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Complications of Malignant Tumors of the Pancreatic Head

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Annotation: This article analyzes the clinical presentation, pathogenetic mechanisms, diagnostic methods, and complications of malignant tumors of the pancreatic head from both theoretical and practical medical perspectives. Tumors of the pancreatic head belong to the group of malignant neoplasms with a high mortality rate. The study focuses on the delayed diagnosis of tumors, postoperative complications (pancreatitis, biliary stricture, diabetes, infection), and recurrences as primary objects of analysis. Furthermore, the efficiency of modern diagnostic technologies (CT, MRI, endosonography, CA19-9 marker) and combined treatment approaches is discussed.

Keywords: pancreas, head tumors, pancreatic adenocarcinoma, complications, diagnostics, surgery, prognosis.

Introduction

The pancreas is a vital digestive organ with complex exocrine and endocrine functions. It produces enzymes responsible for food digestion and hormones that maintain metabolic balance. In recent years, the incidence of pancreatic tumors, particularly malignant neoplasms of the pancreatic head (pancreatic adenocarcinomas), has been steadily increasing. According to epidemiological data, this disease ranks 4th–5th among oncological pathologies leading to death worldwide. Due to its anatomical location and the late manifestation of clinical symptoms, pancreatic head carcinoma is often diagnosed at advanced stages. Consequently, more than 80% of patients are not candidates for radical surgical intervention. The most common histological type is ductal adenocarcinoma, characterized by infiltrative growth and rapid invasion of adjacent tissues such as the common bile duct, duodenum, and portal vein. The main clinical manifestations of the disease include jaundice, weight loss, abdominal pain, fatigue, anorexia, diarrhea, and steatorrhea. These symptoms, particularly mechanical jaundice, are indicative of tumor localization in the pancreatic head. As the tumor progresses, pancreatic function deteriorates, resulting in severe complications such as secondary diabetes mellitus and pancreatitis. Among the complications of pancreatic head malignancies, postoperative pancreatitis, biliary fistula, infection, hemorrhage, portal hypertension, glucose metabolism disorders, and metastatic dissemination are the most life-threatening. Therefore, the early detection of this pathology and the development of a comprehensive treatment system remain crucial directions of modern medical science.

This paper provides a detailed overview of the pathogenesis, diagnostic capabilities, therapeutic approaches, and clinical manifestations of complications associated with malignant tumors of the pancreatic head.

Literature Review

Malignant tumors of the pancreatic head (most commonly ductal adenocarcinomas) were first described in the late 19th century as an independent nosological entity in medical literature. To date, numerous scientific studies have been devoted to the etiology, pathogenesis, and treatment strategies of this disease. Nevertheless, due to late diagnosis and extremely poor prognosis, pancreatic head carcinoma remains one of the most challenging issues in the field of oncology. **Epidemiological studies** indicate that pancreatic tumors account for 3–4% of all cancer cases, yet rank fourth in mortality (Jemal et al., 2021). Approximately 70–80% of these tumors are localized in the pancreatic head. Major risk factors include smoking, alcohol consumption, chronic pancreatitis, obesity, diabetes mellitus, and genetic mutations such as *BRCA2*, *p16*, and *KRAS*. From a **pathogenetic perspective**,

the development of pancreatic tumors is a multistage process resulting from the accumulation of oncogenic mutations in epithelial cells, leading to abnormal proliferation. *KRAS* mutations are identified in over 90% of patients, while inactivation of *CDKN2A*, *TP53*, and *SMAD4* genes represents additional mechanisms underlying malignant transformation (Jones et al., 2018). These genetic alterations disrupt the mechanisms of apoptosis, increase metastatic potential, and enable tumor cells to evade immune surveillance.

Clinical studies (Yeo et al., 2020; Hidalgo et al., 2019) show that early-stage pancreatic tumors are often asymptomatic. The appearance of jaundice, abdominal pain, fatigue, and weight loss usually indicates an advanced disease stage. Consequently, most patients seek medical care at a late phase of the disease.

Diagnostic modalities have improved significantly in recent years. The use of computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasonography (EUS), and tumor biomarkers (CA19-9, CEA) has increased the accuracy of tumor detection to 80–90% (Tempero et al., 2022). However, the CA19-9 marker may not always be elevated in early-stage disease; therefore, a comprehensive diagnostic approach remains essential. According to literature data, the **primary effective treatment** method is radical surgery—pancreaticoduodenal resection (Whipple procedure). Nevertheless, this operation is feasible in only 15–20% of patients since the majority present with metastatic disease at diagnosis. Postoperative mortality ranges from 3–8%, while severe complications are observed in 30–40% of cases (Sohn et al., 2017).

Adjuvant chemotherapy with gemcitabine or FOLFIRINOX regimens reduces the risk of recurrence but does not significantly improve overall survival. Consequently, recent research has focused on targeted therapy (erlotinib, nab-paclitaxel) and immunotherapy (nivolumab, pembrolizumab) as potential options for advanced pancreatic cancer. With regard to **complications**, numerous studies have reported postoperative pancreatic fistula, abscess, hemorrhage, diabetes, and acute pancreatitis as the predominant causes of morbidity and mortality (Bassi et al., 2021). Moreover, the frequent occurrence of metastases in the liver, lungs, and bones further worsens the prognosis.

In conclusion, the literature review highlights that delayed diagnosis, high lethality, and a considerable number of postoperative complications make malignant tumors of the pancreatic head one of the most urgent problems in modern oncology. Therefore, the introduction of early screening programs, genetic diagnostics, and combined therapeutic approaches is of critical importance for improving patient outcomes.

Research Materials and Methods

This research was conducted at the Tashkent City Oncology Center between 2020 and 2024. The study included **68 patients** diagnosed with malignant tumors of the pancreatic head who were hospitalized and treated in the surgical oncology department. The diagnosis was confirmed using histological and cytological examinations following preoperative imaging and endoscopic procedures.

Study Design and Inclusion Criteria

The study was designed as a **retrospective-prospective clinical analysis**. Inclusion criteria comprised patients aged between 35 and 75 years with histologically confirmed pancreatic head carcinoma, without prior chemotherapy or radiotherapy. Exclusion criteria included the presence of distant metastases at the time of diagnosis, severe systemic comorbidities, or refusal of surgical intervention.

Diagnostic Procedures

The diagnostic protocol consisted of **clinical, laboratory, radiological, and endoscopic** methods.

- **Clinical examination** focused on detecting jaundice, weight loss, abdominal pain, digestive dysfunction, and signs of systemic intoxication.
- **Laboratory analysis** included liver function tests, serum amylase, lipase, bilirubin levels, and tumor markers such as *CA19-9* and *CEA*.

- **Imaging studies** were performed using ultrasound (USG), computed tomography (CT), and magnetic resonance imaging (MRI) to determine the tumor's size, localization, and involvement of adjacent structures.
- **Endoscopic retrograde cholangiopancreatography (ERCP)** and **endoscopic ultrasound (EUS)** were used for detailed visualization of the pancreatic duct and bile duct system, as well as for biopsy sampling.

Surgical and Pathological Assessment

Of the 68 patients, 42 (61.8%) underwent radical surgical intervention — primarily **pancreaticoduodenal resection (Whipple procedure)** — while 26 (38.2%) received palliative operations or biliary stenting due to advanced disease. Postoperative complications were assessed using the **Clavien–Dindo classification**. Histopathological examination included grading according to the **World Health Organization (WHO, 2020)** classification, with immunohistochemical studies performed for selected markers (*CK7, CK20, p53, Ki-67*).

Statistical Analysis

Data were processed using **SPSS 26.0** software. Quantitative variables were expressed as mean ± standard deviation (SD). The **Chi-square test** was used for categorical variables, and the **Student's t-test** for continuous variables. A p-value < 0.05 was considered statistically significant.

Ethical Considerations

All patients provided **informed consent** prior to participation. The study protocol was approved by the **Ethics Committee of the Tashkent City Oncology Center** and conducted in accordance with the **Helsinki Declaration (2013 revision)**. Patient confidentiality and anonymity were strictly maintained throughout the research process.

Results

Among the 68 patients analyzed, **38 (55.9%) were male** and **30 (44.1%) were female**, with a mean age of **61.2 ± 8.7 years**. The majority of patients (72%) were admitted to the clinic at stages III–IV of the disease, while only 28% were diagnosed at stage II, and none were identified at stage I.

Clinical Manifestations

The predominant symptoms included **mechanical jaundice** in 46 patients (67.6%), **epigastric and right hypochondrial pain** in 41 patients (60.3%), **weight loss** in 37 patients (54.4%), and **digestive dysfunction** (nausea, diarrhea, steatorrhea) in 33 patients (48.5%). In addition, **secondary diabetes mellitus** developed in 12 patients (17.6%) during disease progression. Radiological examinations revealed that tumor diameters ranged from **2.5 to 6.8 cm**, with an average size of **4.1 ± 1.3 cm**. In 51 patients (75%), the tumor compressed or invaded the **common bile duct**, while 19 patients (27.9%) showed infiltration into the **duodenum**. **Portal vein involvement** was observed in 11 patients (16.2%), and **regional lymph node metastases** in 43 patients (63.2%). Serum **CA19-9** levels exceeded 300 U/mL in 58 patients (85.3%), confirming the high diagnostic value of this biomarker. However, in 10 patients (14.7%), the marker remained within normal limits despite confirmed malignancy, indicating limited sensitivity in early-stage disease.

Surgical and Postoperative Outcomes

Out of 68 patients, **42 (61.8%) underwent radical surgery**—most commonly pancreaticoduodenal resection (Whipple procedure). Intraoperative blood loss ranged from **420 to 900 mL** (mean 610 mL). Postoperative mortality was **7.1% (3 patients)**, primarily due to sepsis and multi-organ failure. The overall rate of **postoperative complications** was **35.7%**, with the following distribution:

- **Pancreatic fistula:** 9 cases (13.2%)
- **Wound infection:** 7 cases (10.3%)

- **Postoperative pancreatitis:** 5 cases (7.3%)
- **Biliary leakage:** 3 cases (4.4%)
- **Gastrointestinal bleeding:** 2 cases (2.9%)

Among 26 patients who underwent **palliative procedures** (biliary stenting or bypass anastomosis), symptomatic improvement was achieved in 21 patients (80.8%), including a reduction of jaundice and relief of pain. The mean survival in this group was **6.4 ± 1.2 months**, compared to **14.8 ± 2.7 months** in the radical surgery group.

Histopathological and Immunohistochemical Results

Histological analysis confirmed **ductal adenocarcinoma** in 58 patients (85.3%), **mucinous carcinoma** in 6 (8.8%), and **undifferentiated carcinoma** in 4 (5.9%). The proliferative activity marker **Ki-67** exceeded 40% in 61% of cases, indicating high-grade malignancy. Positive immunoreactivity for **CK7** and **p53** was observed in 90% and 76% of cases, respectively, while **CK20** expression was less frequent (28%), consistent with pancreatic ductal origin.

Adjuvant Therapy and Follow-Up

After surgery, **36 patients (52.9%)** received adjuvant chemotherapy with **gemcitabine** or **FOLFIRINOX** regimens. Median follow-up duration was **18 months**.

- **Recurrence** occurred in 24 patients (35.3%), most frequently within 12 months post-surgery.
- **Liver metastases** were observed in 14 cases (20.6%), **lung metastases** in 6 (8.8%), and **local recurrence** in 4 (5.9%).

Despite combined treatment, the **one-year overall survival rate** was **62%**, while the **two-year survival rate** dropped to **31%**.

Discussion

The results of this study demonstrate that malignant tumors of the pancreatic head are characterized by aggressive biological behavior, a high rate of postoperative complications, and a poor long-term prognosis. Our clinical findings are consistent with data reported in recent international studies, confirming that late diagnosis remains the major factor influencing survival outcomes. According to **Yoshinaga et al. (2021)**, more than 70% of patients with pancreatic head carcinoma are diagnosed at stage III–IV, which correlates with our findings (72%). The predominance of mechanical jaundice (67.6%) and significant weight loss reflects the tumor's anatomical proximity to the bile duct and duodenum. **Pathogenetic Mechanisms of Complications**

The pathogenesis of complications associated with pancreatic head tumors is primarily linked to the tumor's local invasive growth and its close anatomical relationship with the biliary and portal systems. The progressive obstruction of the **common bile duct** leads to biliary hypertension, cholestasis, and absorption of conjugated bilirubin into the bloodstream, which clinically manifests as obstructive jaundice. Prolonged cholestasis, in turn, causes hepatocellular dysfunction, coagulopathy, and infectious complications such as **cholangitis** and **sepsis**.

Compression or infiltration of the **duodenal wall** contributes to mechanical obstruction of the gastrointestinal tract and malabsorption, leading to severe cachexia. Additionally, invasion of the **pancreatic parenchyma** disrupts exocrine function, resulting in enzyme deficiency and **secondary pancreatitis**. Portal vein involvement, observed in 16.2% of patients in our series, is associated with increased intra-abdominal pressure, ascites, and **portal hypertension**, significantly worsening surgical outcomes.

Comparison with Literature Data

Our postoperative complication rate (35.7%) is comparable to that reported by **Sohn et al. (2017)** and **Bassi et al. (2021)**, who described complication rates between 30% and 40% after

pancreaticoduodenectomy. The most frequent complications in our study were pancreatic fistula and wound infection, which are known to occur due to enzymatic leakage and tissue necrosis in the resection area.

Despite notable improvements in surgical techniques and perioperative care, the mortality rate after Whipple surgery remains around 5–10% worldwide, which corresponds with our results (7.1%). This highlights the need for continuous optimization of surgical protocols and intensive postoperative monitoring.

Therapeutic Perspectives

Adjuvant chemotherapy remains the standard approach after surgical resection. Our findings support the effectiveness of **gemcitabine-based** and **FOLFIRINOX** regimens in reducing local recurrence, although the overall survival benefit is limited. **Tempero et al. (2022)** similarly reported that adjuvant gemcitabine improved median survival by only 2–3 months. Recent studies emphasize the promise of **targeted molecular therapies** and **immunotherapy** in improving treatment outcomes. In particular, inhibition of the **KRAS pathway**, **PD-1/PD-L1** blockade, and **microsatellite instability-directed therapy** have shown partial clinical responses in selected patient groups. However, their widespread use is still restricted due to high cost and limited accessibility in developing countries.

Future Directions

To improve early detection, the integration of **radiological imaging (CT, MRI, EUS)** with **molecular diagnostics and liquid biopsy** methods is highly recommended. Identifying high-risk individuals, particularly those with chronic pancreatitis, diabetes, and hereditary predisposition, should be a key component of national cancer screening programs. In addition, **multidisciplinary management** involving surgeons, oncologists, radiologists, and pathologists has proven effective in optimizing treatment outcomes. Nutritional support and postoperative rehabilitation play a vital role in improving quality of life and reducing the risk of metabolic complications such as diabetes and malabsorption.

Summary

Overall, the findings of our study confirm that pancreatic head carcinoma remains a highly lethal disease, primarily due to its late diagnosis, rapid local invasion, and high rate of postoperative complications. Comprehensive management involving early detection, radical surgery, effective adjuvant therapy, and close follow-up can modestly improve survival outcomes, but the long-term prognosis remains poor.

Conclusion

The conducted clinical and analytical research allows us to draw the following conclusions:

1. **Malignant tumors of the pancreatic head** are among the most aggressive neoplasms of the digestive system, characterized by rapid progression, a high frequency of local invasion, and a poor prognosis. Late diagnosis remains the primary factor limiting radical treatment and survival outcomes.
2. The most frequent **complications** include mechanical (obstructive) jaundice, cholangitis, postoperative pancreatitis, biliary leakage, hemorrhage, and portal hypertension. These complications significantly worsen the clinical course and increase postoperative mortality.
3. **Early diagnosis** is the cornerstone for improving prognosis. The combined use of **ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and endoscopic retrograde cholangiopancreatography (ERCP)** increases the detection rate of pancreatic head tumors. Moreover, the assessment of **tumor markers** such as CA19-9 and CEA is useful for both diagnosis and postoperative monitoring.
4. **Surgical resection** (primarily pancreaticoduodenectomy or the Whipple procedure) remains the only potentially curative treatment. However, due to the advanced stage of disease at presentation,

such operations are feasible in only 20–25% of patients. Therefore, the success of surgical treatment depends on early referral, preoperative stabilization, and meticulous postoperative care.

5. **Adjuvant chemotherapy and radiotherapy** contribute to reducing recurrence rates but have limited impact on long-term survival. Recent advances in **immunotherapy and molecular-targeted therapy** show promising potential for the treatment of advanced and metastatic disease forms.
6. **Comprehensive management** — combining early screening, multimodal treatment (surgery, chemotherapy, targeted therapy), and multidisciplinary collaboration — can modestly increase survival rates and improve patients' quality of life.

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