The Role of Radiotherapy for Pancreatic Malignancies- A Population-based Analysis of the SEER-Medicare Database.

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Research

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Abstract

Background and objective. To investigate the role of adjuvant radiotherapy in patients after surgical resection for pancreatic cancer. *Methods* and patients. The patients with pancreatic cancer from 18 registered institutions in the Surveillance Epidemiology and End Results (SEER) database were retrospectively analyzed. The characteristics of patients who would benefit from adjuvant radiotherapy were screened, as well as whether neoadjuvant or adjuvant radiotherapy conferred to a better clinical outcome.

Results. 30249 patients included in this study (21295 vs 8954 in surgery and adjuvant radiotherapy group) .The median survivals in the surgery (S) group and adjuvant radiotherapy (S+R) group were 24 and 21 months respectively, The 1, 3, and 5-year overall survival (OS) rates in the S group and S+R group were 68%, 40%, 31% ,and 75%, 30%, 20%, respectively ($p<0.001$).Stratified analysis showed patients with histological classified as adenocarcinoma(15 VS 21, $P<0.0001$), infiltrating duct carcinoma (17 VS 21,$P<0.0001$), adenosquamous carcinoma(10 VS 18,$P<0.0001$) could be benefit from adjuvant radiotherapy. Adjuvant radiotherapy was helpful to improve the OS for patients with pancreatic head (19 VS 21, $P=0.0003$) and duct carcinoma (18VS 28, $P=0.0121$). Subgroup stratified assay indicated specific patients with early stage (AJCC 7th I, II, T2, N0) pancreatic carcinoma had better OS after additional radiotherapy than surgery alone.

Conclusion. Additional radiotherapy may contribute to improved prognosis for patients with pancreatic carcinoma of specific histological types (adenocarcinoma/carcinoma, infiltrating duct carcinoma, adenosquamous carcinoma, and squamous), anatomical location, and advanced stage. A specific subgroup of patients with an early stage (I/II, T2) pancreatic cancer should be considered for additional radiotherapy.

1 Introduction

Pancreatic cancer is the seventh leading cause of cancer-related mortality, with an estimated 458918 of new cases and 432242 of deaths worldwide in 2018.[1] It is predicted that pancreatic cancer will become the third cause of cancer-related death in the future.[2] Unfortunately, a multimodal therapy has not been able to improve pancreatic cancer patients' prognosis. Surgery remains the most important treatment, but only 10–15% of patients are candidates for potentially curative resection, given that most patients would have atypical clinical symptoms and therefore present at the late advanced stage of the disease and not amenable for curative surgery. At present, the 5-year survival rate for pancreatic cancers is poor at less than 20%. Adjuvant radiotherapy and chemotherapy have been shown to improve the survival outcome of patients with pancreatic cancers, while neoadjuvant radiotherapy as well as intraoperative radiotherapy have also contributed to the improved prognosis. However, patient selection of suitability for additional radiotherapy or the optimal timing between the application of radiotherapy and surgery remains unclear.

To investigate the impact of adjuvant radiotherapy in patients after surgical resection for pancreatic cancer, we retrospectively analyzed patients from 18 registered institutions in the Surveillance Epidemiology and End Results (SEER) Medicare linked database. We aimed to determine the characteristics of patients that would benefit from adjuvant radiotherapy, and whether neoadjuvant or adjuvant radiotherapy conferred to a better clinical outcome.

2 Methods And Patients

2.1 Data sources

The SEER*Stat software (version8.3.5) was used to retrieve data from the SEER database containing the SEER 18 registries (November 2018 submission). These registries covered approximately 90% of the US population (based on 201 censuses) from 1973–2016.

2.2 Patients

SEER-Medicare patients diagnosed with pancreatic malignancies with site code C25.0-c25.9, and with the International Classification of Disease for Oncology, Third Edition, (ICD-O-3) histological classification codes of 8000 and 9260 were included in our study. Data on diagnosis confirmation, summary stage, American Joint Committee on Cancer (AJCC) 7th Editor all stage, T, N, M stage, histological grade, primary site surgery, regional lymph node surgery, the sequence of surgery and radiotherapy, radio source, chemotherapy, overall survival in months, and survival status were collected. Meanwhile, patient's basic demographics including age, pancreatic cancer diagnosis, and race were also gathered. Patients were excluded if data on survival or any survival status were not available.

Patients who underwent surgery were compared with patients who received surgery and radiotherapy. To identify the characteristics of patients that would benefit from adjuvant radiotherapy, the association of additional radiotherapy on survival with varying tumor histology, AJCC stage, age, race, primary site, grade, surgery primary site, regional lymph node surgery, and chemotherapy were analyzed. Covariates of interest included patient-related factors (age, gender, race), disease-level factors (primary site, stage, grade, histologic classification), treatment-related factors (surgery methods, radiotherapy, the sequence between surgery and radiotherapy, chemotherapy, diagnosis confirmation).

2.3 Statistics

The Fisher Exact Probability and ANOVA test were used to compare differences between categorical variables and continuous variables, respectively. The Cox proportional hazards regression model was used to determine the effects of variables on OS and to visualize the survival curves, which were adjusted for other significant prognostic factors. All calculations were performed with SPSS version 23.0 for Windows software (IBM Corporation, Chicago, IL) and EmpowerStat software, GraphPad prism 7.0.

3 Results

A total of 243417 patients with pancreatic malignancy were identified from the SEER-Medicare data for the years of 1975–2016. Of these, 7864 patients did not have survival data, and 43722 patients whose survival time was 0 month, thus excluded from our analysis. A total of 115371 patients did not undergo surgery, and in 46211 patients, surgical data were not available, thus these were also eliminated. Lastly, 30249 patients met the inclusion criteria and were included in our study. The selection of patients was shown in Figure s1.

3.1 Baseline characteristics of patients.

Of the 30249 patients included in this study, 21295 were in the surgery group (S group), and 8954 were in the combined surgery and radiotherapy group (S + R group). The demographics of the two groups were shown in Table S1.

Patients in the S group were significantly older and more likely to be female than the S + R group. There were more tumors located at pancreatic body and tail in the S group whereas a higher number of pancreatic head tumors were found in the S + R group. Most histological types of adenocarcinoma, carcinoma, and infiltrating duct carcinoma were identified in the S + R group, while there were more neuroendocrine neoplasms recorded in the S group. Patients with local-stage (AJCC 7th stage I, T0-2, N0, M0) disease underwent local excision (including lymph node biopsy) in the S group and patients in the S + R group were mostly with regional-stage (AJCC 7th stage II, T 3–4, N1) and received regional surgery as well as chemotherapy. There were no significant differences in follow time and histologic grade between the 2 groups. More patients were still alive in the S group at the last follow-up.

3.2 Analysis of survival and risk factor

The overall median survival of all patients was 23 months, with the 1, 3, 5-year survival rate of 49%, 32%, and 25% respectively. The median survivals in the S and S + R group were 24 and 21 months respectively, as demonstrated in Fig. 1a. The 1, 2, 3, and 5-year overall survival (OS) rates in the S group were 68%, 49%, 40%, and 31% respectively, while the 1, 2, 3, 5-year survival rates in the S + R group were 75%, 45%, 30%, and 20% respectively, for which the differences in the two groups were statistically significance ($p < 0.001$), given that the 1-year OS appeared superior in the R + S group whereas the 2,3,5-year OSs were better in the S group, as demonstrated in Fig. 1b.

The univariate and multivariate analysis of the entire cohort showed that factors including age, gender, diagnosis year, primary site, ICD-0-3 classification, summary stage, AJCC 7th stage, T, N, M, surgery primary tumor site (surgery T), surgery regional lymph node (surgery N), additional radiotherapy and chemotherapy were related to OS, as shown in TableS2. Factors such as patients in the R + S group (HR 0.89, 95%CI: 0.86–0.92), additional chemotherapy (HR 0.75, 95%CI: 0.72–0.77), diagnosis year between 1999–2006 (HR 0.88, 95%CI: 0.80–0.98) and 2007–2016 (HR 0.80, 95%CI: 0.72–0.89), pancreatic duct tumor (HR 0.82, 95%CI: 0.73–0.92), neuroendocrine neoplasms (HR 0.16, 95%CI: 0.15–0.18), mesenchymal tumor (HR 0.42, 95%CI: 0.32–0.55), mucinous adenocarcinoma (HR 0.63, 95%CI: 0.59–0.68), carcinoma (HR 0.49, 95%CI: 0.43–0.55), and other histologic type (HR 0.60, 95%CI: 0.56–0.64), and

number of dissected lymph node with 1–3 (HR 0.89, 95%CI: 0.83–0.97), and more than 4 (HR 0.78, 95%CI: 0.73–0.83) were associated with lower risk of mortality. On the other hand, factors as independent predictors of higher mortality were age at 20–44 (HR 5.46, 95%CI: 2.82–10.56), 45–64 (HR 7.46, 95%CI: 3.86–14.39), 65–84 (HR 9.28, 95%CI: 4.81–17.9), ≥ 85 (HR 11.86, 95%CI: 6.11–23.03), tumor overlapping lesion of pancreas (HR 1.1,95%CI: 1.02–1.18), adenosquamous carcinoma and squamous (HR 1.12, 95%CI: 0.99–1.27), regional invasion (HR 2.15, 95%CI: 2.03–2.27), distant involvement (HR 3.66, 95%CI: 3.42–3.91), T2 (HR 1.51, 95%CI: 1.33–1.73), T3 (HR 1.69, 95%CI: 1.47–1.96), T4 (HR 1.60, 95%CI: 1.23–2.09), N1 (HR 1.49, 95%CI: 1.41–1.57) and total pancreatectomy (HR 1.14, 95%CI: 1.08–1.21).

3.3 Stratification analysis by subgroup population

Our analysis showed that the median survival and OS of patients in the S group were better than the S + R group ($p < 0.001$), and additional radiotherapy was a reverse risk factor for prognosis. To investigate the specific patient population that benefited from the radiotherapy, stratified analyses of prognosis in different subgroups were performed. The median survival and OS between the two groups were significantly different in the subcategories, as shown in Table S3. First, the median survivals based on histologic types classified by adenocarcinoma/carcinoma, infiltrating duct carcinoma, adenosquamous carcinoma, and squamous in the S group and S + R group were 15 (95%CI: 15–16) vs 21 (95%CI: 20–21) months ($p < 0.0001$), 17 (95% CI: 16–18) vs 21 (95%CI: 21–22) months ($p < 0.0001$), 10 (95% CI: 9–13) VS 18 (95%CI: 14–26) months ($p < 0.0001$), respectively, as demonstrated in Fig. 2a-2c. Second, patients with the pancreatic head (21 months, 95%CI 21–22) and duct tumor (28 months, 95%CI 25–40) had better survival prognosis in the S + R group, compared with 19 (95%CI 18–19) months ($p = 0.0003$) and 18 (95%CI: 15–24) months ($p < 0.0001$) in the S group, respectively, as shown in Fig. 2d,TableS3.However, patients with pancreatic body/tail tumor (56 months,95%CI 51–61) were not survival benefit from adjuvant radiotherapy (22 months, 95% CI 21–24) ($p < 0.0001$), as seen in Fig. 2e.Last, specific tumor stages demonstrated variable benefits to radiotherapy. Patients with regional invasion were the main beneficiaries, as shown in Fig. 2c. Also, patients staged by AJCC 7th II and III had median survivals of 26 (95%CI: 24–27) and 21 (95%CI: 19–25) months in the S + R group respectively, which were significantly better when compared with 22 (95%CI: 21–22) ($p < 0.0001$) and (95%CI: 13–16) 14 months ($p < 0.0001$) in the S group (Fig. 2g,2h). The median survival of T3, T4, N1 in the S + R and S group were 25 (95%CI: 24–26) vs 20 (95%CI: 19–21) months ($p < 0.0001$), 21 (95%CI: 19–24) vs 13 (95%CI: 12–16) months ($p < 0.0001$), and 24 (95%CI: 22–25) vs 18 (95%CI: 18–19) months ($p < 0.0001$), respectively, as shown in Fig. 2i, 2j, and 2 k. Furthermore, the modality of resection as well as chemotherapy had induced variability in patients benefited from radiotherapy. In this instance, patients who underwent a total pancreatectomy and received radiotherapy had a better survival (20 months, 95%CI: 19–21) than those without (19 months, 95%CI: 18–21) ($p = 0.016$), as shown in Fig. 2f, while the addition of chemotherapy conferred to significantly improved survival at 22 (95%CI: 21–23) vs 21 (95%CI: 20–22) months ($p = 0.002$), as demonstrated in Fig. 2l. On the other hand, there was no difference in the survival in the subset analyses of factors including the number of removed lymph nodes, histologic grade, age, and race, as shown in Table S3.

3.4 Interaction analyses for Subgroups and sub-stratification

The stratified analysis showed that patients with the pancreatic body and tail tumors did not benefit from additional radiotherapy, but the subpopulations with specific histologic behavior, stage, and surgical approaches benefited from additional radiotherapy. Therefore, we next investigated whether the additional radiotherapy to survival benefits in the S + R group would be observed at different primary site combined with other features, as shown in TableS4, In this instance, patients with pancreatic head cancer, regional pancreatectomy (22 months, 95%CI: 21–22 vs 19 months, 95%CI: 18–20, p < 0.0001), and the number of lymph node excision of more than 4 (23 months, 95%CI: 22–24 vs 20 months, 95%CI: 19–21, p < 0.0001) derived survival benefits to additional radiotherapy, as shown in Fig. 3a and 3b. On the other hand, patients with pancreatic body/tail histologic classified by adenocarcinoma/carcinoma (21 months, 95%CI: 19–23 vs 15 months, 95%CI: 14–17, P < 0.0001) and infiltrating duct carcinoma (22 months, 95%CI: 20–26 vs 17 months, 95%CI: 16 − 10, P < 0.0001), T4 stage (24 months, 95%CI: 17–34 vs 12 months, 95% CI: 9–13, P = 0.027), III stage (24 months, 95%CI: 18–34 vs 12 months, 95% CI: 9–18, P = 0.018) were identified as highly selection groups that benefited from additional radiotherapy, as shown in Fig. 3c-3 f. Unexpectedly, patients with staged N1 disease (pancreatic body/tail) had no survival benefit from additional radiotherapy. Moreover, more patients with pancreatic head cancer appeared to have a significantly better survival outcome.

3.5 Interaction analyses of the primary site combined histologic subgroup

To further investigate for factors in patients with pancreatic body and tail malignancies that benefited from additional radiotherapy, the three-factor combination among histologic type, primary site, and other clinicopathologic features were additionally refined. In this sub-stratified evaluation, other tumor sites and histologic behavior were excluded due to small sample size, as well as definitive survival benefits from surgery alone and reverse risk for survival, as shown in TableS2 and TableS4. Except for patients with stage T1 disease and infiltrating duct carcinomas, almost all patients with pancreatic head cancer had an improved survival following additional radiotherapy, as demonstrated in TableS5. Unexpectedly, patients with AJCC 7th stage I disease with adenocarcinoma/carcinoma and infiltrating duct carcinoma in both pancreatic heads (21 months, 95%CI: 20–22 vs 15 months, 95%CI: 15–16, p < 0.0001) and body/tail (21 months, 95%CI: 19–23 vs 15 months, 95%CI: 14–17, p < 0.0001) had improved survival prognosis with additional radiotherapy, as shown Fig. 4a-4d. Similar survival benefit from additional radiotherapy was also observed in patients with stage T2 adenocarcinoma of the pancreatic head (29 months, 95%CI: 22–38 vs 20 months, 95%CI: 17–25, p < 0.05), as shown in Fig. 4e. Almost all patients with pancreatic body/tail adenosquamous carcinoma/squamous had no survival benefit from additional radiotherapy, as shown in TableS5. However, a higher number of patients with pancreatic body/tail cancer of adenocarcinoma/carcinoma in staged T3, N1, additional chemotherapy, and any number of

lymphadenectomies showed better survival when received additional radiotherapy, as seen in TableS5, Fig. 4f-4i. From here, a further sub-stratified analysis was not performed due to the small sample size.

3.6 The sequence of surgery and radiotherapy and survival, radio source

Following the identification of a specific patient population that benefited from the additional radiotherapy in addition to surgery, the next concern involving the sequence between surgery and radiotherapy was addressed, as demonstrated in TableS6. A total of 7664 and 1099 patients received adjuvant and neoadjuvant radiotherapy respectively. The median survival was 21 months (95%CI: 20–22) vs 25 months (95%CI: 23–27), while the 1, 3, and 5-year OSs were 74%, 29%, and 20% vs 81%, 35%, and 20% in the adjuvant and neoadjuvant populations respectively, for which the differences were statistically significant (p = 0.001), as shown in Fig. 5a. There were 76 patients that received radiotherapy both before and after surgery, with the median survival of 26 months (95%CI: 20–32) and the 1, 3, and 5-year OS of 85%, 32%, and 19% respectively, which were significantly better than those having either radiotherapy before or after surgery only (p = 0.002), as shown in Fig. 5b. Last, a small proportion of patients had intraoperative radiotherapy with or without further adjuvant radiotherapy, for which the survival difference between these two subgroups was not statistically significant (p = 0.588), as shown in Fig. 5c.

4 Discussion

Adjuvant chemotherapy or radiotherapy in combination with surgery has been the standard of treatment for pancreatic cancer for decades.[3] External beam radiotherapy is one of the most important treatment as it contributes to better survival.[3–16] In this study, we determined the potential patient population who might be benefited from having additional radiotherapy. Our primary survival analysis indicated that the benefit from additional radiotherapy was critically time-dependent and if extending the time window of more than 24 months, the treatment benefit from extension could be reverse. However, the multivariate analysis showed that additional radiotherapy was an independent prognostic factor for OS (HR 0.89, 95%CI 0.86–0.92, P < 0.0001). Moreover, earlier studies have demonstrated that patients treated with radiotherapy had significantly better survival than those without [7,8,11–21]. The conflicting results we observed might be attributed to the differences in the baseline characteristics of patients as a result of retrospective selection bias. Patients who had received additional radiotherapy were of a poor prognostic group with several high-risk factors, including advanced stage, anatomic site, and unfavorable histologic classification. [22–29] Despite these, our study showed that patients with the above unfavorable features could still benefit from additional radiotherapy.

Pancreatic head has been shown to be the most common anatomical site for cancer followed by the pancreatic body and tail, with the latter displaying poorer survival than pancreatic head lesions.[29] Adenosquamous carcinoma of the pancreas has a higher prevalence in the pancreatic tail and

associated with poor survival.[22] In our study, the sample size of adenosquamous/squamous carcinoma was small and the patients with pancreatic body/tail cancer did not appear to benefit from additional radiotherapy. Patients with pancreatic neuroendocrine cancer have a better life expectancy,[24,25] and resection of the primary tumor is associated with longer survival in stages I–III as well as stage IV tumors.[26] Therefore, representing as the third most common tumor type, patients with pancreatic neuroendocrine cancer in our study had extremely good survival prognosis after surgical resection. A similarly favorable survival outcome was observed in patients with mesenchymal tumors or mucinous adenocarcinoma. In short, patients with pancreatic head cancer or cancer of certain histologic subtypes such as non-adenocarcinoma/carcinoma, non-infiltrating duct carcinoma, or non-adenosquamous carcinoma might benefit from additional radiotherapy.

To date, pancreatic adenocarcinoma/carcinoma and infiltrating duct carcinoma are still the most difficult to treat. Also, small pancreatic cancers have been associated with poorer survival prognosis and an extremely high rate of nodal involvement, for which they should not be regarded as early-stage cancers.[30] Similar findings were observed in our study, in which additional radiotherapy significantly contributed to improving survival in patients with stage I/II adenocarcinoma/carcinoma and infiltrating duct carcinoma located in either pancreatic head or body/tail. However, based on the AJCC 7th classification, stage I /II disease indicates a T1/T2 tumor that is localized within the pancreas. Our data showed that additional radiotherapy for patients with T2 tumors in the pancreatic head or T1 tumors in the pancreatic head or body/tail did not confer to survival benefit, though this observation might be attributed to the small sample size. In the current National Comprehensive Cancer Network (NCCN) guideline (https://www.nccn.org), an early-stage pancreatic carcinoma refers to a resectable tumor. Neoadjuvant therapy can be considered in a clinical trial or with chemotherapy alone, or induction chemotherapy followed by chemotherapy, especially in the presence of high-risk factors. In addition, chemoradiation should not be given to patients after surgery except in clinical trials.[31] Importantly, most clinical trials have been focusing on comparing chemotherapy with or without chemoradiotherapy, and few trials have examined the effectiveness of radiotherapy alone. Our study demonstrated that patients with stage I/II or T2 disease had an improved survival from additional radiotherapy, suggesting that those subpopulation patients especially with high-risk features and did not receive neoadjuvant treatment could be considered for adjuvant radiotherapy. The AJCC 8th stage system was prior to current stage for involved in clear T stage, [32] and future prospective clinical study should be designed to take into account patients with diseases of early stages.

Our study demonstrated that locally advanced (T3/4, N^+) pancreatic adenocarcinoma/carcinoma or infiltrating duct carcinoma had improved survival prognosis following additional radiotherapy, regardless of tumor location. Several studies have found adjuvant treatment after surgery contributed to improved survival in advanced pancreatic cancer.[3, 3–7,11,13,33,34] Other clinical trials have confirmed neoadjuvant treatment was prior to adjuvant treatment,[3,5,8,14,21,35]in fact, most patients preferentially received resection, more than 80% of patients were in the station in current study (Table S6). Surprisingly, our study showed that patients who benefited from radiotherapy were those who received chemotherapy, and

this was in keeping with the results of previous studies which demonstrated that chemoradiotherapy or chemotherapy sequencing with radiotherapy was beneficial for survival improvement. An increased number of lymph nodes dissection has been shown to be a poor prognostic factor for OS,[36] with higher lymph node retrieval associated with a higher proportion of positive invasion. Our study showed that patients with more than four lymph node dissection had a favorable survival when treated with additional radiotherapy. Therefore, radiotherapy can improve cancer survival compared with cancer-directed surgery without radiation in patients with adenocarcinoma of the pancreas.[19] Patients with advanced disease regardless of tumor location should be considered for radiotherapy and chemotherapy.

5 Conclusion

Patients with pancreatic cancer of specific histological types (adenocarcinoma/carcinoma, infiltrating duct carcinoma, adenosquamous carcinoma, and squamous), anatomical location, and advanced stage have poor survival and therefore additional radiotherapy may contribute to an improved survival prognosis. A specific subgroup of patients with an early stage (I/II, T2) pancreatic cancer should be considered for additional radiotherapy. Our findings highlight the positive role of radiotherapy in highly selected patients with pancreatic malignancy, suggesting the need for future prospective randomized control study to confirm these findings before recommending such treatment to patients.

Declarations

Ethics approval and consent to participate

The study had been ethics approved for original institution.

Consent for publication

All authors have read and agreed to the published version of the manuscript.

Availability of data and materials

The original data related to the paper can be provided by the corresponding author

Conflict of Interest:

The authors declare no conflicts of interest

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Yunxiu Luo, data analysis and writing; Shengjun Xiao, review and revising.

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Figures

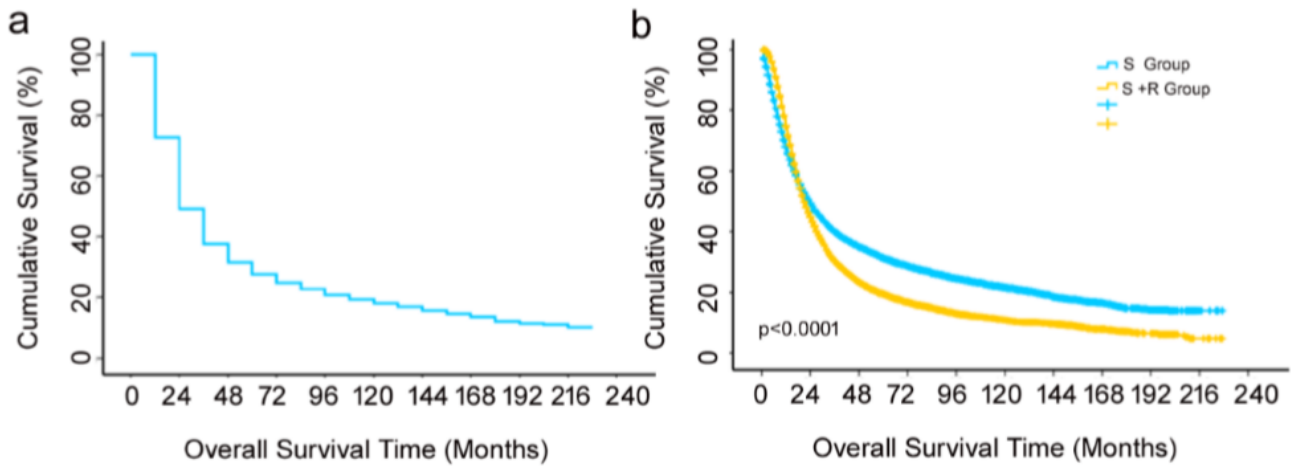

Figure 1

a, cumulative overall survival (OS) curves of all patients with pancreatic cancer; b, OS curves of patients undergoing surgery alone (S) or surgery combined with radiotherapy (S+R). The log-rank test showed that the OS was significantly different between the two groups (P<0.0001).S: surgery, S+R: surgery plus radiotherapy

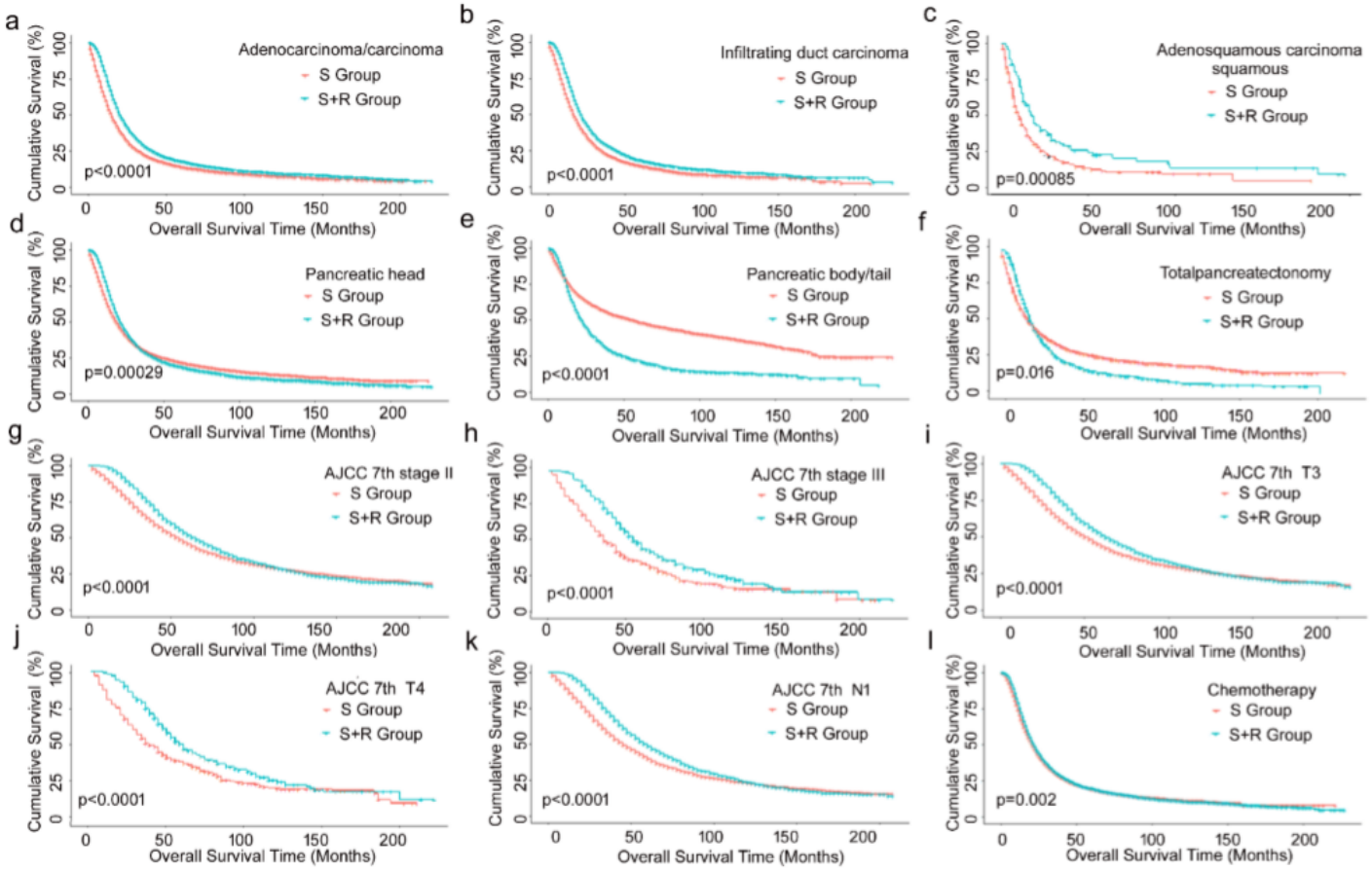

Figure 2

Cumulative overall survival (OS) curves of patients with stratification analysis in surgery alone group and surgery plus radiotherapy group with a log-rank test. a, adenocarcinoma/carcinoma (p<0.0001); b, infiltrating duct carcinoma (p<0.0001); c, adenosquamous carcinoma / squamous (p=0.00085); d, primary site located in pancreatic head (p=0.00029); e, primary site located in pancreatic body/tail (p<0.0001); f, primary tumor with total pancreatectonomy (p=0.016); g, AJCC 7th stage II (p<0.0001); h, AJCC 7th stage III (p= p<0.0001); i, AJCC 7th stage T3 (p<0.0001); j, AJCC 7th stage T4 (p<0.0001); k, AJCC 7th N1 (p<0.0001); l, patients received chemotherapy (p=0.002).

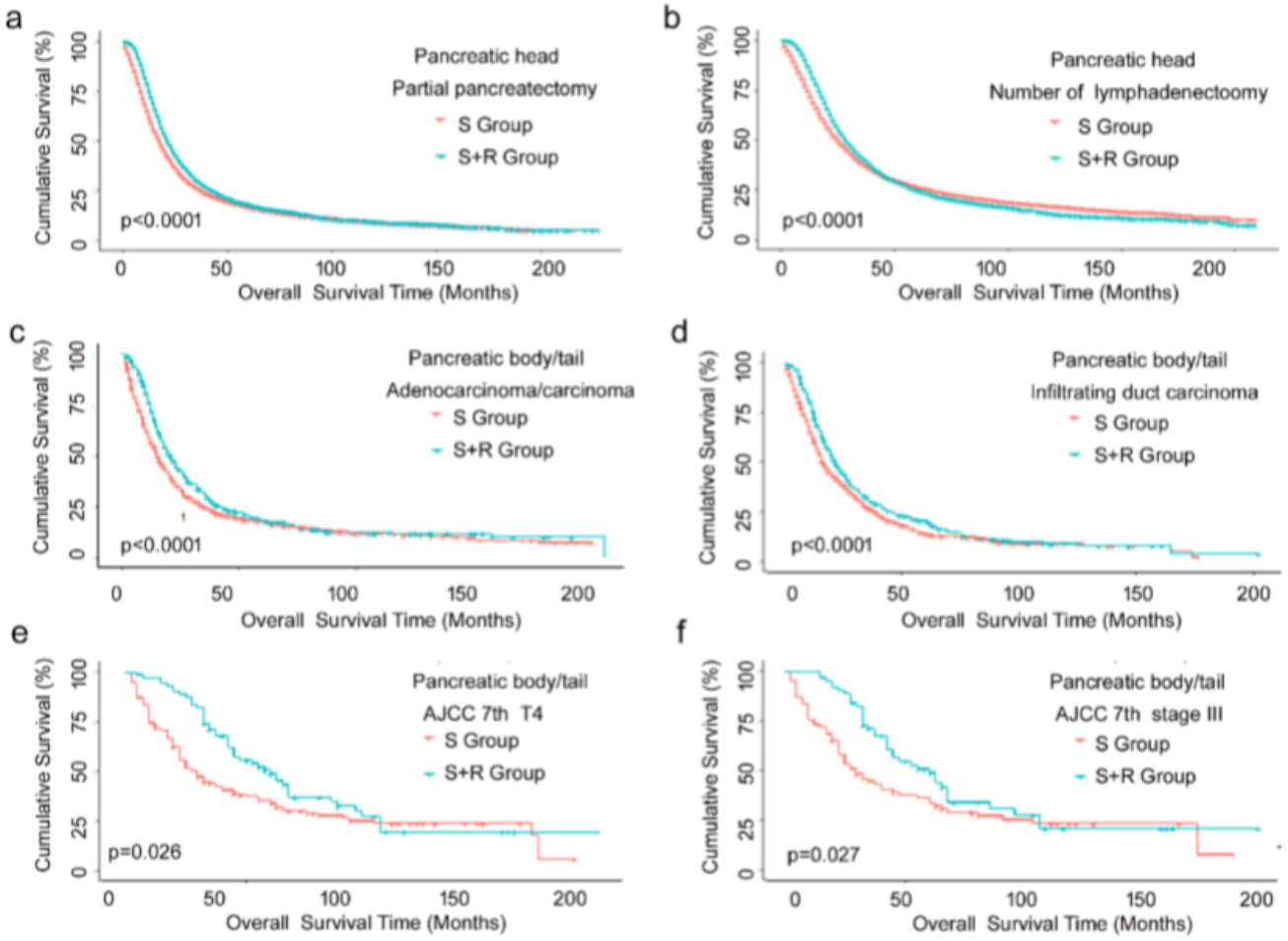

Figure 3

Cumulative overall survival (OS) curves of patients with pancreatic head and body/tail cancer with sub-stratification analysis in surgery alone group and surgery plus radiotherapy group with a log-rank test, which demonstrated a subpopulation of patients that benefited from additional radiotherapy. a, patients with pancreatic head cancer received partial pancreatectomy (p<0.0001); b, patients with pancreatic head cancer dissected more than 4 lymph nodes (p<0.0001); c, patients with pancreatic body/tail adenocarcinoma/carcinoma (p<0.0001); d, patients with pancreatic body/tail infiltrating duct carcinoma (p<0.0001); e, c, patients with pancreatic body/tail cancer staged AJCC 7th T4 (p=0.026); f, c, patients with pancreatic body/tail adenocarcinoma/carcinoma AJCC 7th staged III (p=0.027).

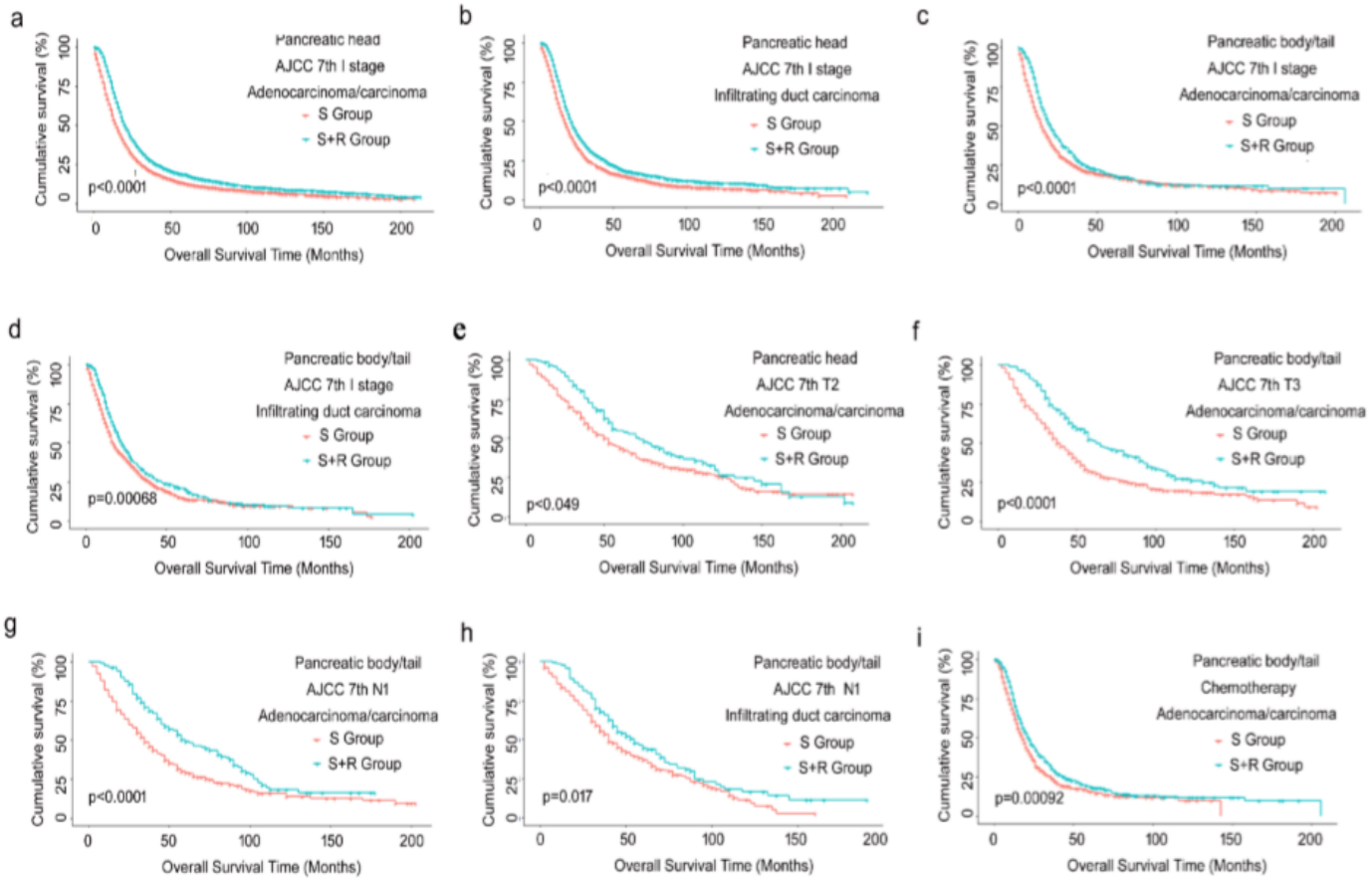

Figure 4

Cumulative overall survival (OS) curves of patients with pancreatic head and body/tail adenocarcinoma/carcinoma or infiltrating duct carcinoma, the sub-stratification analysis in surgery alone group and surgery plus radiotherapy group with a log-rank test, which demonstrated a subpopulation of patients that benefited from additional radiotherapy. a, patients with pancreatic head adenocarcinoma/carcinoma AJCC 7th staged I ($p<0.0001$); b, patients with pancreatic head infiltrating duct carcinoma AJCC 7th staged I ($p<0.0001$); c, patients with pancreatic head adenocarcinoma/carcinoma AJCC 7th staged T2 ($p=0.049$); d, patients with pancreatic body/tail adenocarcinoma/carcinoma AJCC 7th staged I ($p<0.0001$); e, patients with pancreatic body/tail infiltrating duct carcinoma AJCC 7th staged I (p-0.00068)); f, patients with pancreatic body/tail adenocarcinoma/carcinoma AJCC 7th staged T3 ($p<0.0001$); g, patients with pancreatic body/tail adenocarcinoma/carcinoma AJCC 7th staged N1 ($p<0.0001$); h, patients with pancreatic body/tail infiltrating duct carcinoma AJCC 7th staged I ($p<0.0001$); i, patients with pancreatic body/tail adenocarcinoma/carcinoma and received chemotherapy ($p=0.00092$).

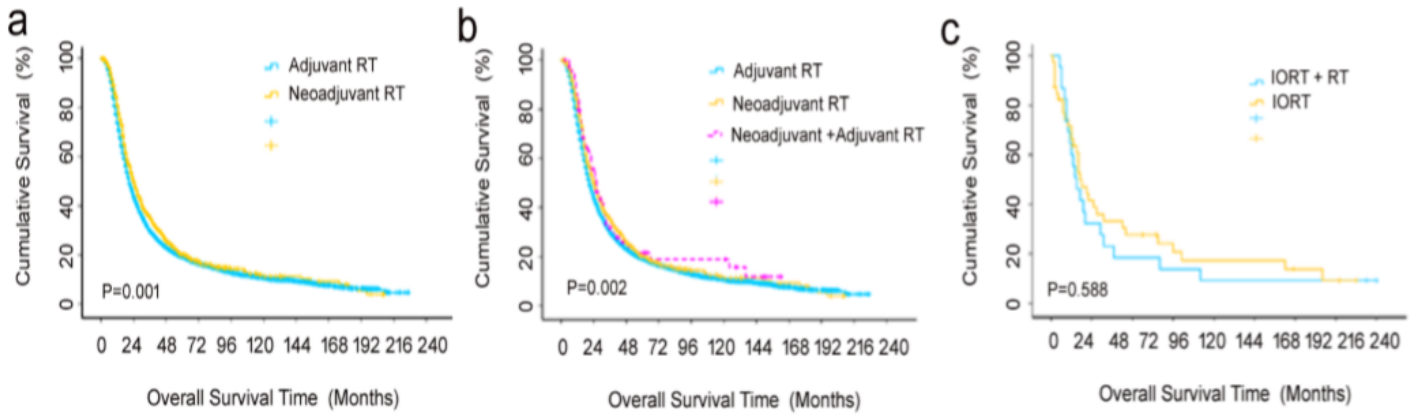

Figure 5

Cumulative overall survival (OS) curves of patients with pancreatic cancer, the sub-stratification analysis of sequence between radiotherapy and surgery with a log-rank test. a, adjuvant and neoadjuvant radiotherapy (p=0.001); b, adjuvant, neoadjuvant, and both; c, intraoperative radiotherapy plus radiotherapy and intraoperative therapy alone (p=0.588).

Supplementary Files

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- SupplementaryTable.xlsx
- figs1.tif