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RESEARCH ARTICLE

# Surgical and Palliative Treatment of Pancreatic Adenocarcinoma in the Yemeni Conflict: A Retrospective Cohort Study

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## Abstract

**Introduction:** Pancreatic cancer is a highly aggressive malignancy with poor survival rates. In Yemen, prolonged war and economic blockade have acted as major additional stressors within a multi-hit aetiological framework, accelerating disease progression and straining healthcare delivery. The Whipple procedure can be curative but is associated with high postoperative morbidity, requiring modern surgical innovations to succeed in resource-limited settings. This study aimed to assess the realities and outcomes of managing pancreatic adenocarcinoma in this complex humanitarian crisis. **Materials and Methods:** A retrospective, multi-centre cohort study was conducted across five tertiary hospitals in Sana'a, Yemen. All consecutive patients with pancreatic adenocarcinoma who underwent surgery or dedicated palliative intervention from March 2015 to February 2025 were included. Demographic, diagnostic, and treatment data, as well as 30-day outcomes, were analysed. **Results:** Of 487 records screened, 224 patients (mean age 55.4±10.2 years; 80.4% male) were included. Major risk factors were smoking (84.8%) and qat chewing (70.5%). Most patients presented with obstructive jaundice (90.2%). Definitive surgery was performed for 100 patients (44.6%), including 89 pancreatoduodenectomies using a Blumgart-style anastomosis. The clinically relevant postoperative pancreatic fistula rate was 2.2% (2/89). Palliative management was offered to 124 patients (55.4%) with advanced disease. Overall 30-day mortality was 10.3%. Mortality was significantly higher among patients aged ≥70 years (27.8% vs. 8.7%, p=0.020) and those requiring vascular resection during Whipple (33.3% vs. 15.0%, p=0.040). **Conclusion:** Radical pancreatic resection with careful technique is feasible in a conflict setting and is associated with a reasonable anastomotic leak rate. However, late-stage presentations are common due to the combined effects of conflict-driven systemic stress and localised carcinogens. Stricter patient selection and improved perioperative care are essential, as demonstrated by the significant fatality rates in older patients and those undergoing vascular resection.

**Keywords:** Pancreatic Cancer- Pancreaticoduodenectomy- Blumgart Anastomosis- Conflict Medicine- Global Surgery

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## Introduction

Pancreatic adenocarcinoma is a major and increasing global health concern, ranking as the second most common gastrointestinal cancer and a leading cause of cancer-related deaths [1, 2]. The global incidence is approximately 8 to 10 cases per 100,000 people, with 510,922 new cases and 467,409 deaths reported in 2022. Projections indicate a 95% increase by 2050 [3]. The disease is strongly associated with older age, with most diagnoses occurring after the age of 65 [4]. Key risk factors include tobacco use, chronic diabetes, pancreatitis, unhealthy dietary habits, and genetic predisposition, reflecting its multifactorial origins [5-7].

Clinically, pancreatic cancer often progresses slowly, with vague early symptoms that result in frequent diagnoses at advanced stages [8]. Common presenting features include painless obstructive jaundice, significant

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weight loss, and abdominal pain [9]. For diagnosis, serum biomarkers such as CA19-9 and CEA assist in monitoring disease progression. Advanced imaging techniques, including computed tomography (CT), magnetic resonance imaging (MRI), and endoscopic ultrasound (EUS), are essential for staging and assessing surgical resectability [10].

Despite advances in diagnostic techniques, only 15 to 20% of patients present with the disease at a stage amenable to potentially curative surgery [11]. Pancreatoduodenectomy, or the Whipple procedure, remains the main option for curative treatment [5]. However, it carries significant risks, including complications such as pancreatic fistula, delayed gastric emptying, and bleeding [12-15]. Consequently, much surgical research focuses on refining techniques and reconstruction methods to improve safety and outcomes. One modification involves the use of a duct-to-mucosa Blumgart-style anastomosis, which aims to reduce the risk of clinically relevant pancreatic fistula [16, 17].

The Republic of Yemen presents a uniquely challenging environment for cancer care. For nearly a decade, the country has endured intense armed conflict and an economic blockade, severely weakening its healthcare system [18]. In this context, the causes and progression of pancreatic cancer can be understood as a multi-hit process. Primary factors, such as heavy tobacco use and regional qat chewing, combine with additional stresses from poor nutrition, environmental instability, and delayed access to specialised diagnostics. These systemic issues contribute to aggressive clinical presentations and complicate the delivery of complex surgical care [19].

This study aimed to assess the realities and outcomes of managing pancreatic cancer in this complex humanitarian crisis. We systematically examined the clinical presentation, diagnostic processes, and treatment options – both radical and palliative – for patients treated at several tertiary centres in Sana'a, Yemen. We focused particularly on assessing the feasibility and safety of performing complex oncological surgery, such as pancreatoduodenectomy, using meticulous techniques despite significant resource limitations. By documenting this experience, we aim to provide a detailed perspective on surgical oncology in conflict zones, highlighting the enduring potential for curative intervention and the critical importance of effective palliative care strategies.

## Materials and Methods

*Ethical Approval and Study Design*

This study adhered to the ethical principles of the Declaration of Helsinki. Approval was obtained from the Institutional Review Board (Ethics Committee) of the 21 September University for Medical and Applied Sciences. The study was a multicentre, retrospective cohort project assessing the clinical presentation, management pathways, and outcomes of pancreatic adenocarcinoma in Yemen. It employed a multi-hit framework to explore how systemic conflict-related stressors act as additional factors alongside primary oncological issues. Given the retrospective design and use of anonymized patient data, the requirement for individual informed consent was waived.

*Study Setting and Period*

The study was conducted in five major tertiary referral hospitals in Sana'a, Yemen: Yemen-German Hospital, European Modern Hospital, Azal Hospital, Al-Thawra Modern General Hospital, and the University of Science and Technology Hospital. The study period extended from March 2015 to February 2025, encompassing a decade of healthcare delivery during ongoing armed conflict and an economic blockade.

*Study Population and Selection Criteria*

The study included all adult patients (≥18 years) with a confirmed histopathological or clear clinical-radiological diagnosis of pancreatic adenocarcinoma who attended the participating centres and received a therapeutic intervention. Patients were included if they underwent surgical exploration with curative intent or received a dedicated palliative procedure. We excluded patients with other pancreatic tumours, those managed with best supportive care only, and cases with insufficient medical records. A total of 487 patient records were screened; 263 were excluded, resulting in a final cohort of 224 patients.

*Data Collection and Variables*

Data were extracted from archived medical records and surgical registries using a standardised data collection form. Two trained research assistants performed the initial data extraction, and the principal investigator verified the data for accuracy. We collected variables including patient demographics, clinical presentation, risk factor history (smoking, qat chewing), diagnostic findings, treatment details, and postoperative outcomes.

*Diagnostic and Staging Protocol*

For all patients, contrast-enhanced multiphase computed tomography (CT) of the abdomen and pelvis was the primary tool for tumour staging and assessing surgical feasibility. Endoscopic ultrasound and routine preoperative biopsy were unavailable in the country during the study period. A serum CA19-9 level above 37 U/mL was considered elevated. We selectively performed preoperative biliary drainage via Endoscopic Retrograde Cholangiopancreatography (ERCP) with stenting for patients with severe obstructive jaundice (total bilirubin above 200 μmol/L) or cholangitis.

*Surgical and Palliative Techniques*

For resectable disease, we performed a standard pancreatoduodenectomy (Whipple procedure). Pancreatico-enteric reconstruction was carried out using a modified duct-to-mucosa Blumgart-style pancreatojejunostomy. In selected cases, we used an "artery-first" approach for early vascular assessment. For unresectable disease, palliative management included endoscopic biliary stenting, open surgical triple bypass, or percutaneous transhepatic biliary drainage (PTD) for high-risk patients.

*Outcome Measures and Statistical Analysis*

The main outcome measures were the rate of major postoperative complications and 30-day or in-hospital mortality. We defined and graded complications using international consensus criteria (ISGPS, Clavien-Dindo). Categorical variables are reported as frequencies and percentages, and continuous variables are reported as mean with standard deviation or median with interquartile range. We used the Chi-square or Fisher's exact test for comparative analyses. We estimated survival probabilities using the Kaplan-Meier method and the log-rank test. A two-sided p-value of less than 0.05 was considered statistically significant, and all p-values are presented as exact values. All analyses were conducted using SPSS software (version 25.0, IBM Corp).

## Results

*Clinical Presentation and Patient Demographics*

There were 224 pancreatic cancer patients in the final analytic cohort. Eighteen patients (8.0%) were older than 70, with a mean age of 55.4 years (range 30 to 80). There was a male predominance (80.4%, n = 180). The Taiz region accounted for the majority of patients (67.0%, n = 150). A history of smoking (84.8%, n = 190) and chewing qat (70.5%, n = 158) were identified as modifiable risk factors. Obstructive jaundice with pruritus (90.2%, n = 202) and significant weight loss (70.1%, n = 157) were the most common presenting symptoms (Table 1).

*Diagnostic Staging and Tumour Characteristics*

All patients underwent contrast-enhanced computed tomography (CT) as their primary staging modality. Serum CA 19-9 levels were elevated (>37 U/mL) in 150 patients (75.0%) out of 200 (89.3%). The tumours were distributed as follows: pancreatic head (53.6%, n = 120), periampullary area (24.1%, n = 54), and body or tail (22.3%, n = 50) (Table 2).

*Management Pathways*

One hundred patients (44.6%) underwent definitive surgical resection. Of these, 89 received pancreatoduodenectomy (Whipple procedure), while 11 underwent distal pancreatectomy. The remaining

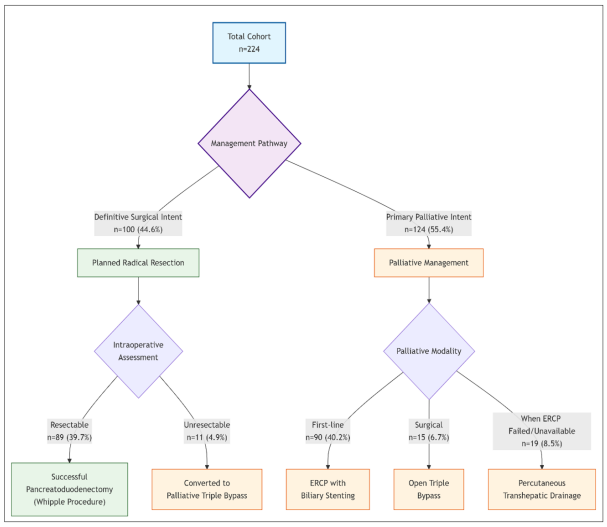



Figure 1. Patient Flow Diagram. CONSORT-style diagram illustrating the screening, eligibility, and management pathways. Of 487 records screened, 224 patients met inclusion criteria. The cohort was stratified into definitive surgical management (n=100, with 89 Whipple procedures) and primary palliative management (n=124, via stenting, bypass, or percutaneous drainage).

124 patients (55.4%) underwent primary palliative care with endoscopic stenting (n = 90), open triple bypass (n = 15), or percutaneous transhepatic drainage (n = 19). Figure 1 shows the patient management protocol, and Table 3 details the distribution of interventions.

*Surgical Results and Specific Complications*

All 89 Whipple procedures were reconstructed with a Blumgart-style duct-to-mucosa pancreatojejunostomy. Two patients (2.2%) developed a clinically significant postoperative pancreatic fistula (CR-POPF, ISGPS Grade B). One was successfully treated with ultrasound-guided percutaneous drainage, while the other required surgical exploration and anastomotic reinforcement. The "artery-first" approach was used on four occasions. The postoperative results are summarised in Table 4.

*Overall Morbidity and Mortality*

The overall 30-day or in-hospital mortality rate was 10.3% (23/224). Patients aged ≥70 years had a substantially

Table 1. Baseline Demographic and Clinical Characteristics (N=224).

| Characteristic | Category | n (%) |
|---|---|---|
| Sex | Male | 180 (80.4) |
| | Female | 44 (19.6) |
| Age (years) | Mean ± SD | 55.4 ± 10.2 |
| | >70 years | 18 (8.0) |
| Region of Origin | Taiz | 150 (67.0) |
| | Other Governorates | 74 (33.0) |
| Risk Factors | Smoking History | 190 (84.8) |
| | Qat Chewing History | 158 (70.5) |
| Presenting Symptoms | Obstructive Jaundice & Pruritus | 202 (90.2) |
| | Significant Weight Loss (>10%) | 157 (70.1) |

SD: Standard Deviation.

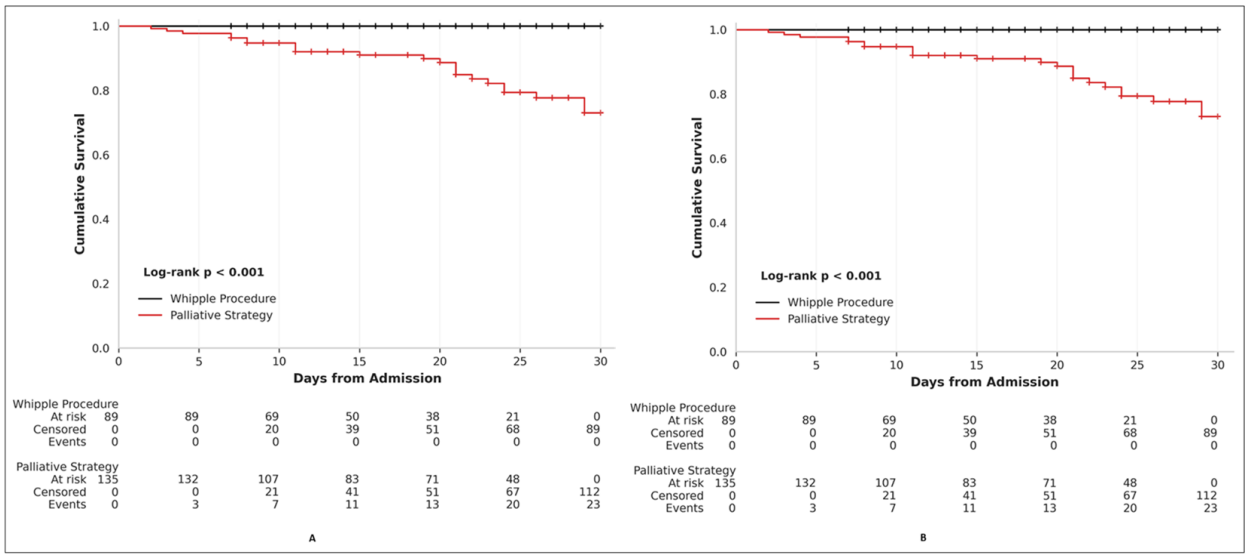



Figure 2. Kaplan-Meier Survival Curves for 30-Day Survival. (A) Age stratification (<70 vs. ≥70 years). (B) Management strategy (Definitive surgery vs. Palliative care). Log-rank p-values are shown. Shaded areas represent 95% confidence intervals.

Table 2. Diagnostic Modality Performance and Tumor Location.

| Parameter | Result |
|---|---|
| CT Scan Sensitivity (Resectability) | 85--90%* |
| Elevated Serum CA 19-9 (>37 U/mL) | 150/200 (75.0%) |
| Tumor Location | n (%) |
| Pancreatic Head | 120 (53.6) |
| Periampullary | 54 (24.1) |
| Body/Tail | 50 (22.3) |

*Sensitivity for determining resectability, based on institutional surgical-pathological correlation. CT: Computed Tomography.

higher mortality rate (27.8%, 5/18) than those under 70 years (8.7%, 18/206; p = 0.020, Fisher's exact test) (Figures 2A and B). Among Whipple patients, mortality was 33.3% (3/9) for those requiring vascular resection, compared with 15.0% (12/80) for those who did not (p=0.040). Two early deaths resulted from haemorrhagic complications following portal vein resection. Detailed mortality analysis is presented in Table 5.

## Discussion

This study provides a critical examination of pancreatic cancer management within Yemen's severely strained healthcare system. Rather than viewing the prolonged conflict solely as a logistical barrier to healthcare delivery, our findings are best interpreted within a multi-hit cancer aetiology paradigm. In this context, initial genetic or toxicological insults act as initiating events, while the persistent chronic stressors of a war-torn environment serve as significant adjuvant factors that accelerate tumour growth and worsen clinical manifestations. Our findings indicate that, despite these complicating factors, radical surgical resection remains feasible when performed with rigorous technique.

The epidemiological profile of our sample reveals a distinct landscape characterised by a marked male predominance (80.4%, with a male-to-female ratio of 4.1:1) and a high prevalence of modifiable risk factors, consistent with global and regional trends [2, 5, 20]. Smoking (84.8%) and khat chewing (70.5%) are the predominant initial "hits" in our patient population. While tobacco is a known carcinogen [21], the widespread cultural use of khat necessitates urgent molecular research. Previous research has linked khat chewing to upper digestive tract cancers across the region [22-24]. When these primary carcinogenic insults are combined with conflict-related secondary adjuvant factors such as severe nutritional deficits, chronic psychological stress, and exposure to environmental toxins (as indicated by the Taiz region's 67.0% concentration of cases), the result is an aggressive disease trajectory. This multi-hit scenario

Table 3. Management Pathways (N=224).

| Management Strategy | Procedure | n (% of Cohort) |
|---|---|---|
| Definitive Surgical Intent | Planned Resection | 100 (44.6) |
| | Whipple Procedure | 89 (39.7) |
| | Distal Pancreatectomy | 11 (4.9) |
| Primary Palliative Intent | ERCP with Stenting | 90 (40.2) |
| | Open Triple Bypass | 15 (6.7) |
| | Percutaneous Drainage | 19 (8.5) |

ERCP: Endoscopic Retrograde Cholangiopancreatography.

Table 4. Postoperative Complications for Whipple Procedures (n=89).

| Complication | ISGPS/Clavien-Dindo Criteria | n (%) | Notes / Management |
|---|---|---|---|
| CR-POPF | Grade B | 2 (2.2) | 1: Percutaneous drainage; 1: Surgical revision |
| Major Complication | Clavien-Dindo ≥IIIa | 15 (16.9) | ** |
| 30-Day Mortality | ** | 15 (16.9)** | ** |
| - With Vascular Resection | ** | 3/9 (33.3) | p=0.04 (vs. 12/80, 15.0%) |

CR-POPF: Clinically Relevant Postoperative Pancreatic Fistula; ISGPS: International Study Group on Pancreatic Surgery.

Table 5. Analysis of 30-Day Mortality (N=224).

| Variable | Category | Mortality, n/N (%) | p-value |
|---|---|---|---|
| Overall Cohort | -- | 23/224 (10.3) | -- |
| Age Group | <70 years | 18/206 (8.7) | 0.02* |
| | ≥70 years | 5/18 (27.8) | |
| Vascular Resection (Whipple only) | Yes | 3/9 (33.3) | 0.04* |
| | No | 12/80 (15.0) | |

*Fisher's exact test.

explains the overwhelmingly late-stage presentation of our patients, with 90.2% presenting with obstructive jaundice and 70.1% with significant weight loss.

Surgical indications in our centres closely followed the NCCN criteria for physically resectable disease [25]. Pancreatoduodenectomy was performed for pancreatic head tumours that did not involve the superior mesenteric artery, while distal pancreatectomy was used for isolated body or tail lesions. Selective vascular reconstruction was undertaken for limited portal or superior mesenteric vein involvement, allowing for margin-negative (R0) resection [26]. This assertive yet selective approach balanced oncological radicality with significant surgical risks. Patients who required vascular resection had a significantly higher mortality rate (33.3%) than those who did not (15.0%, p=0.040), indicating that the feasibility of R0 resection should be prioritised over invasive arterial intervention in a setting lacking effective postoperative rescue therapy.

The Whipple technique continues to encounter significant challenges, including pancreatic anastomotic leaks [27, 28]. Our documented clinically relevant postoperative pancreatic fistula (CR-POPF) rate of 2.2% with a Blumgart-style reconstruction requires careful interpretation. While this suggests the technical effectiveness of a standardised anastomotic approach, systematic evaluations indicate that the true burden of complications in low-resource settings is likely underestimated due to fragmented patient follow-up and diagnostic difficulties [12, 14, 29, 30]. Our group had an overall serious morbidity rate (Clavien-Dindo ≥ IIIa) of 16.9%. This figure accurately illustrates the initial postoperative challenges in a setting where malnutrition and limited recovery protocols place additional strain on physiological healing. Our findings are consistent with regional surgical profiles, such as those reported by Omara et al. [5] and El Nakeeb et al. [31], which detail a broad spectrum of postoperative morbidity.

Thirty-day mortality following pancreaticoduodenectomy is a reliable indicator of surgical outcomes, with benchmarks varying significantly by context [15]. Our observed 30-day mortality rate of 10.3% is at the upper end of rates reported in other low- and middle-income countries [13, 32, 33]. Multivariable analysis showed that vascular resection and advanced age (≥70 years) were independent predictors of early mortality. The mortality rate among older patients was substantially higher (27.8%) than in younger cohorts (8.7%, p=0.020). This aligns with large-scale studies where advanced age remained a significant independent predictor of mortality [34]. These universal risk factors are amplified by the realities of conflict, in which patients are frequently recommended for surgery due to a complete lack of alternative oncological treatments, such as accessible chemotherapy or advanced biliary stenting.

*Study limitations*

Our study is limited by its retrospective design and the inherent constraints of the setting, such as the absence of endoscopic ultrasound for accurate staging and inconsistent access to adjuvant medications, which preclude long-term survival analyses. Nonetheless, the cases described here demonstrate that radical surgery serves a specific and critical role.

In conclusion, our study showed that, with rigorous surgical technique, radical resection for pancreatic cancer can be performed safely in a resource-limited, conflict-affected area. The significant prevalence of late-stage disease, resulting from a combination of regional carcinogens and conflict-related systemic stresses, highlights the urgent need for early detection. The high mortality rate among elderly patients and those requiring complex vascular resection underscores the importance of careful patient selection. Improving outcomes in Yemen requires a dual approach: increasing surgical capacity for patients with resectable disease and establishing comprehensive palliative care networks for the majority with advanced malignancy.

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*Author Contributions*

Conceptualization, manuscript drafting, critical revision, and supervision: Ahmed Ateic, Tofik Almekhlafi, Ali Almassaudi, Faris Alhajami. Data acquisition, analysis, and interpretation: Faisal Ahmed, Qasem Alyhari, Saif Ghabisha, Saleh Alwageeh. All authors reviewed and approved the final manuscript for submission.

*Ethics Statement*

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was granted by the Ethics Committee of the 21 September University for Medical and Applied Sciences (Meeting #202, 19 March 2025). The requirement for individual informed consent was waived due to the retrospective design of the study.

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*Conflicts of Interest*

The authors declare no conflicts of interest.

*Data Availability*

The data that support the findings of this study are not publicly available due to ethical and privacy restrictions but may be made available from the corresponding author upon reasonable request and with permission from the local ethics committee.

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