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Clinical Profile of Dropout Patients with Borderline Resectable Pancreatic Ductal Adenocarcinoma after Neoadjuvant Chemotherapy: A Retrospective Study

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Research Article

Keywords: Borderline resectable pancreatic cancer, neoadjuvant chemotherapy, ECOG performance status, dropout, prehabilitation

Posted Date: June 8th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9658806/v1

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Additional Declarations: No competing interests reported.

Abstract

Background

The recent definition of borderline resectable pancreatic ductal adenocarcinoma (BRPDAC) incorporates anatomical, biological and conditional dimensions. These complex entities demonstrate variable responses to neoadjuvant chemotherapy (NACT). While some patients achieve R0 resection, others drop out due to declining Eastern Cooperative Oncology Group (ECOG) performance status, disease progression, or treatment-related complications. This study aims to characterize the clinical profile of BRPDAC patients who despite having technical resectability (anatomic or biologic criteria), dropout due to declining performance status (conditional criteria) during NACT, focusing on those who might have benefited from upfront surgery.

Methods

A retrospective chart review was conducted at Kathmandu Medical College from 2016 to 2025, analyzing 49 patients with BRPDAC who underwent NACT. Data on demographics, tumor biology, chemotherapy regimens, post NACT ECOG status, and treatment outcomes were evaluated.

Results

Among 49 patients, 19 (38.7%) underwent pancreaticoduodenectomy. Among the remaining 30 patients, 14 exhibited poor tumor biology evidenced by rising Ca 19 – 9, radiological progression or development of distant metastases. Eight patients had incomplete data, with treatment discontinuation attributed to refusal of surgery or chemotherapy due to financial constraints or dissatisfaction with prognosis. Among the remaining eight patients, who had all fulilled the venous criteria for BRPDAC, one died due to chemotherapy toxicity in the setting of significant comorbidities while seven deteriorated to ECOG > 2 despite being technically resectable. Their demographic profile included median age of 60 years, 5 males and 3 females, comorbidities (diabetes: 4, hypertension: 3, cardiovascular disease: 1), and NACT regimens (FOLFIRINOX: 6, gemcitabine-based: 2).

Conclusions

A critical subgroup of BRPDAC dropout patients who see a decline in performance status during NACT may benefit from upfront surgery. Molecular based biomarkers may guide individualized treatment strategy in such patients and preoperative prehabilitation might mitigate functional decline, thus lowering the surgical dropout rate. However, further studies are warranted to refine treatment algorithms and address barriers to care.

Background

Pancreatic ductal adenocarcinoma (PDAC) remains one of the most lethal malignancies, with a 5-year survival rate of approximately 13%.[1] Borderline resectable PDAC (BRPDAC) is defined according to three distinct dimensions by the consensus from the 20th meeting of the International Association of Pancreatology (IAP): anatomical, biological and conditional.[2] Neoadjuvant chemotherapy (NACT) is increasingly utilized to

downstage tumors, improve R0 resection rates, and address micrometastatic disease.[3] Regimens such as FOLFIRINOX and gemcitabine-based therapies have shown promise in improving resectability, particularly for BRPDAC.[4] However, a significant proportion of patients fail to complete NACT due to disease progression, declining performance status or treatment toxicity.[5] The Eastern Cooperative Oncology Group (ECOG) performance status is a critical determinant of treatment tolerance and surgical candidacy.[6] Patients with BRPDAC (anatomical or biological criteria) who drop out of NACT due to detorioration in performance status (conditional criteria) despite being technically resectable represent a unique subgroup where upfront surgery might have been feasible. This study aims to characterize the clinical profile of these dropout patients at Kathmandu Medical College from 2016 to 2025, with a focus on those meeting venous criteria for BRPDAC, to identify factors contributing to treatment discontinuation and inform future management strategies.

Materials and Methods

A retrospective data review was conducted at the Department of Surgery, Kathmandu Medical College, Nepal, from January 2016 to December 2025. The study included 49 patients diagnosed with BRPDAC based on National Comprehensive Cancer Network (NCCN) criteria. BRPDAC was defined by arterial [superior mesenteric artery (SMA) with tumor contact ≤ 180^0 or common hepatic artery (CHA) with tumor contact without extension to celiac artery (CA) or hepatic artery bifurcation] and venous involvement [superior mesenteric vein (SMV) or portal vein(PV) with tumor contact > 180° or tumor contact ≤ 180^0 with counter irregularity of the vein or thrombosis of the vein but suitable for reconstruction].[7] Data were extracted from hospital records, including demographics: age, sex, and comorbidities (e.g., diabetes, hypertension, cardiovascular disease), tumor characteristics: CA19-9 levels, radiological findings (contrast-enhanced computed tomography [CECT]), and presence of metastases, treatment details: NACT regimens (FOLFIRINOX or gemcitabine-based), cycles completed, and reasons for dropout; outcomes: ECOG performance status (after NACT), surgical resection status (R0, R1, or no surgery), and mortality. Patients with histologically confirmed BRPDAC who initiated NACT were included. The choice of neoadjuvant regimen was based on the physician's discretion. Descriptive statistics were used to analyze demographic and clinical characteristics. Continuous variables were reported as medians with ranges, and categorical variable as frequencies and percentages.

Results

Of the 49 BRPDAC patients who underwent NACT, 34 met venous criteria, 9 met arterial criteria and 6 met both arterial and venous criteria. 19 (38.7%) patients underwent resection with pancreaticoduodenectomy (PD), indicating a favorable response to NACT. A total of 8 patients (16.4%) had incomplete data and dropped out of the treatment pathway due to refusal of surgery (n = 3), refusal of chemotherapy after initial cycles (n = 2), financial constraints (n = 2), or dissatisfaction with prognosis (n = 1). Among the remaining 22 patients, 14 (28.6%) exhibited poor tumor biology—evidenced by rising CA19-9 levels, radiological progression on CECT, or development of distant metastases—which rendered them ineligible for surgery. The subgroup of remaining eight patients (16.3%), all of whom had fulfilled the venous criteria for BRPDAC, was the primary focus of this study. Their demographic profile included median age of 60 years (range: 48–75), five males and three females, comorbidities (diabetes: 4, hypertension: 3, cardiovascular disease: 1), and NACT regimens (FOLFIRINOX: 6, gemcitabine-based: 2). Out of these eight patients, seven had decline in performance status (ECOG > 2) during

NACT and one died. The clinical profile of these patients is shown in Table 1. ECOG > 2 was deemed unfit for surgery due to poor performance status, despite radiological evidence of resectability. The deceased patient experienced grade 4 toxicity (FOLFIRINOX-related neutropenic sepsis) exacerbated by comorbidities (diabetes and cardiovascular disease). The 19 patients who underwent resection had stable or improved ECOG status (0–1) post-NACT.

The reasons for treatment dropout across all 49 patients, including those with incomplete data and the BRPDAC focus group is shown in Fig. 1 and the ECOG performance status pre and post NACT is shown in Fig. 2.

Table 1
Demographic and Clinical Profile of BRPDAC Dropout Patients (n = 8)

S.N.	Age (years)	Sex	Co-morbidity	Pre-habilitation	NACT Regimen	Number of completed cycles	ECOG Status (Post NACT)	Outcome
1	48	M	Diabetes	Not done	FOLFIRINOX	3	> 2	Non-resected
2	55	M	Hypertension	Not done	FOLFIRINOX	5	> 2	Non-resected
3	60	F	Diabetes, Hypertension	Not done	Gemcitabine based	4	> 2	Non-resected
4	62	M	None	Not done	FOLFIRINOX	2	> 2	Non-resected
5	65	F	Diabetes	Not done	FOLFIRINOX	5	> 2	Non-resected
6	68	M	Hypertension	Not done	FOLFIRINOX	6	> 2	Non-resected
7	70	F	Diabetes, cardiovascular	Not done	Gemcitabine based	6	> 2	Non-resected
8	75	M	Diabetes, Hypertension	Not done	FOLFIRINOX	4	Died	Death (NACT toxicity)

Discussion

This study identifies a critical subgroup of BRPDAC patients who, despite potential resectability, drop out of NACT due to declining ECOG performance status or treatment-related toxicity potentially benefitting from upfront surgery.

The management of BRPDAC is undergoing a paradigm shift away from upfront surgery and towards a neoadjuvant strategy.[5] The potential advantages of neoadjuvant therapy (NAT) include tumor downstaging, a higher chance of R0 resection, early treatment of micrometastatic disease and better tolerance to systemic chemotherapy when given prior to surgery.[8] The long-term results of the PREOPANC trial demonstrated improved 5 year overall survival with neoadjuvant chemoradiotherapy (NACRT) compared to upfront surgery in

patients with resectable and BRPDAC (20.5% vs. 6.5% respectively). However, among the 91 patients who were started on NACRT in the PREOPANC trial, only 72 underwent resection indicating that 19 patients who initiated chemoradiotherapy did not proceed to surgery. While 10 of these patients were found to have disease progression rendering them unresectable, the remaining nine patients (9.8%) did not undergo resection for reasons not explicitly detailed in the study.[3] Similarly, out of 86 patients included for the full analysis set in ESPAC-5 trial, only 68 underwent surgery. 18 patients (20.9%) did not undergo surgery, 15 due to disease progression while the remaining three (16.6%) due to other causes.[9] These cases likely represent dropout due to treatment-related toxicity, functional decline, or patient refusal which is similar to the 16.3% (n = 8) dropout observed in this study. The NORPACT-1 trial, comparing NAT to upfront surgery in resectable pancreatic head cancer also estimated a 20% dropout in the neoadjuvant arm for similar reasons.[10]

A significant challenge in planning of NACT in aggressive pancreatic tumor is that over half of patients who begin NAT may not be able to have surgery because of a clinical decline in performance status and disease progression.[11] 44.9% (n = 22) of patients in this study could not complete NACT due to chemotherapy related toxicity or tumor progression which is consistent with previous reports showing NACT non-continuation rates of 20–53% in BRPDAC patients.[11,12] Since 88–90% of PDAC patients have a KRAS mutation, targeted therapy and immunotherapy, particularly directed against KRAS, are emerging as treatments for PDAC in addition to chemotherapy. These methods could increase survival and overcome resistance in KRAS mutant PDAC, but their routine usage is currently limited by a lack of clinical data.[13]

Among the 49 patients with BRPDAC in this study, 19 patients (38.7%) underwent PD following NACT, reflecting outcomes comparable to the study by Ali et al, where resection was achieved in 31% of patients receiving NAT.[14] However, Hackert et al in their study of locally advanced pancreatic cancer reported a successful resection in 50.8% of patients (61% following FOLFIRINOX and 46% after gemcitabine and radiation).[4]

In our study, one patient succumbed to FOLFIRINOX-related toxicity, consistent with reported mortality rates of 0–2%.[15,16] Though FOLFIRINOX is effective in downstaging tumor and associated with a survival advantage, it has a significant toxicity when compared to gemcitabine.[16] According to a meta-analysis the pooled rates of all grade 3 or 4 FOLFIRINOX adverse events per 100 patients was 60.4 including neutropenia, thrombocytopenia, diarrhoea, vomitting and fatigue.[17] Furthermore, side effects like gastrointestinal complication, fatigue and neuropathy may lead to deterioration in performance status and quality of life of a patient.[18]

The deterioration to ECOG > 2 in seven and mortality in one patient receiving NACT despite radiological resectibility in this study suggest that upfront surgery could have been a viable option for these patients as they would not risk preoperative clinical detorioration during chemotherapy. There is ongoing research on molecular based biomarkers to guide NAT, which presents a promising route for further exploration.[19] A recent Australian prospective cohort study found that in patients with triple negative PDAC (negative for S100A4, Ca125 and Mesothelin in immunohistochemistry), NACT was associated with worse overall survival (25.2 vs. 33.3 months) when compared with upfront surgery in resectable and BRPDAC, likely due to delay in surgical resection of a biologically favorable tumor, leading to lost opportunity for cure before metastasis developed.[20] This underscores the importance of biological stratification for a neoadjuvant vs surgery first approach in cases of resectable and BRPDAC.

The best way to treat cancer cachexia is to remove the tumor, as was investigated by Aslani et al.[21] Malnutrition often results from cancer related alterations such as protein catabolism, malabsorption, maldigestion, diarrhea and vomiting.[22] Chemotherapy has the potential to reduce the negative effects of cachexia in survival. In one large retrospective analysis, cachectic patients who received chemotherapy had survival rates comparable to those of non-cachectic patients, but cachectic patients who did not receive chemotherapy had significantly lower survival.[23]

Despite increasing utilization and improved survival, there exist significant demographic and socioeconomic disparities in the receipt of NAT independent of tumor factors.[24] Financial issue for NACT is particularly relevant in low-resource settings like Nepal, where access to multidisciplinary care and supportive therapies may be limited. The cost of chemotherapy and associated hospital stay varies significantly according on the regimen utilized; FOLFIRINOX with the highest cost followed by Gemcitabine – nab Paclitaxel and capacetabine.[25] Financial issue for NACT, socioeconomic factor including dissatisfaction with prognosis, contributed to dropout in a subset of our patients, as shown in Fig. 1. Strategies to mitigate dropout include dose-adjusted chemotherapy regimens, enhanced supportive care (e.g., nutritional support, growth factors), and patient counseling to address prognostic concerns.[26]

No patients in this study were enrolled in prehabilitation program. Prehabilitation may be defined as multidisciplinary approaches that mitigate surgery related functional decline and its consequences in the pre-operative period. These programs typically incorporate exercise training, nutritional therapy, smoking cessation and psychosocial support like stress and anxiety reduction.[27] Prehabilitation may modulate systemic inflammation by reducing the production of proinflammatory cytokines like interleukins, TNF-alpha and interferon-gamma, thus potentially lowering the risk of sepsis and death. Furthermore, it may also enhance immunological and cardiovascular function, reduce skeletal muscle loss and promote favorable organ remodelling.[28] A systematic review reported that prehabilitation programs in pancreatic cancer patients improved muscle mass and preoperative quality of life and were associated with better post-operative outcomes like shorter hospital stay and reduced delayed gastric emptying but was silent on postoperative quality of life.[29] These programs may benefit in terms of nutrition and performance status as well but the data are limited.[30] Prehabilitation was found to be safe and feasible especially in patients undergoing NACT as in BRPDAC as a window of 3–6 months is usually available before surgery.[29] However, evidence supporting prehabilitation in pancreatic cancer surgery remains limited with metanalysis reporting evidence ranging from 'moderate' to 'very low', because of small percentage of RCTs, lack of standardized protocols, insufficient sample sizes and a high risk of bias.[31,32] Chemotherapy toxicity limiting participation, lack of standardized prehabilitation protocol and patient adherence remain main challenges to routine implementation of prehabilitation programs.[29,30,33] Furthermore, in a developing country like Nepal, financial constraints, lack of reimbursement, limited access to specialized center and accessibilty issues further complicate these challenges.

This study is subjected to few limitations. First, the retrospective design, small sample size and the absence of long-term follow-up limits generalizability. Second, incomplete data for eight patients may introduce bias, and the lack of molecular profiling (KRAS mutation) precludes analysis of tumor biology beyond CA19-9 and imaging. Third, the hypothetical ECOG scores before NACT were estimated as 0–1 based on typical surgical

candidacy criteria, as exact pre-NACT scores were not provided. Future research should focus on predictive biomarkers for NACT response and toxicity, effect of prehabilitation on quality of life, as well as strategies to maintain ECOG status during treatment. Randomized trials comparing upfront surgery versus NACT in BRPDAC could clarify optimal treatment sequencing. Additionally, addressing socioeconomic barriers through subsidized care or telemedicine could reduce dropout rates in resource-limited settings.

Conclusion

Patients with BRPDAC who fulfill anatomic or biologic criteria but drop out of NACT due to declining ECOG status, despite being technically resectable, represent a critical subgroup that may benefit from upfront surgery. Molecular based biomarkers may guide individualized treatment strategy in such patients and preoperative prehabilitation might mitigate functional decline, thus lowering the surgical dropout rate. However, further studies are warranted to refine treatment algorithms and address barriers to care.

Abbreviations

PDAC
Pancreatic Ductal Adenocarcinoma
BRPDAC
Borderline Resectable Pancreatic Ductal Adenocarcinoma
IAP
International Association of Pancreatology
IRC
Institutional Review Committee
NACT
Neoadjuvant Chemotherapy
ECOG
Eastern Cooperative Oncology Group
NCCN
National Comprehensive Cancer Network
SMA
Superior Mesenteric Artery
CHA
Common Hepatic Artery
CA
Celiac Artery
SMV
Superior Mesenteric Vein
PV
Portal vein
CECT
Contrast Enhanced Computed Tomography
PD

Pancreaticoduodenectomy
NAT
Neoadjuvant Therapy
NACRT
Neoadjuvant Chemoradiotherapy

Declarations

Ethics approval and consent to participate

Ethical approval for this study was taken from Institutional Review Committee (IRC) of Kathmandu Medical College Public Ltd. (Reference number: 10042026/08). Given the retrospective nature of the study, the requirement for individual informed consent to participate was waived by the IRC. This study was conducted in accordance with the ethical standards of the IRC and the Declaration of Helsinki of the World Medical Association, as well as relevant national regulations governing human subject research.

Consent for publication:

Written informed consent for publication of their clinical details was obtained from patients or, where applicable, from their legally authorized representatives. In cases where patients were deceased, critically ill, or lacked decision making capacity, consent was obtained from their next of kin or guardians in accordance with institutional policy.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to patient privacy but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

There was no funding for this study.

Author's contribution

Prabin contributed to the conception and design of the study.

Roshan contributed to the analysis and interpretation of data.

Spandan and Uttam contributed in writing the manuscript.

Dhiresh contributed in revison of the manuscript.

All authors read and approved the final manuscript.

Acknowledgements

Not applicable

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References

1. Siegel RL, Kratzer TB, Wagle NS, Sung H, Jemal A. Cancer statistics, 2026. CA Cancer J Clin.; 76(1). Epub ahead of print January 2026. DOI: 10.3322/caac.70043.
2. Isaji S, Mizuno S, Windsor JA, et al. International consensus on definition and criteria of borderline resectable pancreatic ductal adenocarcinoma 2017. Pancreatology. 2018; 18(1):2–11.
3. Versteijne E, Van Dam JL, Suker ; Mustafa, et al. Neoadjuvant Chemoradiotherapy Versus Upfront Surgery for Resectable and Borderline Resectable Pancreatic Cancer: Long-Term Results of the Dutch Randomized PREOPANC Trial. J Clin Oncol. 2022; 40:1220–30.
4. Hackert T, Sachsenmaier M, Hinz U, et al. Locally Advanced Pancreatic Cancer. Ann Surg. 2016; 264(3):457–63.
5. Janssen QP, O'Reilly EM, van Eijck CHJ, Groot Koerkamp B. Neoadjuvant Treatment in Patients With Resectable and Borderline Resectable Pancreatic Cancer. Frontiers in Oncology; 10. Epub ahead of print 31 January 2020. DOI: 10.3389/fonc.2020.00041.
6. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982; 5(6):649–55.
7. Basturk O, Cardin DB, Gabriela Chiorean E, et al. NCCN Guidelines Version 2.2025 Pancreatic Adenocarcinoma Continue NCCN Guidelines Version 2.2025 Pancreatic Adenocarcinoma, https://www.nccn.org/home/member- (2025).
8. Lee SH. Neoadjuvant Therapy for Resectable or Borderline Resectable Pancreatic Cancer. The Korean Journal of Gastroenterology. 2024; 84(3):103–10.
9. Ghaneh P, Palmer D, Cicconi S, et al. Immediate surgery compared with short-course neoadjuvant gemcitabine plus capecitabine, FOLFIRINOX, or chemoradiotherapy in patients with borderline resectable

pancreatic cancer (ESPAC5): a four-arm, multicentre, randomised, phase 2 trial. Lancet Gastroenterol Hepatol. 2023; 8(2):157–68.

10. Labori KJ, Bratlie SO, Andersson B, et al. Neoadjuvant FOLFIRINOX versus upfront surgery for resectable pancreatic head cancer (NORPACT-1): a multicentre, randomised, phase 2 trial. Lancet Gastroenterol Hepatol. 2024; 9(3):205–17.
11. Gillen S, Schuster T, Büschenfelde CM Zum, Friess H, Kleeff J. Preoperative/neoadjuvant therapy in pancreatic cancer: A systematic review and meta-analysis of response and resection percentages. PLoS Medicine; 7(4). Epub ahead of print April 2010. DOI: 10.1371/journal.pmed.1000267.
12. Murphy JE, Wo JY, Ryan DP, et al. Total neoadjuvant therapy with FOLFIRINOX followed by individualized chemoradiotherapy for borderline resectable pancreatic adenocarcinoma: A phase 2 clinical trial. JAMA Oncol. 2018; 4(7):963–9.
13. Pradeep R, Isbeih NJ, Abraham FF, Noori E, Yeung ZP, Kundranda MN. KRAS Inhibition in Pancreatic Ductal Adenocarcinoma. Journal of Clinical Medicine; 15(2). Epub ahead of print 1 January 2026. DOI: 10.3390/jcm15020873.
14. Aljubran AH, Alata MK, Badran AA, et al. Resectability rate of pancreatic cancer after neoadjuvant therapy. Journal of Clinical Oncology. 2024; 42(16_suppl):e16348–e16348.
15. Rombouts SJ, Mungroop TH, Heilmann MN, et al. FOLFIRINOX in locally advanced and metastatic pancreatic cancer: A single centre cohort study. J Cancer. 2016; 7(13):1861–6.
16. Conroy T, Ychou M, Bouché O, et al. FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer. 364.
17. Suker M, Beumer BR, Sadot E, et al. FOLFIRINOX for locally advanced pancreatic cancer: a systematic review and patient-level meta-analysis. Lancet Oncol. 2016; 17(6):801–10.
18. Sarma G, Bora H, Medhi PP. Optimizing neoadjuvant chemoradiation in resectable and borderline resectable pancreatic cancer: Evidence-based insights. World J Clin Oncol.; 16(7). Epub ahead of print 24 July 2025. DOI: 10.5306/wjco.v16.i7.106107.
19. Endo Y, Kitago M, Kitagawa Y. Evidence and Future Perspectives for Neoadjuvant Therapy for Resectable and Borderline Resectable Pancreatic Cancer: A Scoping Review. Cancers; 16(9). Epub ahead of print 1 May 2024. DOI: 10.3390/cancers16091632.
20. Nahm CB, Turchini J, Sahni S, et al. The Right Treatment Strategy for the Right Patient: A Biomarker-Driven Approach to Neoadjuvant vs. Surgery-First Management of Resectable and Borderline Resectable Pancreatic Cancer. Cancers (Basel).; 14(15). Epub ahead of print 1 August 2022. DOI: 10.3390/cancers14153620.
21. Aslani A, Gill AJ, Roach PJ, Allen BJ, Smith RC. Preoperative body composition is influenced by the stage of operable pancreatic adenocarcinoma but does not predict survival after Whipple's procedure. HPB. 2010; 12(5):325–33.
22. De Luca R, Gianotti L, Pedrazzoli P, et al. Immunonutrition and prehabilitation in pancreatic cancer surgery: A new concept in the era of ERAS® and neoadjuvant treatment. European Journal of Surgical Oncology. 2023; 49(3):542–9.
23. Hendifar AE, Chang JI, Huang BZ, Tuli R, Wu BU. Cachexia, and not obesity, prior to pancreatic cancer diagnosis worsens survival and is negated by chemotherapy. J Gastrointest Oncol. 2018; 9(1):17–23.

24. Chervu N, Kim S, Sakowitz S, et al. Disparities in neoadjuvant chemotherapy for pancreatic adenocarcinoma with vascular involvement. Surg Open Sci. 2024; 20:101–5.
25. Cerullo M, Gani F, Chen SY, et al. Assessing the Financial Burden Associated with Treatment Options for Resectable Pancreatic Cancer. In: *Annals of Surgery*. 267 (3), Lippincott Williams and Wilkins, 2018, pp. 544–51.
26. Sohal DPS, Kennedy EB, Cinar P, et al. Metastatic Pancreatic Cancer: ASCO Guideline Update. J Clin Oncol. 2020; 38:3217–30.
27. Christopher CN, Kang DW, Wilson RL, et al. Exercise and Nutrition Interventions for Prehabilitation in Hepato-Pancreato-Biliary Cancers: A Narrative Review. Nutrients; 15(24). Epub ahead of print 1 December 2023. DOI: 10.3390/nu15245044.
28. Kammerer T, Mahú I, Schier R. Prehabilitation and Inflammation. Annals of Nutrition and Metabolism 2025; 81(4):234–44.
29. Bundred JR, Kamarajah SK, Hammond JS, Wilson CH, Prentis J, Pandanaboyana S. Prehabilitation prior to surgery for pancreatic cancer: A systematic review. Pancreatology. 2020; 20(6):1243–50.
30. Jain AJ, Maxwell JE, Katz MHG, Snyder RA. Surgical Considerations for Neoadjuvant Therapy for Pancreatic Adenocarcinoma. Cancers; 15(16). Epub ahead of print 1 August 2023. DOI: 10.3390/cancers15164174.
31. Refaat M, Modak S, Harivelam C, et al. Can we “prehabilitate” pancreatic cancer patients prior to surgery? A critical appraisal of the literature. Clin Nutr ESPEN. 2024; 63:845–55.
32. Chen Y, Sebio-García R, Iglesias-Garcia E, Reguart N, Martinez-Palli G, Bello I. Prehabilitation for patients undergoing neoadjuvant therapy prior to cancer resection: a systematic review and meta-analysis. Supportive Care in Cancer. 2024; 32(11):749.
33. Hoeijmakers LSM, Driessens H, Buis CI, Olde Damink SWM, Klaase JM, Dulk M den. Prehabilitation before pancreatic surgery in the Netherlands: insights from a nationwide survey among pancreatic surgeons. Perioperative Medicine.; 14(1). Epub ahead of print 31 July 2025. DOI: 10.1186/s13741-025-00569-x.

Figures

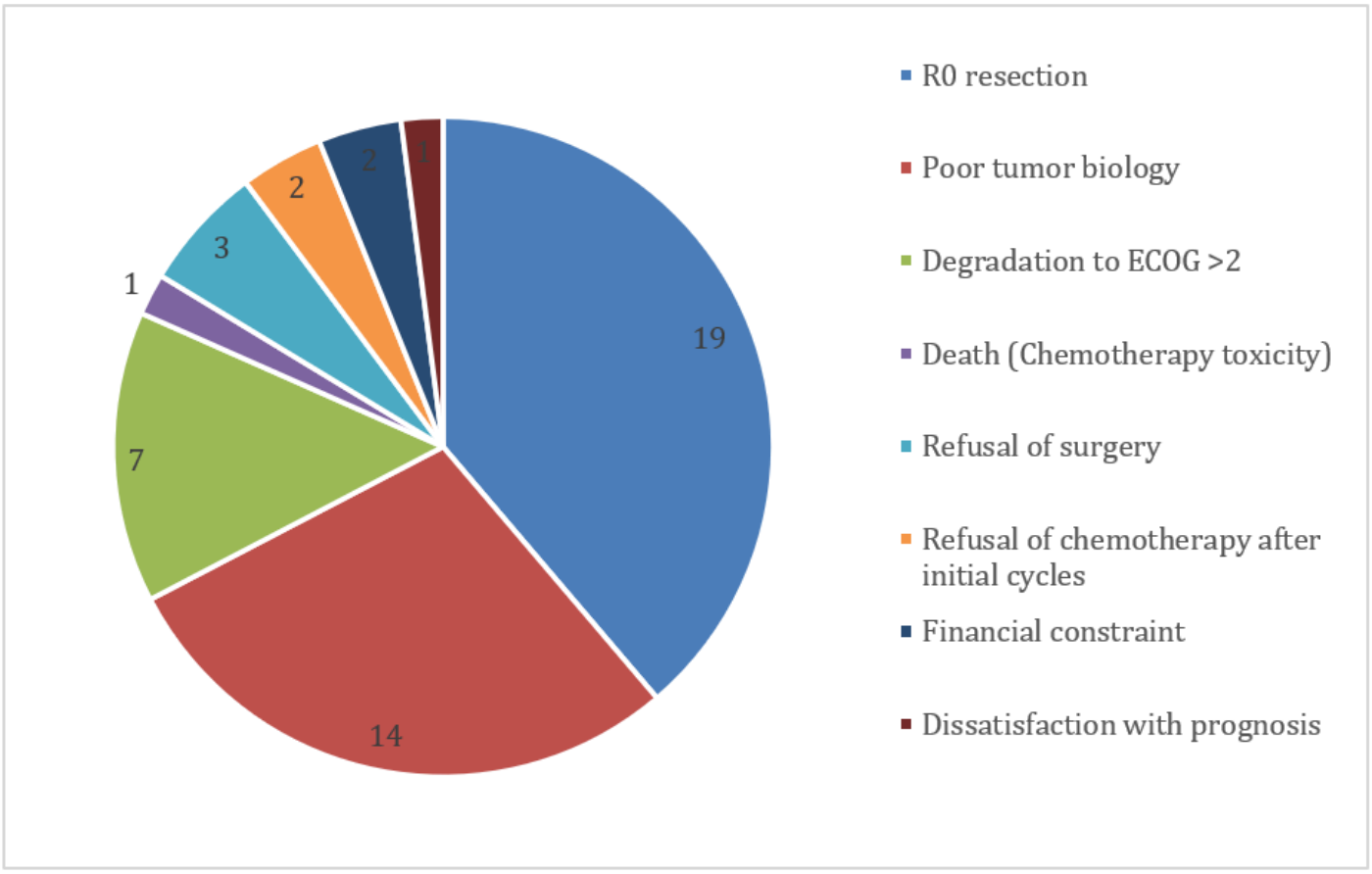


Figure 1

Distribution of Reasons for Dropout in the Entire Cohort (n=49)

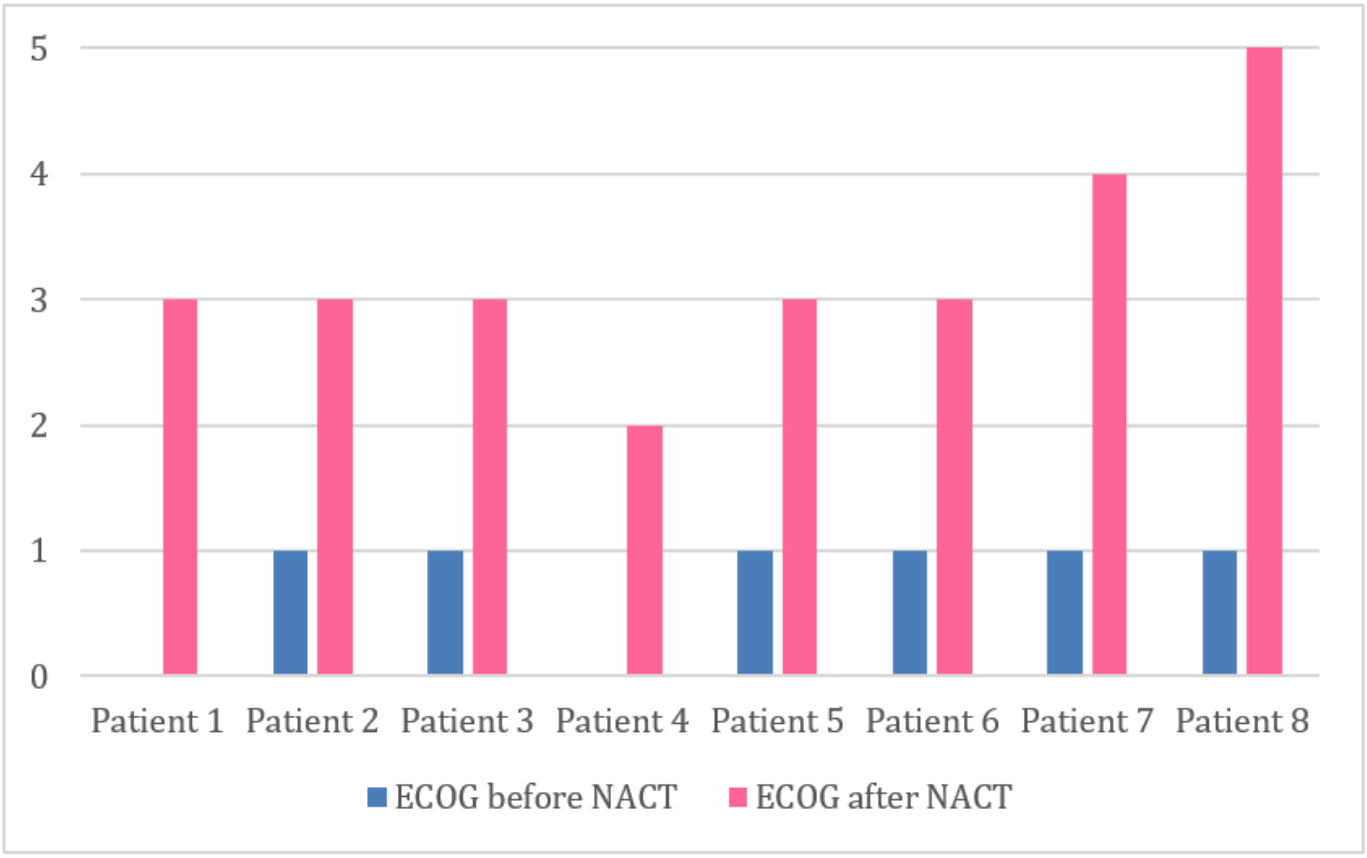


Figure 2

ECOG Performance Status Changes in BRPDAC Dropout Patients (n=8)

Note: ECOG >2 indicate poor performance status, rendering patients unfit for surgery despite technical resectability