

췌장암 Pancreatic Cancer

134

Si Young Song, M.D.

Department of Internal Medicine

Yonsei University College of Medicine, Severance Hospital

E - mail : sysong@yumc.yonsei.ac.kr

Abstract

Pancreatic ductal adenocarcinoma is the fourth to fifth leading cause of cancer death in the Western hemisphere with a median survival of less than 6 months. This highly aggressive cancer is characterized by invasive biology, rapid progression and profound resistance to treatment. Most pancreatic cancers are already unresectable at the time of diagnosis. Also, for the patients who undergo potentially curative resection, the 5 - year survival is only 10~20%. Recently, the incidence of this fatal cancer has been increased remarkably in our country. It is time to start having a serious considerations to pancreatic cancer. Over the past few decades, a lot of trials were performed to improve survival and symptoms in patients with pancreatic cancer, and some improvements occur in patients who also receive chemotherapy and/or radiotherapy. But the impact on long - term survival has been minimal owing to the intense resistance to all extant treatments. Advances in pathological classification and cancer genetics have improved our descriptive understanding of this disease; however, important aspects of pancreatic cancer biology remain poorly understood. Factors associated with an increased risk of pancreatic cancer include smoking, chronic pancreatitis, diabetes, prior gastric surgery, and exposure to radiation or chemicals such as chlorinated hydrocarbon solvents. A number of syndromes are identified with an increased incidence of pancreatic cancer. Surgical operation has been the dominant procedure for treating pancreatic cancer. But, it is notoriously difficult to detect at its initial condition, and most pancreatic cancers are already unresectable at the time of diagnosis. Until now, gemcitabine has been established as a new standard for the treatment of unresectable pancreatic cancer in terms of clinical benefit response, time to progression, and survival. However their effects were modest. Advancement in the understanding of the biology of pancreatic cancer has helped identify several molecular targets for the development of novel therapies. Gene therapy and immunotherapy are currently in the spotlight as promising new methods for cancer cure. Many studies have revealed the potential of their therapy for the treatment of pancreatic cancer, and early clinical trials are taking place to evaluate the success of each therapy. A better understanding of pancreatic cancer biology will lead the way to more effective treatments, however, we should keep in mind that the single most important factor to improve the survival of pancreatic cancer patient is the early diagnosis in a radically resectable condition.

Keywords : Pancreatic cancer; Early diagnosis; Treatment

4~5

28,000~

32,000 가

가

가 10

2 가

가 가

2010 4,000 가

가 가

, 2

10%

가 90%

15

가 20

“90 ”

가

10

가

가

35%

7~14%

(3).

?

가 가

가 가

5

10~18%

(4).

(UICC)

가

, UICC

I

(T1 - 2 N0 M0)

가 2 cm

가?

(T1a),

가 2 cm

(T1b)

(T2)

가 2 cm

5

15~25%

5

가

가

가

I

가 2 cm

50%

가

(1, 2),

가 1 cm

K - ras

22

1

가

가 16 (73%)

(5). , 1960 1989 16
가 1 cm Niderau 2,429
가 90% 86 (3.5%)
. Ariyama 77 (7).
가 1 cm 가
5 100% 가 ,
, perineural invasion .
(6).
? 5~10%
가
가 7.8% 0.6%
(8, 9).
45 , hereditary pancreatitis,
, , , ataxia - telangiectasia, hereditary nonpolyposis colo-
, , , , rectal carcinoma(HNPCC), Von Hippel - Lindau
가 . , familial atypical mole - multiple melanoma
(FAMMM)
1. Hereditary pancreatitis autosomal dominant
WHO
, 가 , 가
, , (10). 14
가 가 , 57 70
, 가 가 40~75% . Heredi-
10~20 , , tary pancreatitis 7q355 cationic
가 trypsinogen gene
, 가 3% 가

(11~13).

HNPCC 가 가 , autosomal dominant , , nu- cleotide repeat mismatch repair 1.

Von Hippel - Lindau

가 BRCA2 99% 5~10%

20

가 CA 19 - 9 가 CA 19 - 9

CA

19 - 9가 가 (1).

40 (1) CA 19 - 9

(10% CA 19 - 9 mucin sialylated Lewis

), mice mo-

(), , monoclonal ,

amylase, elastase I 가 , . Lewis a - b -

5% CA 19 - 9

가 가 CA 19 - 9

가 95%

70~90%, 90%

가

1~2

CA 19 - 9 elastase - 1

가

가

(14). CA 19 - 9

가

1,000 IU/ml
 가가 ,
 CA 19 - 9 가
 가
 CA 19 - 9
 CA 19 - 9
 . CA 19 - 9
 가

1. Classification of pancreatic tumor markers

Category	Tumor markers
Complex glycoconjugates	CA 19 - 9, CA 125, CA 242, CA 72 - 4 (TAG - 72), CA 494, CAM 17.1, CA 50, SPAN - 1, DUPAN - 2, TPA, TPS
Oncofetal proteins	CEA, AFP, POA
Tumor suppressor gene	p53
Oncogenes	K - ras
Enzymes	Elastase, Ribonuclease, Amylase, Lipase, Telomerase, GT - II
Hormones and peptides	Amylin (IAPP), TATI, Insulin, Gastrin, Glucagon

(2) CEA

Carcinoembryonic antigen(CEA)

cut off 5 ng/ml

58% 75%

61%

CEA

CEA

가 2 cm

83%

93%

가

(15).

(3)

Amylin, CA 494, CAM 17.1

beta

insulin

amylin

가

. CA 494

BALB7c

가 90%,

94%

glycoprotein

monoclonal antibody

CAM

17.1 67~86%

90%

(4)

가

. K - ras

90~95%

p53

, p16, DPC4, BRCA2

. Amylin islet amyloid polypeptide

가 , 가 2 cm 가

2.

가

가 , 가

가

Helical(Spiral) CT가

가

. Helical CT

CT

2~3

가

2

3

가

가

(ERCP),

(MRI),

, PET(positron

emission tomography)

(MRCP : Magnetic Resonance Cholangiopancreatography)

가 가

Helical CT

가 가

가

.가

가 ,

Helical CT

(IDUS : Intra-
ductal pancreatic ultrasonography) 20~30 MHz

가 가

가 가

가 ,

18F - fluo- 6~12 , 가
rodeoxyglucose PET scanning In - 111 - octreotide
imaging PET

90% 가 가

PET 가
(16), (des-
moplastic reaction)가

1.

가 thymidylate synthase
가 (resec- 5 - fluorouracil(5 - FU) 가
table), (locally advanced) 5 - FU
(far advanced) 3가 가

5 - FU doxorubicin, mito-
mycin C, cisplatin, streptozocin, paclitaxel

5 - FU 가 ,

가 ,

가 .

1990 pyrimidine

gemcitabine(Gemzar, Eli Lilly, Indianapolis, IN, USA) , 5 - FU (clinical benefit response)

가 , 1997 FDA

gemcitabine FDA

가 ,

Gemcitabine deoxycytidine deoxycytidine , 20 가

dCTP . DNA 가

, ribonucleotide dNTP . , 1

Burris 3 126

gemcitabine 5 - FU 70% 4

4.4 5 - FU

gemcitabine 5.7

. 1

5 - FU 2% gemcitabine 18% 가 ,

5 - FU 5%, gemcitabine 24%

. 19

(17).

gemcitabine 10%

1

gemcitabine

5 - FU, platinum , irinotecan, docetaxel, capecitabine, trastuzumab cetuximab

Gemcitabine 5 - FU 가

, 5 - FU 가 (

), ,

가 ,

gemcitabine

Cisplatin oxaliplatin platinum

(

2). Platinum DNA 가 가 DNA

, gemcitabine gem-

citabine DNA platinum DNA

, DNA

platinum DNA exo-

nuclease

platinum

2.	Gemcitabine	Platinum	2	
		(%)	()	
Gemcitabine/cisplatin	41	11	8.2	Heinemann, et al
	42	26	7.1	Philip, et al
	52	31	-	Colucci, et al
	16	31	9.6	Brodowicz, et al
Gemcitabine/oxaliplatin	64	29	-	Louvet, at al
Gemcitabine/cisplatin/epirubicin/5 - FU	49	58	11	Reni, et al

가 , , platinum 가 epidermal growth factor receptor(EGFR) 가 Trastuzumab Cetuximab . gemcitabine 4 , 1 EGFR HER - 2/neu 3 1,000 mg , cis- platinum 4 80 mg EGFR 40%, 5.6 , 가 8.2 가 Iressa . platinum oxaliplatin 100 mg citabine 3 1 2 가 gem- 26~31%, p53, p16, DPC4 6 71% , metalloprotease inhibi- 2 topoisomerase irinote- tor, Cox - 2 inhibitor, Ras farnesyl- can(CPT - 11), taxane paclitaxel docetaxel, transferase inhibitor, flutamide fluoropyrimidine capecitabine(Xeloda), gemcitabine pemetrexed(ALIMTA), polyamine , DNA Troxacitabine, Pectin GBC - 590, Acylfulvenes gem- citabine 가

2.

가 (radio-
가 resistance)

DNA

가

가

(p53

MDM2가)

DNA

radical scavenger

가 가

S

가

, Raf Ras

가

pH

가

가

가

1)

2)

가

가

가

(locally advanced)

가

가

‘enhancer’, ‘potentiator’

‘radiosensitizer’,

가

가

margin positive resec-

tion

가

가

5 - FU

gemcitabine

gemcitabine

가

radiosensitizer

가

gem-

citabine

Whipple

가

가

가

1997 1

2001 12

48

가

가

gemcitabine

doxifluridine,

paclitaxel

doxifluridine

(5 ,

가

4,500 cGy)

13

15

, 1

50%

62.5%

(18).

가

가

가

desmoplastic reaction

가가

가

가

가

2

가

☺

1. Tsuchiya R, Tsunoda T. Tumor size as a predictive factor. *Int J Pancreatol* 1990 ; 7 : 117
2. Satake K, Nishiwaki H, Yokomatsu H. Surgical curability and prognosis : standard resection versus extended resection for T1 carcinoma of the pancreas. *Surg Gynecol Obstet* 1992 ; 175 : 259
3.
1994 ; 26 : 1010 - 20
4. Yamamoto M, Ohashi O, Saitoh Y. Japan pancreatic cancer registry : Current status. *Pancreas* 1998 ; 16 : 238 - 42
5. Demeure MJ, Doffek KM, Komorowski RA, Wilson SD. Adenocarcinoma of the pancreas : detection of occult metastases in regional lymph nodes by a polymerase chain reaction - based assay. *Cancer* 1998 ; 83 : 1328 - 34
6. Ariyama J, Suyama M, Satoh K, Sai J. Imaging of small pancreatic ductal adenocarcinoma. *Pancreas* 1998 ; 16 : 396 - 401
7. Niederau C, Grendell JH. Diagnosis of pancreatic carcinoma. *Pancreas* 1992 ; 7 : 66 - 86
8. Lynch HT. Genetics and pancreatic cancer. *Arch Surg* 1994 ; 129 : 266 - 8
9. Lynch HT, Fusaro L, Lynch JF. Familial pancreatic cancer. A family study. *Pancreas* 1992 ; 7 : 511 - 5
10. Comfort MW, Steinberg AG. Pedigree of a family with hereditary chronic relapsing pancreatitis. *Gastroenterology* 1992 ; 21 : 54 - 63
11. Ekblom A, McLaughlin JK, Karlsson B, Nyren O, Gridley G, Fraumeri JF, et al. Pancreatitis and pancreatic cancer : A population - based study. *J Natl Cancer Inst* 1994 ; 86 : 625 - 7
12. Lowenfels AB, Maisonneuve P, Cavallini G, Ammann RW, Lankisch PG, DiFrancesco V, et al. Pancreatitis and the risk of pancreatic cancer. *N Engl J Med* 1993 ; 328 : 1433 - 7
13. McKusick VA. Mendelian inheritance in man, ed 9. Baltimore : Johns Hopkins University Press, 1990
14. Satake K, Takeuchi T, Homma T, et al. Ca 19 - 9 as a screening and diagnostic tool in symptomatic patients : The Japanese experience. *Pancreas* 1994 ; 9 : 703 - 6
15. Matsumoto S, Harada H, Tanaka J, Ochi K, Seno T, Kunichika K, et al. Evaluation of cytology and tumor markers of pure pancreatic juice for the diagnosis of pancreatic cancer at early stages. *Pancreas* 1994 ; 9 : 741 - 7
16. Bang SM, Chung HW, Park SW, Chung JB, Kang JK, Song SY, et al. The usefulness of 18 FDG - PET scan in determination of treatment response in pancreatic cancer. *Gastroenterology* 2003 ; 124(Suppl 1) : A - 188
17. Burris HA 3rd, Moore MJ, Andersen J, Green HR, Rothenberg ML, Van Hout DD, et al. Improvements in survival and clinical benefit with gemcitabine as first - line therapy for patients with advanced pancreas cancer : a randomized trial. *J Clin Oncol* 1997 ; 15 : 2403 - 13
18. Chung HW, Park JY, Kim SA, Shin Y, Park SW, Song SY, et al. Comparison of concurrent chemoradiation between paclitaxel/furtulon and gemcitabine/furtulon for the locally advanced pancreatic carcinoma. *Gastroenterology* 2002 ; 122(Suppl 1) : A - 337