



Insights into Duodenal Adenocarcinoma: Clinical Presentation, Survival Outcomes, and Treatment Trends—A Long-Term Follow-Up Study

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Abstract

Introduction Duodenal adenocarcinoma (DA) is a rare and aggressive malignancy, representing less than 0.5% of all gastrointestinal cancers. It constitutes a significant portion (55.7%) of small bowel adenocarcinomas, most of which arise in the second part of the duodenum, followed by the third and fourth parts. Despite its rarity, DA presents substantial challenges in diagnosis and treatment due to its aggressive nature and often insidious onset.

Objectives The aim of the study is to investigate the clinical presentation, prognostic factors, survival outcomes, and treatment strategies in DA, with a focus on surgical and adjuvant therapeutic interventions. Additionally, the study aims to elucidate patterns of recurrence and identify areas for future research to optimize therapeutic approaches and enhance patient care.

Materials and Methods This retrospective observational study (2015–2023) analyzed patients aged 18 to 90 years with DA. Data from case sheets, laboratory investigations, and medication charts were reviewed. This study aims to explain demographic characteristics, clinical presentations, treatment trends, and survival outcomes to improve therapeutic strategies and patient care in DA patients, excluding other gastrointestinal cancers

Results The study examined 10 cases of DA diagnosed between 2015 and 2023. The patient cohort had an equal gender distribution, with ages ranging from 53 to 83 years. Chief presenting symptoms included abdominal pain (90%) and vomiting (50%). Tumor markers were elevated in 40% of patients. Tumor locations predominantly included the D2 region. Three patients underwent Whipple's surgery and three received chemotherapy with curative intent.

Conclusion The study highlights the challenges associated with DA, including its rare incidence, clinical presentations, and variable treatment outcomes. Surgical interventions such as the Whipple procedure and adjuvant chemotherapy show promise in

Keywords

- ▶ duodenal adenocarcinoma
- ▶ gastrointestinal malignancies
- ▶ small bowel cancer

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improving survival rates. Further studies with larger cohorts are essential to better understand the disease, refine therapeutic strategies formulate separate guidelines for DA, and enhance patient outcomes.

Clinical trial registry number: N/A.

Introduction

Small bowel cancers (SBCs) are rare, constituting just 2% of all gastrointestinal cancers. The ileum is the primary site of malignancy, followed by the duodenum and the jejunum. Adenocarcinoma is the most common type of duodenal cancer, while the majority of ileal tumors have neuroendocrine origins. In total, 55.7% of small bowel adenocarcinomas are located in the duodenum. Duodenal adenocarcinoma (DA) is a rare and aggressive malignancy, constituting a small fraction of periampullary adenocarcinomas and gastrointestinal cancers. The majority arise in the second part of the duodenum, followed by the third and fourth parts. Incidence rate accounts for less than 0.5% of all gastrointestinal malignancies. DA poses challenges in diagnosis and treatment. Surgical intervention, often necessitating pancreaticoduodenectomy for tumors in the proximal duodenum and segmental duodenal resection for distal tumors, offers a curative option for many patients, with 5-year survival rates ranging from 45 to 71%. However, prognostic factors such as extent of tumor spread are still combative, complicating treatment decisions. Notably, lymph node metastasis significantly influences outcomes, although other determinants remain less clear.¹⁻⁹

Adjuvant therapy's efficacy and patterns of recurrence post-resection are poorly understood, further highlighting the need for comprehensive studies. The CAPOX (capecitabine and oxaliplatin) regimen is used in both curative and palliative settings for DA, with four to six cycles being common. Its mechanism combining the DNA cross-linking effects of oxaliplatin with the tumor-specific action of capecitabine makes it effective in systemic disease management. Additionally, CAPOX's oral administration of capecitabine offers convenience, improving patient compliance compared with infusional regimens like FOLFOX.¹⁰ Early-stage DA may present insidiously, with symptoms including nausea, abdominal pain, constipation, and digestive disruptions. Risk factors, including advanced age, genetic predisposition, dietary habits, tobacco use, alcohol consumption, and concurrent gastrointestinal conditions, contribute to its etiology. Multinodal treatment approaches involving surgery, chemotherapy, and radiation therapy are tailored based on disease staging and individual patient characteristics. Understanding the intricate nature of duodenal cancer is essential for refining therapeutic strategies and improving patient outcomes in this challenging clinical context.¹¹⁻¹³

Materials and Methods

Study Design and Participants

It is a retrospective, observational study conducted at Father Muller Medical College Hospital, Mangalore. The study

included patients aged 18 to 90 years who had a confirmed diagnosis of DA and were admitted to the hospital from the year 2015 to 2023. Patients of duodenal cancers other than adenocarcinoma were excluded.

Ethical approval to conduct the research and publish the findings was obtained from the Institutional Ethics Committee (IRB number: FMIEC/CCM/348/2024; date of approval: May 15, 2024). A waiver of consent was granted by the institutional review board for this study, considering the retrospective nature of the data collection and analysis.

Sample Collection

Data were gathered from the hospital's wards, including detailed case sheets, comprehensive laboratory investigations, and medication charts. A review of medical records using a structured data collection form designed to capture essential details such as patient demographics, clinical presentations, specific treatment employed, and subsequent follow-up outcomes was used.

Inclusion and Exclusion Criteria

Inclusion Criteria

- Patients aged 18 to 90 years.
- Both male and female genders.
- Patients with a confirmed diagnosis of DA who were admitted to either the inpatient or outpatient departments of the hospital. (*This study specifically targets individuals with DA from the year 2015 to 2024.*)

Exclusion Criteria

- Pregnant and lactating women.
- Patients diagnosed with other types of gastrointestinal cancers, including stomach (gastric) cancer, liver cancer (hepatocellular carcinoma), intestinal cancer (such as colorectal cancer), pancreatic cancer (pancreatic adenocarcinoma), and ampullary adenocarcinoma, were excluded from this study.

Primary and Secondary Outcome

Primary Outcome

- To analyze the demographic characteristics and their clinical presentation.
- To analyze survival outcomes.

Secondary Outcome

- To study the treatment trends.

Statistical Analysis

Data were analyzed using SPSS software. Demographic characteristics, clinical presentations, prognostic factors, and treatment types were descriptively summarized. Differences in clinical outcomes and survival rates were assessed using the Kaplan–Meier survival analysis.

Ethical Approval

All procedures performed in studies involving human participants were conducted in accordance with the ethical standards of the Father Muller Institutional Ethics Committee (FMIEC) of Father Muller Research Centre, Mangalore, Karnataka, India. This study also complies with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards (IRB approval number: FMIEC/CCM/348/2024; date of approval: May 15, 2024).

Results

A cohort of 10 patients with DA were identified. Among the cohort of 10 patients, gender distribution was equal, with 5 males and 5 females. The age range spanned from 53 to 83 years, with six patients falling between 50 and 60 years and the remaining four patients older than 70 years. All individuals adhered to a mixed dietary pattern comprising both vegetarian and nonvegetarian diets (► **Table 1**).

Clinical Characteristics and Laboratory Investigations

The prevalent chief complaints noted upon admission included abdominal pain, which manifested in nine instances, often described as persistent, gradually increasing in severity. Vomiting was documented in five cases, with reports of multiple episodes, sometimes nonbilious. Three cases had jaundice and one case had chronic constipation.

Tumor markers were noted to be elevated in 4 of 10 patients (40%), with cases exhibiting elevated levels of either carcinoembryonic antigen (CEA) greater than 3 ng/mL (4 of 10 patients) or carbohydrate antigen 19–9 (CA 19–9) greater than 37 U/mL (4 of 10 patients).

Table 1 Demographic and clinical characteristics of patients with duodenal adenocarcinoma (DA)

Characteristic	Value	
DA, <i>n</i>	10	
Age (y), median (range)	63 (53–83)	
Gender	Male	5 (50%)
	Female	5 (50%)
Dietary pattern	Vegetarian diet	0
	Mixed diet	10 (100%)
Clinical symptoms	Abdominal pain	9 (90%)
	Vomiting	5 (50%)
	Jaundice	3 (30%)
	Constipation	1 (10%)

Location of Tumor

The frequency of tumor locations was as follows: 3 in the D2 region, 3 in the D1–D2 junction, 1 in D3, and 1 case in the D2–D3 junction. The location was not distinguishable in two cases.

Tumor Staging and Grading]: Nonmetastatic versus Metastatic

The tumor staging data indicated that six cases were identified as metastatic (M1) and four cases were nonmetastatic (M0; ► **Table 2**).

Treatment: Surgery

Surgeries performed included Whipple's procedure with pancreaticoduodenectomy (*n* = 3), open palliative gastrojejunostomy (*n* = 2), and triple bypass surgery (*n* = 1). The remaining patients were not amenable to surgery.

Chemotherapy

The intent of chemotherapy differed based on the treatment goals, ranging from curative (*n* = 3) to palliative (*n* = 1). Chemotherapeutic regimens for (adjuvant) curative intent included CAPOX (oxaliplatin and capecitabine; *n* = 1), carboplatin with gemcitabine (*n* = 1), and single-agent capecitabine (*n* = 1). The chemotherapy regimen for palliative intent included CAPOX (*n* = 1). The number of chemotherapy cycles ranged from four to six cycles.

Survival Rates: Metastatic and Nonmetastatic

The data on survival rates for patients with DA between metastatic and nonmetastatic cases were calculated. Metastatic patients had a median survival time of 5 months. Nonmetastatic patients exhibited a longer mean survival time of 18.3 months, although with a wide confidence interval (0–42 months), reflecting high variability in survival. However, the median survival time for nonmetastatic patients is 6 months, with a confidence interval of 0 to 14 months. These statistics highlight the generally poorer prognosis for metastatic patients and the substantial variability in survival times among nonmetastatic patients.

Discussion

Among the array of symptoms reported, weight loss, abdominal pain, anemia, and jaundice emerge as the most prevalent clinical presentations. However, due to the heterogeneous nature of symptomatology, determining a definitive

Table 2 Tumor characteristics

Tumor staging	Nonmetastatic	Metastatic
Cases	4	6
Details	T3N0M0 (<i>n</i> = 3)	T3N0M1 (<i>n</i> = 3)
	T2N0M0 (<i>n</i> = 1)	T3N1M1 (<i>n</i> = 1)
		T2N0M1 (<i>n</i> = 2)

Abbreviations: M, metastasis; N, nodes; T, tumor.

diagnostic framework remains challenging. Complicating matters, the available literature primarily consists of small personal series or retrospective multicentered studies spanning several decades, highlighting the difficulty in obtaining robust data for meaningful analysis. This scarcity of comprehensive data impedes the establishment of standardized treatment protocols. Consequently, clinicians often face the dilemma of navigating treatment decisions based on limited evidence.^{1,11} Early studies often categorized DA alongside other periampullary tumors, thereby complicating management discussions. The etiological factors contributing to DA remain indefinable, with associations noted with dietary patterns, alcohol, tobacco use, and certain genetic syndromes like familial adenomatous polyposis (FAP) and Gardner's syndrome. However, the majority of cases do not have identifiable causative agents.^{1,2,11,14}

DA presents a complex landscape of treatment options, with surgical interventions serving as the cornerstone of management. Alongside the well-established Whipple's procedure, alternative surgical approaches such as endoscopic resection, partial (wedge) resection, and segmental (limited) resection are typically recommended for select DAs without the risk of lymph node metastasis.^{10,15}

Based on the study done by Ecker et al, radiation treatment (CRT) did not demonstrate a significant survival advantage over chemotherapy alone across most patient subgroups. While CRT did not lead to worse outcomes, it also did not yield a notable improvement in overall survival compared with chemotherapy alone.¹⁶ In a study by Kelsey et al,⁶ adding chemotherapy and radiation (CT-RT) to surgery did not significantly improve overall survival, disease-free survival, or local control when compared with surgery alone. Clinical outcomes were similar between patients who had a Whipple procedure and those who had a segmental resection, with no significant differences in survival or local control. For patients who had an R0 resection, the 5-year overall survival rate was 64%, disease-free survival was 61%, and local control was 70%. These patients had significantly better 5-year overall survival compared with those who had R1/R2 resections. In patients with R0 resection, there was a trend toward better survival with adjuvant CT-RT (83 vs. 53%, $p=0.07$), but the difference was not statistically significant.^{6,17} Furthermore, it is crucial to note that while major surgical procedures used for DA share similarities in postoperative complications with other periampullary cancers like postoperative pancreatic fistula and delayed gastric emptying, proper management of these complications is vital for enhancing recovery and preserving quality of life.¹⁸

Because DA is so rare, there is limited evidence to recommend the best possible therapy based on outcome. Whipple's surgery is still the sole effective treatment option for DA that produces comparable results. In a study done by Meijer et al, approximately 71% of patients who underwent either pancreaticoduodenectomy or segmental resection had a significantly better survival rates (46% 5-year survival) compared with those who had palliative treatment (1% survival). The study also indicates that there is no survival benefit with neoadjuvant chemotherapy.⁵

The role of chemotherapy and the ideal regime in patients with DA in both curative and palliative setting is limited, from patients receiving unspecified chemotherapy regimens to the absence of prospective, randomized evidence.¹⁹ Although chemotherapy may improve overall survival in patients with advanced DA compared with no chemotherapy, there is not enough information to determine the significance of chemotherapy in palliative care.^{5,19,20}

Conclusion

The study highlights the complexities and challenges associated with DA, emphasizing its rarity, diverse clinical presentations, and variable treatment outcomes. Surgical interventions, particularly Whipple's procedure, combined with adjuvant chemotherapy, show the best management and survival in patients with DA.

Consent

A waiver of consent was granted by the Father Muller Institutional Ethics Committee (FMIEC) of Father Muller Research Centre (IRB approval number: FMIEC/CCM/348/2024; date of approval: May 15, 2024).

Authors' Contributions

J.F.J. contributed to concepts, design, definition of intellectual content, literature search, clinical studies, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, manuscript review. S.R.C. contributed to concepts, design, literature search, clinical studies, data analysis, manuscript preparation, manuscript editing, manuscript review. N.S. contributed to concepts, design, definition of intellectual content, literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, manuscript review. D.S. contributed to concepts, design, manuscript preparation, manuscript review.

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Conflict of Interest

None declared.

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