적다. 그러나 unresectable disease의 경우 질환이 진행함에 따라 duodenal obstruction이 더 많은 환자에서 발생한다.

pancreas cancer 환자에서는 흔히 gastroparesis가 동반되는데 이는 neurogenic cause에서 기인하며 nausea, vomiting의 증상을 유발하므로 true mechanical duodenal obstruction과 감별이 필요하다.

incidence of DO during the course of the disease

Sarr and Cameron, 1983

-- 13% (8000 surgical cases)에서 gastrojejunostomy (GJ)가 시행됨.

20%의 환자는 사망 시 duodenal obstruction symptom (+)

Singh and Rever, 1989 -- 21%에서 late stage에 GJ 필요

Watanapa and Williamson, 1992

-- biliary bypass만 시행했던 환자 중 17%(1600 cases)에서 평균 8.6 개월 후 GJ 필요

Espat et al., 1999 -- 3%

Lillemoe et al., 1999 -- 19%

2. Options for surgical bypass

Gastrojejunostomy (GJ)

: 가장 흔하게 시행됨

Antecolic or Retrocolic GJ

: antecolic - to avoid placement of GJ anastomosis in the bed of tumor

Lillemoe et al., 1993

-- retrocolic GJ: decreased incidence of delayed emptying (6% vs 17%), and late gastric outlet obstruction (2% vs 9%)

Antrectomy

: delayed gastric emptying in GJ (Doberneck and Berndt, 1987 -- 26%)

Lucas et al., 1991 -- advocate antrectomy as procedure of choice

Vagotomy in GJ to prevent stomal ulceration

: not justified ← further aggravation of delayed gastric emptying routine anti-ulcer medication 실시

3. Prophylactic bypass in the absence of demonstrated obstruction

--- questionable

NO: development of DO in less than 20% of patients

high postoperative mortality (Doberneck and Berndt, 1987 -- 18%)

development of postoperative delayed gastric emptying, and subsequent increased operation mortality (Doberneck and Berndt, 1987 -- 33%)

aggressive biologic nature of pancreas cancer

→ not indicated routinely

YES: Lillemoe et al., 1999, prospective, randomized trial of 87 patients

- similar hospital stay (8 days)

DO requiring bypass in 8 of 43 patient without GJ

no increase in morbidity in routine GJ group

* Summary

Duodenal obstruction in unresectable pancreas cancer demonstrated by preoperative diagnostic modalities (including diagnostic laparoscopy)

→ non-operative stenting bypass

if failed, surgical bypass

Duodenal obstruction or impending obstruction in unresectable disease demonstrated during laparotomy

→ gastrojejunostomy

cf) prophylactic surgical bypass in the absence of obstruction

-- controversial

: decision by physician's experience, condition and desire of patient

Surgical Palliation of Pain

* Pain in advanced pancreas cancer

: most disturbing, incapacitating symptom → extremely poor quality of life significant pain

in 30~40%, minimal complain of pain in 30% at the begining of management

cause - secondary to tumor invasion of celiac and mesenteric nerve plexus

* Palliation of pain

: surgical - Intraoperative chemical splanchnicectomy (celiac plexus block)

Thoracoscopic splanchnicectomy

non-operative

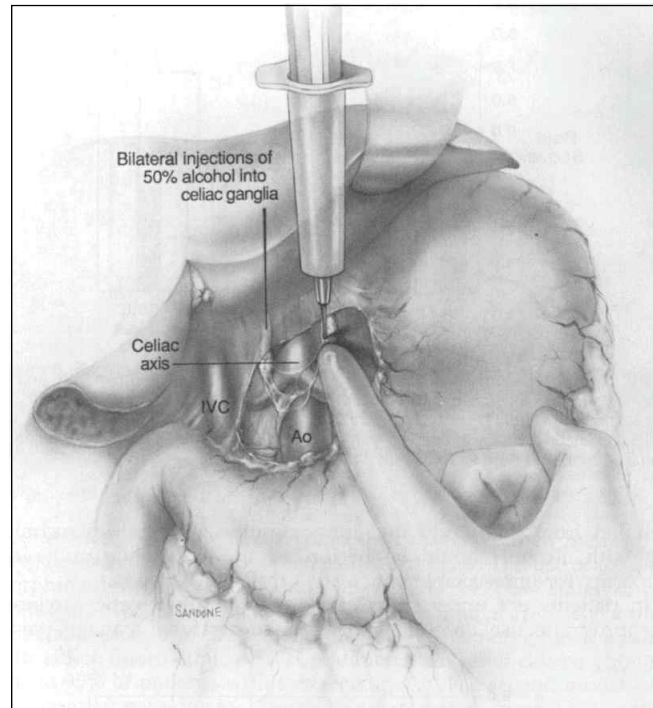
- Narcotic analgesics

Percutaneous chemical splanchnicectomy

External beam radiation

1. Intraoperative chemical splanchnicectomy

Method



Result

effective short-term analgesia (70~90%),

significant reduction of conventional narcotic medication,

substantial improvement of quality of life

Lillemoe et al., 1993, prospective, randomized, placebo-controlled study

-- intraoperative chemical splanchnicectomy group (20 ml of 50% alcohol)
vs placebo group(saline)

: hospital mortality, postoperative Cx., return to oral intake,
length of hospital stay -- no difference

in splanchnicectomy group

-- lower mean pain scores at 2, 4, 6 month follow-up and final follow-up prior to death

- delay or prevention of subsequent onset of pain in patients without preoperative pain

- reduced existing pain in patients with significant preoperative pain

marked improvement of survival

in patients with significant preoperative pain

(cf. actuarial survival of all group - similar)

→ recommend intraoperative chemical splanchnicectomy for all patients with unresectable pancreas cancer undergoing laparotomy

2. Thoracoscopic splanchnicectomy

: excellent short-term analgesia (up to 99%)

long-term analgesia rate of 40% in the 4 month after procedure

* Results of palliation of pain in pancreas cancer

Study	No. subjects	Procedure	Short-term analgesia (<3 mo; %)	Long-term analgesia (>3 mo; %)	Complications
Ihse et al ¹¹ (1999)	45	Bilateral thoracoscopic splanchnicectomy	99	55	9% thoracic bleeding requiring thoracotomy
Eisenberg et al ⁹ (1995)	1145	Neurolytic celiac plexus block	89	60~75	96% local pain 44% transient diarrhea 38% transient hypotension 1% pneumothorax 1% neurologic deficit lower extremity
Noppen et al ⁵⁸ (1998)	8	Thoracoscopic splanchnicectomy	80	50	10% trocar site significant pain
Rykowski et al ⁵⁹ (2000)	50	Neurolytic celiac plexus block	N.A.	74	28% transient back pain 24% transient urinary retention 18% transient diarrhea
Pietrabissa et al ⁶⁰ (2000)	24	Thoracoscopic splanchnicectomy	100	100	4% need for chest tube postoperatively

*** Conclusion

* Surgical palliation of pancreas cancer의 decision은 환자에 따라 개별화하여 가장 적절한 방법으로 시행해야 한다.

-- decision influenced by; diagnostic accuracy, patient's symptom and clinical condition, clinical situation, experience of surgeon (acceptable operative morbidity and mortality), availability of non-operative palliation

* Major advantages of surgical palliation

1. Ability to combine adequate long-term palliation for all 3 primary symptoms
2. Surgical exploration only
 - potentiality of curative resection
 - confirm the unresectable status of the disease exactly in many cases

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