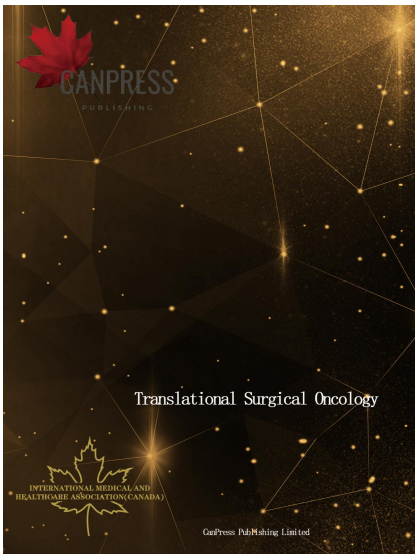
Diagnosis and treatment of pancreatic metastases from renal cancer



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Abstract

Pancreatic metastases from renal cancer represent a rare clinical scenario that poses diagnostic and therapeutic challenges for clinicians. With advances in imaging techniques and the development of new treatment modalities, significant progress has been made in managing this unique patient population. In this review we highlight the latest diagnostic techniques and treatment strategies for pancreatic metastases from renal cancer. The application of Computed Tomography (CT), Magnetic Resonance Imaging (MRI), and Positron Emission Tomography-Computed Tomography (PET-CT) provides powerful tools in the diagnosis of pancreatic metastases from renal cancer, while recent advancements in surgical treatment, targeted therapy, and immunotherapy bring hope for treating this condition. Additionally, we discusses prognostic factors for patients with pancreatic metastases from renal cancer and propose the directions for future studies in the field.

Keywords: Renal cancer, Pancreatic metastases, Diagnosis, Treatment, Prognosis

Introduction

Kidney cancer is a common tumor worldwide, and ranks the 14th in the incidence and the 16th in the mortality among all cancer types. In Asia, new kidney cancer patients account for 34.8% of the global cases, while new deaths represent 38.0% of all kidney cancer deaths worldwide. Regarding the 5-year prevalence, there are 448,321 kidney cancer patients in Asia, making up 32.7% of the global cases[1]. Overall, the 5-year survival rate for kidney cancer is approximately 78%[2]. Pathologically, clear cell carcinoma is the most common type, accounting for 75%-85% of all renal cancers, followed by papillary carcinoma, chromophobe cell carcinoma, eosinophilic cell carcinoma, and collecting duct tumors, as well as molecular classifications of renal cancer[3,4]. Currently, the primary treatments for kidney cancer include surgical intervention, targeted therapy, immunotherapy, and a combination of targeted drugs and immunotherapy. Surgery remains the main treatment approach for kidney cancer. Targeted therapy includes the inhibitors of the mammalian target of rapamycin (mTOR) and the inhibitors targeting angiogenesis, such as sunitinib, pazopanib, sorafenib, and axitinib. Immunotherapy primarily relies on Programmed Death-1 (PD-1) monoclonal antibodies[5]. Although surgical treatment offers a potential cure for the majority of patients, about 7%-30% patients may experience local recurrence within 5 years, and 20%-40% may develop distant metastasis, making a challenge for the treatment of distant metastasis in renal cancer[6].

Distant metastasis of kidney cancer

Among all metastatic sites for kidney cancer, the lungs, bones, liver, and brain are the most common, with the incidence of pancreatic metastasis ranging from 2% to 5%[7-9]. Notably, different pathological types of renal cancer show consistency in the distribution of these common metastatic sites. Specifically, in chromophobe cell carcinoma and papillary carcinoma, the most common metastatic sites are the lungs, bones, liver, and brain[10]. Currently, approximately 7% to 30% of patients treated surgically may experience local recurrence within five years, while 20% to 40% develop distant metastases[11]. In advanced kidney cancer, pancreatic metastases represent a slightly different proportion of kidney

cancers of different pathological types. The proportion of pancreatic metastases in clear cell renal carcinoma is about 5%, whereas it is approximately 1% and 2% for papillary and chromophobe cell carcinoma, respectively[10]. This difference highlights the uniqueness and importance of pancreatic metastasis in the pathological classification of renal cancer.

Surgery is currently the treatment of choice for pancreatic metastases from renal cancer, and the incidence of pancreatic metastases increases progressively over time after surgery on the primary site of renal cancer[10]. Patients with pancreatic metastasis from renal cancer tend to first metastasize to the pancreas and then spread to other organs. Konstantinidis et al.[12]found that in patients with pancreatic metastases from surgically resected renal cell carcinoma, the pancreas was the first site of renal cancer recurrence in 85% of patients, while 5% of patients had renal cancer complicating pancreatic metastases at the time of initial diagnosis.

Among all metastatic sites of kidney cancer, combined pancreatic metastases are usually associated with a favorable prognosis. Grassi et al.[13]analyzed 24 patients with pancreatic metastases from kidney cancer and 330 patients with metastases from other sites of kidney cancer, and found that the median survival time for patients with pancreatic metastases from kidney cancer was 39 months, while the median survival time for patients with combined metastases from other sites of kidney cancer was 23 months. Thus patients with pancreatic metastases from kidney cancer had a significantly better prognosis than patients with metastases from other sites (P=0.0004). Blas et al.[14]reached a similar conclusion through a multicenter retrospective analysis of 23 institutions in Japan, finding that pancreatic metastasis was a protective factor for improved survival in both univariate and multivariate analyses. Shin et al.[15]studied 300 cases of renal cancer metastases in Korea, and patients with combined pancreatic metastases showed a better prognosis. Shaya et al.[16]retrospectively included data from 12 previous phase II and III clinical studies with 235 patients with pancreatic metastases and 4,501 patients with non-pancreatic metastases, and the median survival time of patients with pancreatic metastases was significantly longer (41.7 months vs. 19.0 months). In multivariate analysis, the improvement in survival time in patients with pancreatic metastases remained statistically significant.

Pathogenesis of pancreatic metastases from renal cancer

Pancreatic metastasis in combination with renal cancer is a marker of better prognosis in distant metastases of renal cancer. Cignoli et al.[17]found that patients with pancreatic metastases had better tumor staging and grading, with a lower frequency of tumor necrosis, sarcomatoid features, and lymphovascular invasion in the specimens. Patients with pancreatic metastases from renal cancer also had a lower rate of lymph node metastasis, which may be a contributing factor to their better prognosis. Madkhali et al.[18]analyzed 29 patients with secondary malignancies of the pancreas, and found no lymph node metastases in the renal cancer group, whereas the rate of lymph node positivity was significantly higher in the non-renal cancer group, which could be another reason for the better prognosis of pancreatic metastases from renal cancer. Overall, renal cancer combined with pancreatic metastasis is characterized by lower lymph node metastasis rate and better tumor stage and grading.

Primary renal cancers that developed pancreatic metastasis showed frequent PBRM1 gene mutations, 3p deletion, and 5q amplification, as well as a lower frequency of BAP1 gene mutations and deletions of 9p, 14q, and 4q, which were tumor invasive features[19]. Meanwhile, pancreatic metastases of renal carcinoma showed limited genetic changes relative to primary renal carcinoma, and the tumor cells maintained genetic stability during the metastatic process, showing low activity of effector T cells and strong angiogenic capacity at both the gene expression level and histopathological level. This partly explains the clinical phenomenon that patients with pancreatic metastases from renal cancer have a good prognosis, are sensitive to anti-angiogenic therapy, and are resistant to immunotherapy[20].

There is a certain pancreatic orientation to renal cancer. The proportion of renal cell carcinoma in patients with secondary malignancies of the pancreas often exceeds 50%. Patients with pancreatic metastases from renal cancer tend to develop pancreatic metastases first, followed by extra-pancreatic metastases. By analyzing 1,034 cases reported in the literature between 1952 and 2019, Sellner et al. found that tumor risk factors traditionally thought to be associated with prognosis, such as the number and size of metastases, whether they appeared synchronously with the primary tumor, or the interval between metastatic occurrences, did not directly determine the prognosis for patient survival. Based on this finding, they proposed the seed-soil hypothesis to explain the observation that cancer cells can successfully form metastases only in an adapted organ microenvironment. In particular, in the specialized microenvironment of the pancreas, renal cancer cells are able to complete the entire process of metastasis, whereas in other organs, these cells may be removed or remain dormant. This emphasizes the key role that the pancreatic microenvironment may play in promoting or restricting the survival and proliferation of tumor cells, suggesting a decisive role of the microenvironment in the formation of pancreatic metastases from renal cancer[21,22].

Overall, pancreatic metastases from kidney cancer mark a special case of good prognosis in clinical practice. This may be due to the fact that kidney cancer patients with pancreatic metastases exhibit lower lymph node metastasis rates and superior tumor staging and grading. Studies at the molecular level have revealed that pancreatic metastatic renal cancers have specific genetic changes, such as mutations in the PBRM1 gene and 3p deletion, which reflect the molecular characteristics of renal cancer cells and may influence their invasiveness and metastatic propensity. Such molecular features provide important clues in explaining why renal

cancer cells preferentially metastasize to the pancreas. In addition, the seed-soil hypothesis further explains the ability of renal cancer cells to successfully form metastatic foci in the specialized microenvironment of the pancreas, whereas in the microenvironments of other organs, these cells may not be able to survive or only remain dormant. Currently, studies on the mechanisms of pancreatic metastasis of renal cancer are still in the preliminary stage, and the hypotheses need to be verified by more in-depth studies.

Clinical manifestations of pancreatic metastases from renal cancer

Symptoms of pancreatic metastasis from kidney cancer mainly depend on the size, location, and number of metastases and may be affected by complications such as pancreatitis or biliary obstruction. Generally speaking, most patients with pancreatic metastasis from kidney cancer do not exhibit obvious clinical symptoms in the early stages and usually require imaging tests for diagnosis. It has been found that patients with metastatic symptoms may present with clinical manifestations of jaundice, gastrointestinal bleeding, anemia, abdominal pain, back pain, and weight loss[23-25]. Among these symptoms, jaundice may be associated with compression or invasion of the bile ducts by the metastases; anemia may be related to gastrointestinal bleeding; gastrointestinal bleeding may be due to invasion of the duodenal mucosa by the pancreatic metastases; abdominal and back pain may be related to localized nerve invasion; and weight loss may be associated with tumor-induced malnutrition or deterioration of systemic status. Metastatic pancreatic lesions may present with less abdominal pain and obstructive jaundice than other types of pancreatic disease, such as adenocarcinoma and neuroendocrine tumors[26,27]. Yoon et al.[28]showed that patients with metastasis-related symptoms at the time of diagnosis are usually associated with a poor prognosis. These findings suggest that early diagnosis and treatment of pancreatic metastases from renal cancer are crucial and may help to improve patient survival and prognosis.

Imaging features and diagnosis of pancreatic metastases from renal carcinoma

The diagnosis of pancreatic metastases from renal cancer is a complex and challenging process because it shares clinical, radiological, and cytological characteristics with other pancreatic tumors, particularly pancreatic neuroendocrine tumors. To accurately diagnose renal cancer pancreatic metastasis, a comprehensive use of various diagnostic tools is necessary.

Imaging studies, such as Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), are foundational in the diagnostic process. These methods can reveal the morphological and contrast enhancement characteristics of tumors, with renal cancer pancreatic metastases showing a "fast in, fast out" enhancement pattern[29,30]. Enhanced CT during the arterial phase demonstrates significant enhancement, with density differences exceeding 100 Hounsfield Units (HU), indicating higher contrast agent uptake compared to normal pancreatic tissue[31]. However, imaging characteristics alone may not suffice to distinguish some renal cell carcinomas from neuroendocrine tumor[32].

Endoscopic Ultrasound (EUS) combined with Fine-Needle Aspiration (FNA) or Fine-Needle Biopsy (FNB) offers an effective means of diagnosis, providing tissue samples for cytological and immunohistochemical analysis crucial for differentiating renal cell carcinoma from other pancreatic tumors[33,34]. However, due to the rich vascular supply of renal cancer pancreatic metastatic lesions, the risk of bleeding from the procedure may be higher, thus not necessarily recommended as a routine examination method[29].

Positron Emission Tomography-Computed Tomography (PET-CT) also holds significant value in diagnosing renal cancer pancreatic metastasis. Although the 18F-Fluorodeoxyglucose (18F-FDG) tracer may present a negative response in some cases, the positive reaction with 68Gallium-DOTA-conjugated peptides in these cases reveals the potential complementary effect between different tracers, highlighting the importance of further research into PET-CT tracer selection[35,36].

Pancreatic metastasis from renal cancer can occur up to 32.7 years postoperatively, making long-term imaging follow-up of renal cancer patients post-surgery particularly crucial[37-39]. Combining the patient's history of renal cancer with the features of tumors with rich blood supply as revealed by enhanced CT and MRI plays a critical role in the early diagnosis of renal cancer pancreatic metastasis.

In summary, the diagnosis of renal cancer pancreatic metastasis involves integrating imaging studies, endoscopic ultrasound-guided tissue biopsy, and subsequent cytological and immunohistochemical analysis. This multimodal diagnostic approach helps improve diagnostic accuracy, providing vital information for the clinical management and treatment decision-making for patients.

Therapeutic strategies for pancreatic metastases from renal cancer

The treatment methods for pancreatic metastases from renal cancer have made significant progress, including surgical treatment and pharmacological treatment. Surgical treatment aims to extend the patient's survival and improve the quality of life by removing tumor metastases, while pharmacological treatment primarily relies on targeted drugs and immunotherapy to control the progression and spread of the disease. Although surgical treatment can significantly improve the prognosis for specific patients, pharmacological treatment has shown better efficacy and adaptability for patients in certain cases. Considering the specific characteristics of the disease and the overall condition of the patient, the optimal treatment regimen for patients with pancreatic metastases

from renal cancer may need to be re-evaluated. Currently, the treatment strategy for pancreatic metastases from renal cancer should be based on individual considerations, integrating the latest research results to tailor the most appropriate treatment plan for the patient.

Surgical treatment

In the course of treatment for renal cancer, surgical treatment has always held a central position, and this is also the case for the treatment of pancreatic metastases from renal cancer. Takashi et al.[40]included 6 patients who underwent complete resection of renal cancer metastases and 6 patients with palliative resection of metastases or combined with other site metastases. Patients who underwent complete resection of metastases demonstrated better survival rates, and the difference was significant, making it one of the early studies to prove the effectiveness of surgical resection for treating distant metastases of renal cancer. Sohn[41]performed retrospective analysis of 10 patients who underwent surgical treatment for pancreatic metastases from renal cell carcinoma. The average follow-up time was 30 months, and 8 patients were alive at the final follow-up. Among them, the longest survivor lived for 117 months after the resection surgery, suggesting that an aggressive surgical treatment strategy might be beneficial for patients with pancreatic metastases from renal cell carcinoma.

Faure et al.[42]included 8 patients with pancreatic metastases from renal cancer, with an average survival period of 48 months. At the end of the study, 6 patients were alive and 2 patients died at 13 and 70 months, respectively. Pathological examination showed that all cases were lymph node-negative, also proposing that surgery for pancreatic metastases from renal cancer may not need to involve lymph node dissection. Akatsu et al.[43]included 22 patients with secondary malignant tumors of the pancreas, of which 10 were secondary metastases from renal cell carcinoma. Seven patients underwent surgical treatment, and three did not undergo surgery. The median survival time for all patients was 61 months, with the surgical treatment group having a median survival time of 61 months and the non-surgical treatment group having a median survival time of 20 months. Although there was no statistical difference in survival time between the two groups, the survival time of the surgical treatment group showed a trend of being superior to that of the non-surgical treatment group.

Reddy et al.[44]found that lymph node involvement and vascular invasion were significantly associated with prognosis for renal cell carcinoma patients. Koide[45]included 58 patients, of which only 1 was found to have positive lymph node metastasis, further confirming that routine lymph node dissection may not be necessary for surgery. Tanis et al.[46]conducted a systematic review of previous studies, including 394 patients with pancreatic metastases from renal cancer, of which 321 underwent surgical treatment and 73 underwent non-surgical treatment. Among those who underwent surgical treatment, 231 patients had partial pancreatectomy, and 58 had total pancreatectomy. The 5-year survival rate for patients undergoing partial pancreatectomy was 75%, and for those undergoing total pancreatectomy was 70%. Among the 73 patients who received non-surgical treatment, survival data was provided for 57 patients, with a 5-year survival rate of 14%, indicating that surgical treatment might be more effective than non-surgical treatment for patients with pancreatic metastases from renal cancer. Yazbek et al.[47]included 11 patients, of which 6 underwent standard pancreatic resection and 5 underwent non-standard resection. The median survival time for the standard resection group was 8 years, and for the non-standard resection group was 4.5 years. Although the survival time of the standard resection group appeared to be longer than that of the non-standard resection group, the difference in survival between the two groups was not significant. Santoni et al.[48]]included 103 patients, of which 59 received targeted therapy and 44 underwent surgical treatment. The median survival time for the surgical treatment group was 103 months, while the median survival time for the non-surgical group receiving targeted drug treatment was 86 months. Although the survival time for the surgical group was slightly longer, statistically, there was no significant difference in survival between two groups. Rückert et al.[49]presented an analysis of peri-pancreatic lymph node samples from 21 patients, of which 5 had tumor-positive cells, suggesting the advisability of performing peri-pancreatic lymph node dissection. Zhang et al.[50]conducted a retrospective analysis of 18 patients with pancreatic metastases from renal cancer, including 5 who underwent surgery and 13 who received targeted therapy, and showed that the benefit of surgical treatment may not be significant compared to targeted therapy. Additionally, compared to surgical treatment, targeted therapy may have a more pronounced advantage in patients with late recurrence.

Reviewing the development of surgical treatment for pancreatic metastases from renal cancer, patients with renal cancer accompanied by pancreatic metastases have a better prognosis post-surgery, and patients can achieve long-term survival following surgical treatment. In recent years, with the development of targeted and immunotherapy drugs, there has gradually emerged a viewpoint that surgery may not necessarily offer benefits superior to those of non-surgical treatments, and as the interval between pancreatic metastasis extends, the benefits of targeted therapy may become significant. At present, whether surgery should be performed for pancreatic metastases from renal cancer remains a topic worthy of further discussion, and the indications for surgical treatment still warrant further clarification (Table 1).

Targeted therapies

Targeted therapy blocks tumor growth by targeting key molecular pathways involved in cell growth and angiogenesis. Tyrosine kinase inhibitors (TKIs) are the most commonly used drugs in targeted therapy for kidney cancer. Since their

approval by the FDA in 2006, they have been the standard choice for the first-line treatment of metastatic kidney cancer. Compared with interferon-alpha, sunitinib showed a significant improvement in progression-free survival and objective response rates. A phase III clinical trial by Motzer et al.[51]included equal numbers of patients in the sunitinib treatment group and the interferon-alpha treatment group, with the sunitinib group showing a median progression-free survival of 11 months compared to 5 months in the interferon-alpha group, demonstrating a significant extension in progression-free survival. The objective response rate (including complete and partial responses) was 31% in the sunitinib group compared to 6% in the interferon-alpha group, showing the substantial advantage of sunitinib in treating renal cancer.

Medioni et al.[8]included 15 patients with pancreatic metastases from renal cancer, with a median age of 61 years, among whom, 14 were diagnosed with clear cell carcinoma, and 1 had an unspecified pathological type. All 15 patients received sunitinib treatment, and according to the RECIST criteria, 2 patients achieved Complete Response (CR), 2 achieved Partial Response (PR), and the remaining 10 had Stable Disease (SD), suggesting the potential effectiveness of sunitinib in treating pancreatic metastases from renal cancer.

Gravis et al.[52]conducted a multicenter analysis, including 138 patients with glandular metastases from renal cancer and 421 patients with non-glandular metastases. During treatment, all patients received at least one of the following treatments: Anti-Vascular Endothelial Growth Factor (Anti-VEGF), Tyrosine Kinase Inhibitor - Vascular Endothelial Growth Factor Receptor (TKI-VEGFR), or mammalian Target Of Rapamycin Inhibitor (mTOR inhibitor). The results showed that the median survival for patients with glandular metastases was 61.5 months, significantly longer than the 37.4 months for patients with non-glandular metastases, indicating a survival advantage for patients with glandular metastases from renal cancer. For patients with advanced renal cancer, including glandular metastases, targeted therapy may offer better outcomes.

Chrom et al.[53]included 34 patients with pancreatic metastases from renal cancer and 287 patients with non-pancreatic metastases, all of whom received at least one of the listed drug treatments: Anti-Vascular Endothelial Growth Factor, Tyrosine Kinase Inhibitor - Vascular Endothelial Growth Factor Receptor, or mammalian Target Of Rapamycin Inhibitor. The results showed that the median Overall Survival (OS) for the pancreatic metastasis group was 46.1 months, significantly longer than the 22.5 months for the non-pancreatic metastasis group. However, after adjustment through Inverse Probability of Treatment Weighting (IPTW), the survival difference between the two groups was not significant, indicating that under the background of targeted therapy, patients with pancreatic metastases from renal cancer may have a better prognosis compared to those with non-pancreatic metastases, but this difference may be influenced by other covariates. In summary, compared to patients with non-pancreatic metastases from renal cancer, targeted therapy for pancreatic metastases may offer relatively better efficacy, potentially requiring further clinical research for confirmation, and its specific mechanisms warrant further exploration.

Immunotherapy

Immune checkpoint inhibitors such as nivolumab (Nivolumab) and ipilimumab (Ipilimumab) have shown significant efficacy in treating advanced renal cancer. At the current stage, compared to the use of targeted therapy alone, the combination of targeted therapy and immunotherapy provides patients with greater survival benefits. In the CLEAR trial, a total of 1,417 patients were enrolled, including 355 patients in the lenvatinib plus pembrolizumab group (targeted therapy combined with immunotherapy group) and 357 patients in the sunitinib group. In terms of Progression-Free Survival (PFS), the median follow-up time for the lenvatinib plus pembrolizumab group was 27.8 months, compared to 19.4 months for the sunitinib group. The median PFS for the lenvatinib plus pembrolizumab group was 23.3 months, and for the sunitinib group was 9.2 months. In terms of Overall Survival (OS), although the median survival time for both groups has not been reached, patients using lenvatinib plus pembrolizumab showed an improvement in survival compared to those using sunitinib[54]. Overall, the results of the CLEAR study indicate that, compared to sunitinib, patients treated with lenvatinib plus pembrolizumab show improvements in both PFS and OS.

For patients with pancreatic metastases from renal cancer, the reactivity to immune checkpoint inhibitors (Programmed Cell Death 1(Ligand), PD-(L)1) may be poore[17]. In the aspect of combination therapy within immunotherapy, the combination of targeted therapy and immunotherapy has shown to be more effective than the use of targeted drugs alone in the treatment of advanced renal cancer. Moreover, for patients with pancreatic metastases from renal cancer, studies have confirmed that the combination treatment of anti-PD(L)1 with anti-vascular endothelial growth factor can potentially improve the prognosis of patients with pancreatic metastases[17,55]. Negishi et al.[56]included 68 patients with advanced renal cancer who switched to treatment with immune checkpoint inhibitors (Nivolumab) after receiving one or more types of targeted therapy. The overall response rate (ORR) for the pancreatic site was 33%. In summary, the combination of targeted therapy and immunotherapy may enhance the efficacy for patients with pancreatic metastases from renal cancer. However, the exact role of immunotherapy in this context remains controversial and requires further in-depth studies to clarify the effects and underlying mechanisms of treatment.

Prognostic factors of pancreatic metastases from renal cancer

Volk et al.[62] included 14 patients with pancreatic metastases from renal cancer who underwent surgery, finding differences in survival curves related to tumor size greater than 2.5 cm and the number of pancreatic metastases. Yoon et al.[28] showed that patients with renal cell carcinoma as the primary tumor, without symptoms related to pancreatic metastases, without extrapancreatic involvement, and who received surgical treatment had a better prognosis. Schwarz et al.[58] included 62 surgical patients and found that lymph node metastasis and extrapancreatic metastasis were associated with poorer prognosis. Dong et al.[63]included 7 patients with renal cancer pancreatic metastases and found that asymptomatic metastasis and surgical treatment were important factors for improving survival rates. Ito et al.[25] reported that lymph node metastasis and extrapancreatic metastasis prior to renal cancer pancreatic metastasis could affect the prognosis of patients with renal cancer pancreatic metastases. Blanco-Fernández et al.[64]included 118 Canadian patients and found that the factors affecting renal cancer pancreatic metastases were the type of pancreatic surgery and the interval of metastasis. Shin and colleagues analyzed 300 cases in Korea and found that pancreatic metastasectomy was associated with extended survival in patients with metachronous pancreatic metastases from renal cancer[65].Aa meta-analysis by Hirashita et al.[59]covering 8 studies with a total of 331 patients showed that patients who underwent surgery had a significantly higher 5-year survival rate compared to those who did not undergo surgery. Sellner et al.[21,22]systematically analyzed 1,034 cases of renal cancer pancreatic metastases and found that the size and number of metastatic lesions and the interval of metastasis did not affect overall survival rates.

In summary, potential prognostic factors affecting the long-term survival of patients with pancreatic metastases from renal cancer include the pathological type of the primary tumor, the number, size, and distribution of pancreatic metastatic lesions, the presence or absence of extrapancreatic metastases, symptoms of metastasis, lymph node metastasis, surgical treatment, and targeted drug therapy. However, some studies have found that the impact of these factors is not significant or that there is an interaction between them. Further clarification of prognostic factors of patients with renal cancer pancreatic metastases requires extensive, multicenter studies with larger sample sizes.

Concluding remarks

Pancreatic metastases from renal cancer, as a relatively uncommon form of distant metastasis within renal cancer patients, exhibit unique clinical, radiological, and treatment response characteristics. Although surgical treatment has traditionally been regarded as an effective means to improve patient survival time and quality of life, drug treatment has shown great potential in controlling disease progression and extending patient survival. Particularly, the combined application of targeted therapy and immunotherapy has provided new treatment options for patients with advanced renal cancer, including those with pancreatic metastases. Moreover, the prognosis of patients with renal cancer pancreatic metastases is influenced by multiple factors, including but not limited to the size and number of metastatic lesions, the presence or absence of extrapancreatic metastases, symptoms of metastasis, and lymph node metastasis.

Future studies should further explore molecular mechanisms of renal cancer pancreatic metastases to develop new therapeutic targets and drugs. Additionally, large-scale, multicenter clinical trials are required to verify the effectiveness and safety of different treatment strategies and to personalize treatment plans based on the specific conditions of patients, thereby maximizing treatment effects and improving patient quality of life. Furthermore, the collection of long-term follow-up and survival data for renal cancer pancreatic metastases will help us better understand the natural course of this disease and provide patients with accurate prognostic information. Through multidisciplinary approach, we anticipate to develop effective and safe treatment methods to patients with pancreatic metastases from renal cancer in the near future, and significantly improve their prognosis.

Table.1 Comparison of survival of renal cancer patients with pancreatic metastases by different treatments

Study	Year	Treatment Method	Number of Patients	5-Year Survival Rate	Median Survival (months)	Remarks
Tanis et al.[46]	2009	Surgical Treatment	321	Partial Pancreatectomy: 75% Total Pancreatectomy: 70%	-	-
Santoni et al.[48]	2015	Surgical Treatment	44	-	103	No statistically significant difference in survival time compared to the non-surgical group (P=0.201)
Santoni et al.[48]	2015	Non-Surgical Treatment (Targeted Therapy)	59	-	86	No statistically significant difference in survival time compared to the surgical group
Zhang Zhiyang et al.[50]	2020	Surgical Treatment	5	75%	-	No significant difference in survival rate compared to non-surgical treatment (P=0.952)
Zhang Zhiyang et al.[50]	2020	Non-Surgical Treatment (Targeted Therapy)	13	83%	-	No significant difference in survival rate compared to surgical treatment (P=0.952), indicating potential advantages of targeted drug therapy in patients with late-stage recurrences

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