

가

Effect of Intraoperative Radiation Therapy (IORT) in Unresectable Pancreatic Cancer

Chun Hwan Lee, MD, Nam Ryeol Kim, MD, Chul Yong Kim, MD¹, Dae Sik Yang, MD¹, Min Young Cho, MD, Young Chul Kim, MD, Cheung Wung Whang, MD, and Sung Ock Suh, MD.

Purpose: Pancreatic cancer is a devastating disease and the complete resection is difficult due to its the aggressive histologic behavior. Among the possible treatments for the unresectable pancreatic cancer, intraoperative radiation therapy (IORT) has the several advantages. But the impacts of the IORT on survival and local control are not clear. We analyzed the effects of the IORT on pain control, survival duration and local control in patients with unresectable pancreatic cancer.

Methods: We reviewed 6 years of the medical records of 94 patients who had undergone operations involving the pancreatic adenocarcinoma (33 patient IORTs, 39 palliative surgeries only and 22 curative resections involving a curative resection). The clinicopathologic factors and outcomes of the 33 patients treated with the IORT were compared with those of the palliative surgery groups.

Results: The age and sex distribution and tumor stage were same for the two groups. The average tumor size in the IORT group was larger than those of the palliative surgery group. The preoperative serum CA19-9 level in the IORT group was higher than the other group. The most common reason for unresectability in the IORT group was local invasion to the adjacent organs including of the great vessels. On the contrary, distant metastasis was a more common cause unresectability in the palliative surgery group. The postoperative complications and operative times were similar in both groups. Pain relief after treatment was observed in 12 cases of the 26 patients in the IORT group, and 5 of

29 patients in the palliative surgery group ($P < 0.05$). The cases of minor and partial remission were more common in the IORT group than the palliative surgery group. However, the survival rate of the IORT group was no better than the palliative surgery group.

Conclusion: This study suggests that IORT may have an important palliative role especially in ameliorating visceral pain in patients with unresectable pancreatic cancer. However, IORT appears to have no significant effect on overall survival. (*J Korean Surg Soc* 2002;63:51-56)

Key Words: Pancreatic cancer, IORT (intraoperative radiation therapy)

Departments of Surgery and ¹Radiation Oncology, Korea University College of Medicine, Seoul, Korea

가 126-1
Ⓢ 136-705,
Tel: 02-920-5303, Fax: 02-928-1631
E-mail: myfellow@hitel.net
: 2002 2 19 , : 2002 5 29
2001

가 가 가
25% ,
(1-7)
가 가
가 가
(8,9) 가
(10-12) 가
가

1994 1 1998 12 5
 94
 가 가 가 33
 가 39
 가 가 22
 가 가 33 12
 21
 .94 22
 23.4% . IORT 33 14
 39 12 4,500 cGY
 5,400 cGY 가 . IORT 33
 6 , 39 12 5-fluorouracil
 가 , 가 , 가 ,
 , , 가 ,
 .
 , ,
 .
 1 3
 1 () 10 ()
 (visual analogue pain scale) 가
 , ,
 (pain scale 1 3),
 가 ()
 4 6) , 가
 (7 10) .
 가 5 9 cm

20 30 cGy 9 20 MeV
 AJCC (1988)
 ±
 SPSS 9.0 for Windows
 Chi-square
 Kaplan-Meier
 Log-rank test P
 0.05
 58.9 64 ,
 2.13 : 1 .
 30 1 66 10.8
 94 54 (58%)
 23 (24%), 15 (16%)가
 2 78 (83%)
 가 (52%)
 (Table 1).
 7.6 cm
 (P=0.013).
 5.5 cm
 19 가 4 14 가 3 ,
 21 IV 18 가
 (P > 0.05).
 CA 19-9 CEA가
 가 CA 19-9 . IORT

Table 1. Patient characteristics

| | IORT (n=33) | Palliative surgery (n=39) | P-value |
|--------------------|-------------|---------------------------|---------|
| Mean age (years) | 58.3±7.5 | 59.9±9.5 | NS* |
| Sex ratio (M : F) | 23 : 10 | 25 : 14 | NS |
| Symptoms and signs | | | NS |
| Abdominal pain | 25 | 30 | |
| Weight loss | 19 | 16 | |
| Anorexia | 11 | 8 | |
| Jaundice | 7 | 11 | |
| Mass | 1 | 5 | |
| Tumor location | | | NS |
| Head | 16 | 10 | |
| Body | 14 | 24 | |
| Tail | 3 | 5 | |

*NS = statistically not significant by Chi-Square test.

Table 2. Analysis of size, stage and tumor marker

| | IORT (n=33) | Palliative surgery (n=39) | P-value |
|--|----------------|------------------------------|---------|
| Tumor size (cm) | 7.6±3.8 | 5.5±2.4 | 0.013 |
| Stage (AJCC) | | | NS* |
| I | 0 | 0 | |
| II | 0 | 0 | |
| III | 14 | 18 | |
| IV | 19 | 21 | |
| Tumor marker | | | |
| CA 19-9 | 924.6±949.0 | 202.7±284.3 | 0.045 |
| CEA | 82.1±276.1 | 11.2±27.6 | NS |
| Adjuvant chemotherapy | | | NS |
| Not done | 27 | 27 | |
| Done | 6 | 12 | |
| Postoperative external RT [†] | | | NS |
| Not done | 19 | 27 | |
| Done | 14 | 12 | |

*NS = statistically not significant by Chi-Square test; [†] RT = radiation therapy.

cGY 14 12 4500 cGY 5400

6 , 39 12 . IORT 33

(Table 2).

가 가

가 27 ,

가 6

가

21 18 (P=0.003)

(Table 3).

3.12±4.25

2.65±1.98

0.21 unit 0.14

unit 가 . 3.21±4.10 , 3.71±3.94 가 .

(Table 3).

3

1

12 46.2%,

29 5

17.2%

(P <

Table 3. Comparison of cause of unresectability, operation time, complication and survival rate between two groups

| | IORT (n=33) | Palliative surgery (n=39) | P-value |
|---|----------------|------------------------------|---------|
| Cause of unresectability | | | 0.003 |
| Distant metastasis | 6 | 21 | |
| Local invasion | 27 | 18 | |
| Operative time (hour) | 3.12±4.25 | 2.65±1.98 | NS* |
| Transfusion (unit) | 0.21 | 0.14 | NS |
| Ileus (day) | 3.21±4.10 | 3.71±3.94 | NS |
| Complication (case) | | | NS |
| Wound infection | 5 | 5 | |
| Intraabd. abscess | 1 | 1 | |
| Bleeding | 1 | 0 | |
| Renal complication | 0 | 0 | |
| Pul. complication | 3 | 4 | |
| Pain relief (%) | (n=26) | (n=29) | 0.04 |
| Good (no pain) | 3 (11.5%) | 1 (3.4%) | |
| Fair (better than before op) | 9 (34.6%) | 4 (13.8%) | |
| Poor (same or worse) | 14 (53.8%) | 24 (82.8%) | |
| Distant metastasis during follow up periods | | | NS |
| Liver | 12 | 16 | |
| Lung | 2 | 1 | |
| Peritoneal seeding | 1 | 2 | |
| Bone | 1 | 0 | |
| Minor or partial remission (%) | 6 (18.2%) | 2 (5.1%) | NS |
| Median survival time (months) | 6.50 | 9.17 | NS |

*NS = statistically not significant by Chi-Square test.

0.05)(Table 3).

12 , 2 , 1 , 16 , 1 , 2

가 50%

99% (PR: partial remission) 50% minor remission 가

6 , 2 가

(Table 3).

6.5 ,

9.1

(Fig. 1, Table 3).

가 가

가

가 가

. Mariya (20)

8 12

1 3

가
가

가

33 6 (18.2%)

가

2 (5.1%)

가

가

6.50 9.17

(21,22)

가

가

가

가

(22-27)

1994 1998

가

39

33

가

가

가

REFERENCES

- 1) Niederhuber JE, Bremman MF, Menck HR. The national cancer data base report on pancreatic cancer. *Cancer* 1995;76: 1671-7.
- 2) Lee KU, Moon BI, Kang HS, Kim JB. Chronological Changing Pattern of the Management of Pancreatic Carcinoma. *J Korean Surg Soc* 1995;48:416-27.
- 3) Gudjonsson B. Cancer of the pancreas. 50 years of surgery. *Cancer* 1987;60:2284-303.
- 4) Connolly MM, Dawson PJ, Michelassi F, Moosa AR, Lowenstein F. Survival in 1001 patients with carcinoma of the pancreas. *Ann Surg* 1987;206:366-73.
- 5) Gudjonsson B, Livstone EM, Sapiro HM. Cancer of the pancreas: diagnostic accuracy and survival statistics. *Cancer* 1978; 42:2494-506.
- 6) Kalser MH, Barkin J, MacIntyre JM. Pancreatic cancer. Assessment of prognosis by clinical presentation. *Cancer* 1985; 56:397-402.
- 7) Kawamura M, Kataoka M, Fuji T. Electron beam intraoperative radiation therapy for localized pancreatic carcinoma. *Int J Radiat Oncol Biol Phys* 1992;23:751-7.
- 8) Mohiuddin M, Rosato F, Barbot D. Long term results of combined modality treatment with I-125 implantation for carcinoma of the pancreas. *Int J Radiat Oncol Biol Phys* 1992;23: 305-11.
- 9) Kim CY, Kim YC, Suh SO, Kim CD, Choi MS. Intraoperative radiotherapy for T3-T4 biliary tract carcinoma. *Progress in Radio-Oncology VI* 1998;457-60.
- 10) Moertel CG, Childs DS Jr, Reitmeier RJ, Colby MY, Holbrook MA. Combined 5-fluorouracil and supervoltage radiation therapy of locally unresectable gastrointestinal cancer. *Lancet* 1969; 2:865-7.
- 11) Yoon SM, Lee HS, Hur WJ, Choi YM, Kim HJ, Kim JS, et al. Results of treatment in unresectable pancreatic cancer. *J Kor Soci Hyperthermia and Oncology* 1999;4:105-23.
- 12) Gastrointestinal Tumor Society Group. A multi-institutional comparative trial of radiation therapy alone and in combination with 5-fluorouracil for locally unresectable pancreatic carcinoma. *Ann Surg* 1979;189:205-8.
- 13) American joint committee on cancer. *AJCC Cancer Staging Manual*. 5th ed. Philadelphia: Lippincott-Raven; 1997.
- 14) Kim HD, Lee BK, Choi KH, Lee SD, Seo JK, Park YH. Clinical study of pancreatic cancer. *J Korean Surg Soc* 1992; 42:179-88.
- 15) Beazley RM, Cohn I. Tumors of the pancreas, gallbladder and extrahepatic ducts. In: Holleb AI, Fink DJ, Murphy GP, editors. *Textbook of Clinical Oncology*. 1st ed. Atlanta: American Cancer Society; 1991. p.219-30.

- 16) Davidson BS, Jeffrey EL, Peter WT, Frederick CA, Douglas BE. Teaching complex surgery: A standard approach to pancreaticoduodenectomy. *Surgical Rounds* 1995;450-7.
 - 17) Haskell CM, Lavey RS, Ramming KP. Exocrine Pancreas. In: Haskell CM, Berek JS, editors. *Cancer treatment*. 4th ed. Philadelphia: W.B. Saunders; 1995. p.502-12.
 - 18) Lamerz R. Role of tumor markers, cytogenetics. *Ann Oncol* 1999;10Suppl 4:S145-9.
 - 19) Kim KH, Lee HS, Kim CD, Ryu HS, Hyun JH. Clinical evaluation of serum CEA and CA 19-9 in the staging of pancreatic cancer. *Korean J Gastroenterol* 1998;30:390-6.
 - 20) Mariya Y, Aoki M, Anabai A, Matsukura H, Abe Y, Kimura T, et al. Response of unresectable pancreatic cancer to intraoperative radiotherapy. *Radiat Med* 1998;16:195-200.
 - 21) Cienfuegos JA, Manuel FA. Analysis of intraoperative radiotherapy for pancreatic carcinoma. *Eur J Surg Oncol* 2000;26Suppl A:S13-5.
 - 22) Sindelar WF, Kinsella TJ. Studies of intraoperative radiotherapy in carcinoma of the pancreas. *Ann Oncol* 1999;10Suppl 4:226-30.
 - 23) Miyamatsu A, Morinaga S, Yukawa N, Akaike M, Sugimasa Y, Takemiya S. Intraoperative radiation therapy (IORT) for locally unresectable pancreatic cancer. *Gan To Kagaku Ryoho* 1999;26:1846-8.
 - 24) Dubios JB. Intra-operative radiation therapy in tumors of the digestive tract. *Bull Cancer* 2001;88:155-62.
 - 25) Takeda S, Inoue S, Kaneko T, Harada A, Nakao A. The role of adjuvant therapy for pancreatic cancer. *Hepatogastroenterology* 2001;48:953-6.
 - 26) Reni M, Panucci MG, Ferreri AJ, Balzano G, Passoni P, Cattaneo GM, et al. Effect on local control and survival of electron beam intraoperative irradiation for resectable pancreatic adenocarcinoma. *Int J Radiat Oncol Biol Phys* 2001;50:651-8.
 - 27) Tanada M, Takashima S, Endoh H, Hyoudou I, Jinno K, Kataoka M. Multimodal treatment including intraoperative irradiation for advanced pancreatic cancer with extended metastasis. *Gan To Kagaku Ryoho* 2001;28:1681-3.
-