The effect of combined treatment methods on survival and toxicity in patients with pancreatic cancer

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Key words: *chemoradiation; pancreatic cancer; chemotherapy; survival.*

Summary. *In Lithuania, there were 476 new pancreatic cancer cases in 2005. Based on international scientific literature and the results of our retrospective studies, a prospective study has been designed. The aim of study was a prospective evaluation of the impact of two concomitant chemoradiation methods on the survival and the time to disease progression in patients diagnosed with resectable and unresectable pancreatic cancer and prospective evaluation of the safety of two concomitant chemoradiation methods for the treatment of resectable and unresectable pancreatic cancer.*

Material and methods. During the period of 2000–2005 at the Clinic of Oncology, Kaunas University of Medicine Hospital, we performed a prospective randomized study to analyze two concomitant chemoradiation treatment methods. The patients were stratified according to the resectability of the tumor: with resectable tumor (stage I–IVA) and with unresectable tumor (stage III–IVA). Treatment for each group of patients was selected randomly choosing concomitant chemoradiation treatment: radiation therapy and 5-fluorouracil or radiation therapy and gemcitabine. Criteria of the efficacy of the treatment methods were median survival, time to disease progression, and treatment safety (qualitative and quantitative analysis).

Results and conclusions. The treatment methods – radiotherapy and 5-fluorouracil or radiotherapy and gemcitabine – were equally effective when assessing the survival and time to disease progression in patients diagnosed with pancreatic cancer. Treatment of patients diagnosed with pancreatic cancer with radiotherapy and 5-fluorouracil was a safer approach than treatment with radiotherapy and gemcitabine, which induced more severe toxic adverse effects.

Introduction

Treatment of pancreatic cancer is an important medical problem. In Lithuania, there were 476 new pancreatic cancer cases in 2005 (1).

During the last decades, new diagnostic and treatment methods have been developed, but these new advances did not make the treatment of this form of cancer more effective. Median survival of patients diagnosed with pancreatic cancer, depending on the stage of the disease, the metastasis of the tumor, the treatment method, and the functional status of a patient, is about 6–12 months (2). Only 20% of newly diagnosed cases with pancreatic cancer are resectable at the diagnosis (stages I–III), and 25% to 40% of these patients will survive for 5 years (2, 3).

At present, pancreatic cancer is treated by applying combination therapy – surgery, radiation therapy (RT), and chemotherapy – although so far surgery remains the main treatment of pancreatic cancer. However, insignificant changes in survival rates following resections, the emergence of new chemotherapy preparations, and the progress of the RT technique prompt the analysis of the benefit of combination treatment for this patient group. Another important factor of the need for adjuvant treatment is the course of the pancreatic cancer, relapses, rapid development of metastases and micrometastases that are via molecular biology techniques histologically detected in N0 lymph nodes (50–70%), bone marrow, and other sites (4, 5).

At present, the actively discussed issues are whether pancreatic cancer in its early stages necessitates adjuvant treatment or whether surgical treatment alone is sufficient, what adjuvant therapy should be selected (chemotherapy alone or in combination with radiotherapy), and what – longer survival or the quality of life – is more important for the patient.

The superiority of chemoradiation (ChRT) treatment was first proven in 1967 by Moertel *et al.*, when application of ChRT in treating unresectable pancreatic cancer yielded better results than did RT alone (6).

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After the first successful results of ChRT treatment, the GITSG (*Gastrointestinal Tumor Study Group*) further studied the effect of concomitant ChRT treatment on the life expectancy of patients with unresectable pancreatic cancer.

ChRT therapy yielded better results, compared to RT or chemotherapy applied separately. The application of RT combined with 5-Fu increased median survival up to 8–9 months.

After clinical studies proved better survival results in patients with unresectable pancreatic cancer, studies on adjuvant therapy were performed. During the last decades, three larger randomized clinical studies were performed on the application of adjuvant concomitant ChRT therapy (GITSG 9173 clinical trial, EORTC, and the most recent and largest – ESPAC-1 (*European Study Group for Pancreatic Cancer*). In 2002, the journal of ASCO (*American Society of Clinical Oncology*) published the meta-analysis of the results of the recent clinical studies on the application of chemotherapy and RT. The generalization of these clinical studies lead to the conclusion that following resection, the best choice for adjuvant therapy is chemotherapy, and concomitant ChRT therapy is recommended for selected patient groups (7, 8).

When generalizing the results of the analysis of these clinical studies, one can state that at present, the choice of adjuvant therapy is not clear yet, and no treatment standards have been established. The recommended options for the adjuvant treatment of resectable pancreatic cancer are either concomitant ChRT therapy or chemotherapy alone depending on patient's condition and therapeutic experience, capacities, and traditions of the hospital. The treatment options for unresectable pancreatic cancer are the same; only here, general patient's condition and the safety of treatment are of greater importance.

Until 2000, in Lithuania, according to the data of several retrospective studies, pancreatic cancer at the Kaunas University of Medicine Hospital was most frequently treated by applying palliative surgery plus RT or 5-fluorouracil (5-Fu). It was only after 2000, when increasing possibilities for chemotherapy (gemcitabine (Gem)) and RT, new treatment planning and technique allowed for the initiation of the application of ChRT therapy.

Based on international scientific literature and the results of our retrospective studies, a prospective study has been designed.

Our study aimed at a prospective evaluation of the impact of two concomitant ChRT methods on the survival and the time to disease progression in patients diagnosed with resectable and unresectable pancreatic cancer and the safety of two concomitant ChRT methods for the treatment of resectable and unresectable pancreatic cancer.

Materials and methods

During the period of 2000–2005 at the Clinic of Oncology of Kaunas University of Medicine Hospital, we performed a prospective randomized study in order to analyze two concomitant ChRT treatment methods. The clinical study was approved by the Local Ethics Committee; protocol No. 42/2001.

In the prospective study, patients diagnosed with resectable and unresectable pancreatic cancer were analyzed. For the research, patient inquiry and clinical data for the observation period were used.

The main inclusion criteria were the following: histologically and/or cytologically confirmed pancreatic cancer (adenocarcinoma, *etc.*); early or locally advanced resectable or unresectable pancreatic cancer (stages I–IVA); the stages of pancreatic cancer were evaluated according to the pancreatic cancer staging rules for 2000; no distant metastases; no previous treatment with 5-Fu or Gem.

A total of 60 patients were treated during the period of the study. Forty-one patients were diagnosed with resectable pancreatic cancer and 19 patients with unresectable pancreatic cancer. Twenty-three patients with resectable pancreatic cancer were treated with RT and 5-Fu and 18 patients with RT and Gem (78.2% and 61.1% of patients died, respectively). Ten patients with unresectable pancreatic cancer were treated with RT and 5-Fu and nine patients with RT and Gem (80% and 77.7% of patients died, respectively).

Treatment methods

The patients were stratified according to the resectability of the tumor: with resectable tumor (stage I–IVA) and with unresectable tumor (stage III–IVA). Treatment for each group of patients was randomly selected by choosing closed envelopes containing indicated treatment methods – concomitant ChRT treatment: RT and 5-FU or RT and Gem.

Treatment arms:

1. 5-Fu 350 mg/m^2 IV on days 1–5, and 31–35 of RT (the first and fifth week of RT) or 500 mg/m^2 IV on days 1–3, and 31–33 of RT (TFD 50 Gy, 25 fractions during 5 weeks).
2. Gem 250–300 mg/m^2 IV once a week during RT (TFD 50 Gy, 25 fractions during 5 weeks).

Upon diagnosis of distant metastases, patients of both groups were treated with Gem in standard doses

(1000 mg/m^2 IV once weekly for 7 weeks, followed by additional five 3-week courses with 2-week breaks).

Criteria of the efficacy of the treatment methods

Median survival was the time interval during which 50% of patients of the analysis group survived.

Time to disease progression was time from the diagnosis to the progression of the disease (local progression or distant metastasis). The progression of the disease was evaluated if local recurrence or distant metastases were clinically diagnosed and confirmed by instrumental studies (abdominal ultrasound and/or computed tomography). If the patient survived beyond the duration of the study, he/she was observed further. The dates of patients' deaths were verified in the Cancer Registry, Institute of Oncology, Vilnius University.

Treatment safety was defined as treatment-related toxicity, its severity and change immediately after treatment and at 1 and 3 months after treatment. Adverse reactions resulting from each studied treatment method were evaluated according to the World Health Organization (WHO) criteria. Indicators were assessed on a scale ranging from 0 to 4 points (from total absence to the severe manifestation of the indicator). Signs of toxicity resulting from the treatment were evaluated on the last day of the application of ChRT, then after 1 month (early toxicity), and after 3 months (late toxicity) following the treatment.

Statistical analysis

In the study, two groups were compared using cross-tabulation method; statistical significance was determined using chi-square test and chance proportion. For this purpose, sign frequency characteristics were used. Statistical analyses were performed using Statistical Package for Social Sciences software (SPSS, Version 11). Survival was estimated by the Kaplan-Meier method and performed using STATA. MS and survival to disease progression was estimated by the Kaplan-Meier method and compared by the log-rank test. Analysis of treatment toxicity was evaluated using patient questionnaire, and statistical analysis was performed using SPSS (Version 11).

Results

1. Survival (median survival)

We compared median survival of patients treated with RT and 5-Fu and with RT and Gem.

The median survival of patients who underwent radical surgery and RT combined with 5-Fu was 518 days (17.2 months), whereas the median survival of those who underwent radical surgery and RT combined with Gem – 364 days (12.1 months). The difference was not statistically significant (P=0.84). The survival curves of these patients are presented in Fig. 1.

The median survival of patients who underwent palliative surgery and RT combined with 5-Fu was 286 days (9.5 months), whereas the median survival of those who underwent palliative surgery and RT combined with Gem – 273 days (9.1 months). The difference was not statistically significant (P=0.79). The survival curves of these patients are presented in Fig. 2.

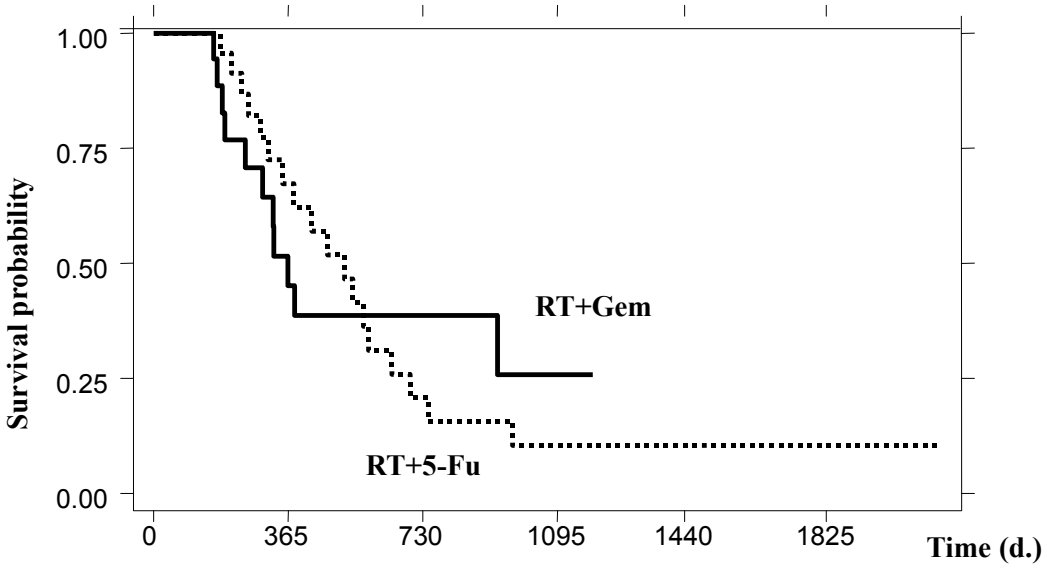

Fig. 1. **Survival curves of patients diagnosed with resectable pancreatic cancer and treated with radiotherapy (RT) and 5-fluorouracil (5-Fu) or radiotherapy and gemcitabine (Gem)**

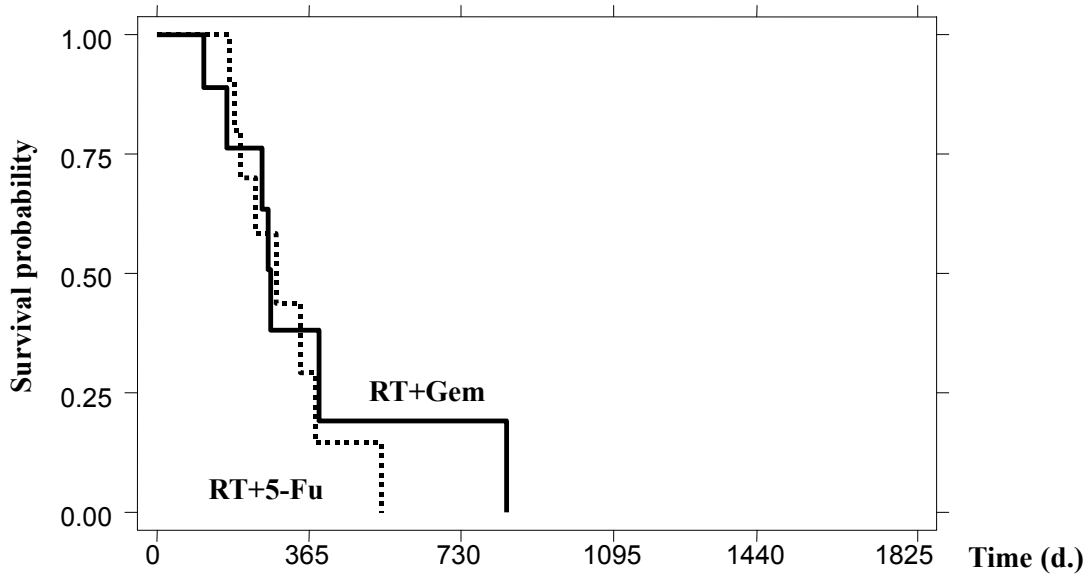

Fig. 2. **Survival curves of patients diagnosed with unresectable pancreatic cancer and treated with radiotherapy (RT) and 5-fluorouracil (5-Fu) or radiotherapy and gemcitabine (Gem)**

2. Time to disease progression

When analyzing the results of the treatment of resectable and unresectable pancreatic cancer cases, we investigated the time to disease progression. The time to disease progression of all patient groups is presented in Table 1.

In cases of resectable pancreatic cancer, the time to disease progression was longer in patients treated with RT and 5-Fu (14.3 months) than in patients treated with RT and Gem (10.8 months) (P=0.8). In cases of unresectable pancreatic cancer, the time to disease progression was also longer in patients treated with RT and 5-Fu (8.6 months) than in patients treated with RT and Gem (5.6 months) (P=0.8).

3. Assessment of the safety of the two treatment methods

We analyzed the adverse effects of two treatment methods, evaluated the hematological and gastroenterological (including hepatobiliary) toxicity, and performed the qualitative and quantitative analysis of the toxicity of both treatment methods.

a) Qualitative analysis of treatment toxicity

The main hematological parameters evaluated were the following: leukopenia, neutropenia, anemia, and thrombocytopenia. Statistically significant difference was observed in leukopenia between the groups diagnosed with resectable pancreatic cancer (P= 0.011). No difference in other parameters of hematological toxicity or gastroenterological toxicity between two groups was detected. The comparison of all adverse effects between two treatment methods immediately after ChRT and at 1 and 3 months following the treatment in cases of resectable pancreatic cancer yielded no statistically significant differences (P=0.27; 0.20; 0.97, respectively; Table 2). In cases of unresectable pancreatic cancer, the comparison of the toxicity of two treatment methods immediately after ChRT (P=0.34), at 1 month (P=0.41), and 3 months following the treatment yielded no statistically significant differences either (Table 3).

b) Quantitative analysis of treatment toxicity

The grade of toxicity was evaluated using the

Table 1. **Time to disease progression of all patient groups**

Treatment method	Min survival, days	Max survival, days	Median survival, days (months)	P
RT+5-Fu, resectable	124	2138	429 (14.3)	0.8
RT+Gem, resectable	163	1136	325 (10.8)	
RT+5-Fu, unresectable	175	539	260.5 (8.6)	0.8
RT+Gem, unresectable	112	839	168 (5.6)	

RT – radiation therapy; Gem – gemcitabine; 5-Fu – 5-fluorouracil.

***Table 2*. Toxic side effects of two treatment methods in patients with resectable pancreatic cancer**

Side effect	RT+5-Fu, resectable, %			RT+Gem, resectable, %		
	1*	2*	3*	1*	2*	3*
Leukopenia	8.6	8.6	0	61.1	0	0
Neutropenia	4.3	0	0	50	0	0
Anemia	13	13	9.5	44.4	12.5	25
Thrombocytopenia	0	4.3	0	5.5	0	0
Nausea/vomiting	21.7	0	0	33.3	0	0
Diarrhea	8.6	4.3	0	22.2	0	0
GPT/GOT increase	4.3	8.6	4.7	0	6.2	16.6
AP increase	0	0	4.7	0	18.7	16.6

GPT – glutamic-pyruvic transaminase; GOT – glutamic-oxalacetic transaminase; AP – alkaline phosphatase; RT – radiation therapy; Gem – gemcitabine; 5-Fu – 5-fluorouracil.
1* – after chemoradiation; 2* – 1 month after chemoradiation; 3* – 3 months after chemoradiation.

***Table 3*. Toxic side effects of two treatment methods in patients with unresectable pancreatic cancer**

Side effect	RT+5-Fu, unresectable, %			RT+Gem, unresectable, %		
	1*	2*	3*	1*	2*	3*
Leukopenia	0	0	0	22.2	11.1	0
Neutropenia	0	0	0	0	0	0
Anemia	0	22.2	40	0	22.2	0
Thrombocytopenia	0	0	0	0	0	0
Nausea/vomiting	30	0	0	22.2	0	0
Diarrhea	10	0	0	11.1	0	0
GPT/GOT increase	0	0	0	0	33.3	0
AP increase	0	11.1	0	0	11.1	0

GPT – glutamic-pyruvic transaminase; GOT – glutamic-oxalacetic transaminase;
AP – alkaline phosphatase; RT – radiation therapy; Gem – gemcitabine; 5-Fu – 5-fluorouracil.
1* – after chemoradiation, 2* – 1 month after chemoradiation, 3* – 3 months after chemoradiation.

WHO scale. No treatment-related deaths were registered. Most frequently, grade 1 and grade 2 toxicity was observed. No grade 4 toxicity was detected. Severe grade 3 toxicity was analyzed in detail.

The general survey of all toxic effects by grade showed that the more toxic effects of higher grade were observed, the greater toxicity, in general, was in the treatment group. In patients with resectable pancreatic cancer, more toxic adverse effects were observed in patients treated with RT and Gem, although toxicity immediately after ChRT and at 1 month following the treatment was not statistically significantly different. However, after 3 months following the treatment with RT and Gem, the toxicity in this group was more severe than in the group who underwent treatment with RT and 5-Fu (Fig. 3).

In the group of patients diagnosed with unresectable pancreatic cancer, more severe toxicity was observed in patients treated with RT and Gem. The difference in toxicity was not statistically significant immediately after the treatment, but toxicity after 1 month following the treatment with RT and Gem was statistically significantly worse than that observed in the group of patients treated with RT and 5-Fu (Fig. 4).

Discussion

The analysis of the survival results

The survival results and prognosis differed between patient groups with resectable and unresectable pancreatic cancer. These results were analyzed separately.

No statistically significant differences in median survival have been detected between patients with re-

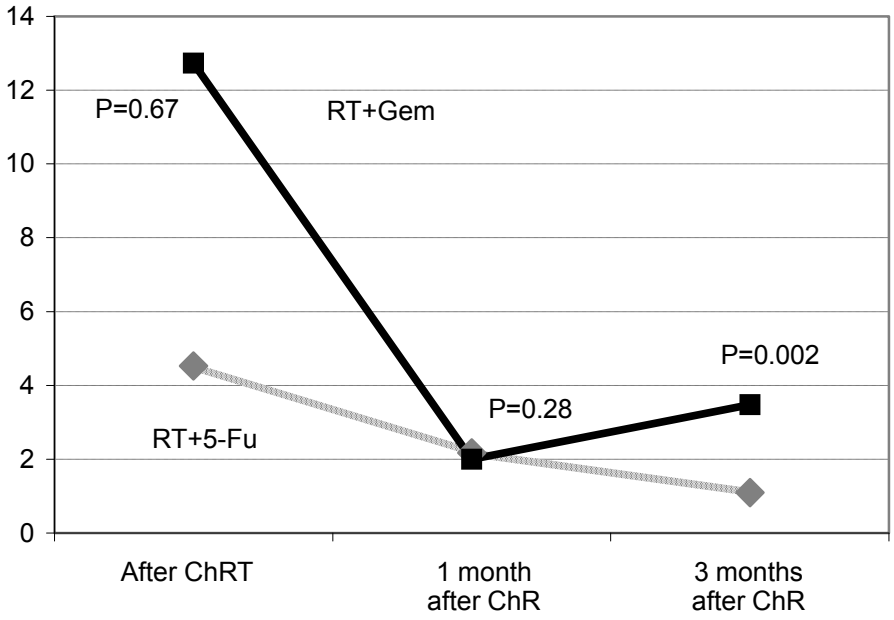

Fig. 3. **Comparison of safety of two concomitant chemoradiation (ChRT) methods in a group of patients diagnosed with resectable pancreatic cancer**

RT – radiation therapy; 5-Fu – 5-fluorouracil; Gem – gemcitabine.

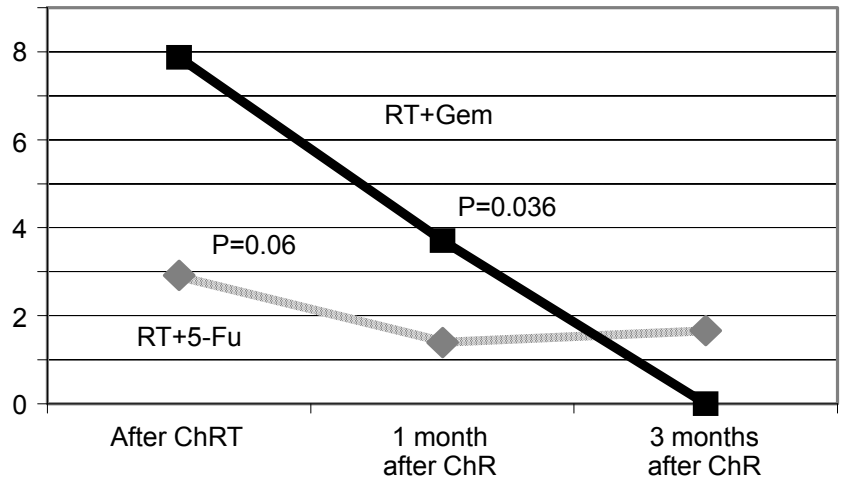

Fig. 4. **Comparison of safety of two concomitant chemoradiation (ChRT) methods in a group of patients diagnosed with unresectable pancreatic cancer**

RT – radiation therapy; 5-Fu – 5-fluorouracil; Gem – gemcitabine.

sectable pancreatic cancer treated with radiation therapy and 5-Fu or with RT and Gem. The results of patients' survival improved: from the median survival of 12 months during the first analyzed clinical studies (determined during the retrospective clinical study) to 17 months (determined during the prospective study in patients who underwent radiation therapy and 5-Fu) (9, 10). Better results may be explained by the superiority of the prospective study and the improvement of treatment techniques.

Three larger randomized clinical studies of ChRT treatment have been performed. According to their findings, the median survival in the presence of resectable pancreatic cancer is 1–2 years: the median survival determined during the GITSG clinical trial was 20 months and during the EORTC study – 17 months (7, 8). Although the ESPAC-1 clinical trial (11) and meta-analysis (7, 8) proved the superiority of chemotherapy as an adjuvant treatment, but the evaluated median survival (MS) of patients who under-

went ChRT therapy was 16 months. During these randomized clinical trials, patients mostly underwent radiation therapy and 5-Fu, and the dosage and treatment regimens were similar to those applied in our study (11–13).

The number of clinical studies on the application of the combination of radiation therapy with Gem is very scarce. The total duration of the survival of patients with resectable pancreatic cancer treated with Gem (300 mg/m^2) together with radiation therapy (total focal dose – 45 Gy) during phase II multicenter study was 19 months (14). These results are better than those obtained during our study (MS – 12 months), and longer survival period might have been influenced by differences in the treatment techniques.

The results of our study are similar to those obtained during the GITSG clinical trials that investigated patients with unresectable pancreatic tumor and treated with radiation therapy and 5-Fu, where the median survival was 8–9 months (15–17, 19). We selected similar treatment techniques: the radiation therapy dosage corresponds to the conventional doses, *i.e.* 40–60 Gy (in our clinical study – 50 Gy) (15–18). 5-Fu was administered intravenously at conventional dosage (13, 19, 20). The dosage of Gem was 150–500 mg/m^2 (as indicated in literature) administered once per week together with radiation therapy (in our study, it was 250–300 mg/m^2 once weekly). Several randomized clinical also trials analyzed the effect of radiation therapy and Gem in the treatment of unresectable cancer. Literature sources describe only phase I–II clinical trials, and therefore we could only perform a more detailed comparison of doses in this regimen. The total focal dosage of radiation therapy applied in combination with Gem was conventional; meanwhile, the dosage of Gem was also similar to the dosage applied during our clinical study (21–26).

Literature describes several clinical trials whose model was similar to the one used in our study. During the retrospective randomized clinical study, the median survival of patients treated with RT combined with Gem was 11 months. Meanwhile, the median survival of patients treated with RT combined with 5-Fu was 9 months. The difference was not statistically significant (27). Although median survival in both groups was similar, significant conclusions are not presented due to greater toxicity of RT and Gem. Another randomized prospective clinical trial analyzed patients with unresectable pancreatic cancer, treated with RT and 5-Fu or Gem. A better median survival was found in patients treated with RT and Gem (14.5 months) than in those treated with RT and 5-Fu (6.7 months, P=0.027) (28).

Both clinical studies yielded better results in treating unresectable pancreatic cancer with the combination of RT and Gem, compared to the findings of our study. This suggests that either the dosage of Gem (which was greater in both studies) or the continuation of Gem treatment following ChRT therapy influenced the results of the study.

We analyzed the time to disease progression in all four groups of patients during different periods of observation. A part of patients in all groups died early. We think that these were patients with poor prognosis, whose survival was not influenced by additional factors (such as treatment, *etc.*). In other patients who survived the MS period, the probability of survival increased. These were the patients with favorable prognosis, since their life expectancy (time to disease progression – MS) was continuously increasing. The main factor that conditioned the results in this group was ChRT treatment. Although no statistically significant difference was found between the two treatment methods, we think that adjuvant treatment may modify the results of survival (in this case – the time until disease progression).

During the randomized clinical trial (ESPAC-1), the time to disease progression in patients with resectable pancreatic cancer and treated with RT and 5-Fu was about 11 months (in our study 14.3 months) (11). In other phase II studies, the mean time to the progression of the disease in patients with resectable pancreatic cancer, treated with RT and Gem, was 6 and 14.5 months (in our study 10.8 months) (14, 26). According to the findings of a small-scale prospective clinical trial, the mean time to disease progression in patients with unresectable pancreatic cancer, treated with RT and Gem, was statistically significantly longer compared to patients treated with RT and 5-Fu (7.1 and 2.7 months, respectively; P=0.019) (28). Although literature data on the evaluation of time to disease progression are scarce, RT and 5-Fu seems to be superior in its efficacy in cases of resectable pancreatic cancer.

The evaluation of our findings shows that patients' survival time to disease progression differs largely, especially in case of resectable pancreatic cancer. The difference is not statistically significant, and therefore, we cannot state that one treatment method is superior to the other; on the other hand, the influence of both treatment methods (as adjuvant therapy) on life expectancy is significant.

The analysis of the safety of the two treatment methods

Qualitative analysis of treatment toxicity

We separately analyzed and compared adverse events that were prevalent in each group of subjects. In addition, we evaluated the hematological and gastroenterological toxicity of the treatment.

In the presence of resectable pancreatic cancer, more cases of hematologic toxicity (leukopenia, neutropenia, and anemia) were detected in patients treated with RT combined with Gem. The survey of all cases of resectable pancreatic cancer revealed the following characteristics: during the early posttreatment period, the signs of hematological (leukopenia, neutropenia, and anemia) and gastroenterological (nausea/vomiting and diarrhea) toxicity predominated. These manifestations of early toxicity may be explained by the effect of radiotherapy and chemotherapy preparations on the blood-forming system and the mucosa of the gastrointestinal tract. During the later period (at 3 months following the treatment), anemia persisted (resulting from the sum of the effect of the treatment or the cancerous intoxication due to the progression of the disease), and hepatic dysfunction became more prominent (resulting from the effect of the chemotherapy and/or the progression of the disease). No statistically significant difference in the manifestations of toxicity between two groups was found. However, the analysis of separate signs of toxicity (*e.g.* leukopenia) showed that the number of cases of this kind of toxicity was statistically significantly greater in patients treated with the combination of RT and Gem, since this therapy had a greater effect on the blood-forming system than on gastrointestinal one.

The generalization of the signs of toxicity on the treatment of unresectable pancreatic cancer showed that during the early period, the predominant manifestations were leukopenia (in patients treated with RT and Gem), and nausea/vomiting and diarrhea. During the later posttreatment period, anemia and changes in liver function became more prominent. Such manifestations indicate that the treatment has a toxic effect on the blood-forming system and the mucosa of the gastrointestinal tract, as well as on the patients' compensatory capacities. Although no statistically significant differences in the manifestations of toxicity were found between two treatment techniques in case of unresectable pancreatic tumor, we presume that treatment with RT and Gem resulted in more cases of leukopenia and liver dysfunction and treatment with RT and 5-Fu – in more cases of anemia lasting for 1–3 months following the treatment.

Quantitative analysis of the toxicity of the treatment

The generalization of the results revealed that more cases of grade 3 hematological toxicity were detected in patients with resectable pancreatic cancer and more cases of gastroenterological toxicity – in patients with unresectable pancreatic cancer, treated with RT and Gem.

We compared the degrees of the signs of toxicity resulting from the application of the two treatment methods, as well as the changes in these degrees within a set period. According to the data presented in foreign scientific literature, prescribing ChRT therapy also includes the description of its hematological and gastroenterological toxicity. A phase I clinical study even describes grade 4 gastroenterological toxicity of treatment in the presence of resectable pancreatic tumor when the total focal dose of RT was 60 Gy and the dose of Gem – 200 mg/m^2 (29). Another phase II clinical study of patients treated with radiotherapy plus Gem found grade 3–4 toxicity that again was both hematological (in 36% of cases) and gastroenterological (in 32% of cases) (26).

We reviewed the results or the toxicity of treatment of unresectable pancreatic cancer, described in several aforementioned clinical trials. The treatment methods applied in these trials were the same as those applied in our study. The retrospective clinical study, where patients were treated either with the combination of RT and 5-Fu or RT and Gem, showed that early toxicity (gastroenterological – nausea, vomiting) was more prominent in patients treated with RT and Gem (23% *vs.* 2%, P<0.001). Late toxicity (gastroenterological) was also more pronounced in patients treated with RT and Gem, whereas no cases of late toxicity were observed in patients treated with RT and 5-Fu (30). Other randomized clinical trial also detected grade 3–4 hematological (neutropenia – in 34% of patients treated with RT and Gem and in 19% of patients treated with RT and 5-Fu) and gastroenterological (nausea) toxicity. No statistically significant difference between these indices was found (28). In this case, toxicity caused by both treatment methods was similar.

We analyzed the relationship between toxicity and the dose of radiotherapy or chemotherapy preparation. Literature indicates that the most common adverse effects of treatment with Gem are leukopenia, thrombocytopenia, *etc.*, and the adverse effects of 5-Fu are more common toxic effects on the gastrointestinal tract. It is indicated that when a single once-weekly dose of Gem in combination with RT is 600–700 mg/m^2 is applied, one can already expect pronounced hematological and gastroenterological toxicity (21). In our

clinical study, the detected manifestations of toxicity were similar to those observed in such treatment regimens, although both treatment methods proved to be not very toxic.

Conclusions

1. The treatment methods – radiotherapy and 5-fluorouracil or radiotherapy and gemcitabine – were equally effective when assessing the survival and time to disease progression in patients diagnosed with pancreatic cancer.

2. Treatment of patients diagnosed with pancreatic cancer with radiotherapy and 5-fluorouracil was a safer approach than treatment with radiotherapy and gemcitabine, which induced more severe toxic adverse effects.

Kasos vėžio kompleksinio gydymo įtaka ligonių gyvenimo trukmei ir gydymo saugumui

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Raktažodžiai: chemospindulinis gydymas, kasos vėžys, chemoterapija, išgyvenimas.

Santrauka. Lietuvoje 2005 m. užregistruoti 476 nauji kasos vėžio atvejai. Išanalizavus tarptautinę literatūrą, mūsų atliktų retrospektyviųjų klinikinių tyrimų duomenis, suplanuotas prospektyvusis klinikinis tyrimas.

Tyrimo tikslas – atlikti prospektyvųjį tyrimą ir nustatyti dviejų chemospindulinio gydymo metodų, skirtų rezektabiliam ir nerezektabiliam kasos vėžiui gydyti, efektyvumą įvertinus ligonių gyvenimo trukmę ir laiką iki ligos progresavimo; atlikti prospektyvųjį tyrimą ir ištirti dviejų chemospindulinio gydymo metodų, skirtų rezektabiliam ir nerezektabiliam kasos vėžiui gydyti, saugumą.

Medžiaga ir metodai. 2000–2005 metais Kauno medicinos universiteto klinikų Onkologijos klinikoje atliktas prospektyvusis randomizuotas klinikinis tyrimas. Analizuoti du sutaptinio chemospindulinio gydymo metodai. Ligoniai buvo suskirstyti pagal naviko rezektabilumą: rezektabilus – I–IVA stadija; nerezektabilus – III–IVA stadija. Kiekvienos grupės ligoniams gydymas parinktas randomizacijos būdu ir skirtas sutaptinis chemospindulinis gydymas: spindulinis gydymas ir 5-fluorouracilas arba spindulinis gydymas ir gemcitabinas. Dviejų gydymo metodų efektyvumo vertinimo kriterijai: išgyvenimo mediana, laikas iki ligos progresavimo ir gydymo saugumas (kokybinė ir kiekybinė gydymo toksiškumo analizė).

Rezultatai ir išvados. Rezektabilaus ir nerezektabilaus kasos vėžio gydymo metodai (spindulinis gydymas ir 5-fluorouracilas arba spindulinis gydymas ir gemcitabinas) buvo lygiaverčiai ligonių bendrojo išgyvenimo bei laiko iki ligos progresavimo požiūriu. Spindulinio gydymo ir 5-fluorouracilo derinys buvo saugesnis gydant kasos vėžiu sergančius ligonius, nes spindulinio gydymo ir gemcitabino derinys lėmė sunkesnį toksiškumą.

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