Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Timing of Drain Amylase Measurement for Predicting Clinically Relevant Pancreatic Fistula After Pancreaticoduodenectomy

Omer Akay

omer_akay_38@hotmail.com

Kocaeli City Hospital

Mert Guler

Gaziosmanpaşa Taksim Eğitim ve Araştırma Hastanesi

Husnu Ozan Sevik

Basaksehir Cam and Sakura City Hospital

Mert Mahsuni Sevinc

Istanbul Teaching and Research Hospital

Muhammed Gurluk

Istanbul Teaching and Research Hospital

Ufuk Oguz Idiz

Istanbul Teaching and Research Hospital

Cihad Tatar

Taksim Acibadem Hospital

Research Article

Keywords: Periampullary tumors, pancreaticoduodenectomy, pancreatic fistula, postoperative complications, drain amylase

Posted Date: May 29th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9600786/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Background

Postoperative pancreatic fistula (POPF) remains one of the most significant complications following pancreaticoduodenectomy (PD). The optimal postoperative day for drain amylase measurement to predict clinically relevant POPF remains unclear. This study aimed to determine the most informative time point for early detection of symptomatic POPF.

Methods

This retrospective cohort study included 144 patients who underwent PD for periampullary tumors between 2018 and 2024. For patients with multiple drain amylase measurements within the first five postoperative days, the highest recorded value was analyzed, and patients were categorized according to the postoperative day (POD1–POD5) on which this peak occurred. Clinically relevant POPF (Grades B–C) was defined according to International Study Group of Pancreatic Surgery (ISGPS) criteria. Diagnostic performance was evaluated using receiver operating characteristic (ROC) analysis.

Results

Clinically relevant POPF occurred in 17 patients (11.8%). Elevated drain amylase measured on POD3 demonstrated high diagnostic accuracy, with an AUC of 0.886 (95% CI: 0.780–0.991), sensitivity of 90.5%, and specificity of 85% at a cut-off value of 118.5 U/L ($p < 0.001$). Although POD4 showed a slightly higher AUC (0.904), POD3 represented an earlier clinically actionable time point with comparable discriminatory performance.

Conclusion

Drain amylase measurement on postoperative day 3 provides high diagnostic accuracy for identifying clinically relevant pancreatic fistula and may serve as a clinically useful early assessment point to guide postoperative management after PD.

Introduction

Periampullary tumors (PBT) are malignancies arising within approximately 2 cm of the major papilla and account for 0.5–2% of all gastrointestinal cancers. These tumors include neoplasms of the pancreatic head, ampulla of Vater, distal bile duct, and duodenum, with pancreatic head and ampullary tumors being the most frequently encountered subtypes [1].

Pancreaticoduodenectomy (PD) remains the standard curative treatment for resectable periampullary malignancies. Despite advances in surgical technique and perioperative care, PD continues to be associated with considerable morbidity due to its anatomical complexity and the technical challenges of reconstruction. Although postoperative mortality has decreased significantly in high-volume centers, morbidity rates remain high, affecting approximately 30–45% of patients [2–3].

Among postoperative complications, postoperative pancreatic fistula (POPF) represents the most clinically significant and feared. According to the International Study Group of Pancreatic Surgery (ISGPS), POPF is defined as drain fluid with an amylase concentration greater than three times the upper limit of normal serum amylase levels, accompanied by a clinically relevant condition [4]. Clinically relevant POPF (Grades B–C) occurs in approximately 15–20% of patients after PD and is associated with prolonged hospitalization, increased healthcare costs, and a mortality rate that can reach 20–40% if not promptly recognized and adequately drained [5–8].

Early identification of patients at risk for developing POPF is therefore crucial to improving postoperative outcomes. Drain amylase measurement is widely used for this purpose; however, the optimal postoperative day for measuring amylase levels remains unclear. Current practices vary between centers and even among surgeons, and most existing studies evaluate drain amylase values on fixed days rather than determining the most informative time point for clinical decision-making.

The aim of this study was to evaluate the diagnostic performance of drain amylase measurements obtained on different postoperative days following pancreaticoduodenectomy and to determine a clinically relevant and informative time point for the early detection of clinically significant POPF.

Materials and Methods

This retrospective study was conducted following approval from the Ethics Committee of the University of Health Sciences, Istanbul Training and Research Hospital. A total of 168 consecutive patients who underwent pancreaticoduodenectomy (PD) for periampullary tumors between January 1, 2018 and April 1, 2024 were screened. Patients with missing clinical or laboratory data, no documented drain amylase measurements, or benign final pathology were excluded. After applying these criteria, 144 patients were included in the final analysis.

At the end of each operation, two closed-suction drains were routinely placed: one adjacent to the pancreatoenteric anastomosis and another near the bilioenteric anastomosis. Postoperative management followed standard institutional practice.

Drain amylase levels were not measured on fixed postoperative days for all patients. Measurement frequency varied according to surgeon preference and the patient's clinical condition, resulting in heterogeneity in both the timing and number of assessments. Given the retrospective nature of the study and the absence of standardized daily measurements, a uniform day-by-day comparison was not feasible. To allow for a consistent analytical framework, the highest recorded drain amylase value within

the first five postoperative days was selected for patients with multiple measurements. Patients were then categorized according to the postoperative day (POD1–POD5) on which this peak value was observed. This approach was chosen to reflect the earliest clinically relevant elevation in drain amylase that could potentially trigger clinical attention or intervention, rather than to model daily amylase trends. This methodology may introduce measurement-related bias and limits direct comparison of diagnostic accuracy across individual postoperative days; therefore, it is acknowledged as an inherent limitation of the retrospective design, and may favor detection of later peaks over earlier transient elevations, which should be considered when interpreting time-based comparisons.

Clinically relevant postoperative pancreatic fistula (POPF) was defined according to the 2016 International Study Group of Pancreatic Surgery (ISGPS) criteria, with Grades B and C classified as symptomatic POPF [4].

The primary outcome of this study was to evaluate the association between the postoperative day on which elevated drain amylase was detected and the occurrence of clinically relevant POPF (Grades B–C). The retrospective nature of the study warrants cautious interpretation; however, the findings offer meaningful insight into the timing of drain amylase assessment for early identification of patients at increased risk for clinically relevant POPF.

Statistical Analysis

Categorical variables were compared using the Chi-square test. Diagnostic performance for each postoperative day was assessed using receiver operating characteristic (ROC) analysis, from which AUC, sensitivity, specificity, PPV, and NPV were calculated. Because key operative and gland-related variables (e.g., duct diameter, gland texture, blood loss, FRS) were not available for all patients, multivariable analysis could not be performed and this was acknowledged as a limitation. A p-value < 0.05 was considered statistically significant.

Results

A total of 144 patients were included in the analysis. Of these, 92 patients (63.9%) were male and 52 (36.1%) were female, with a mean age of 62.2 ± 12.7 years. Tumor localization was as follows: pancreatic head in 71 patients (49.3%), distal bile duct in 14 (9.7%), ampulla of Vater in 46 (32%), and duodenum in 13 (9%). The distribution of POPF grades according to ISGPS 2016 criteria was: Grade A in 51 patients (35.4%), Grade B in 15 patients (10.4%), and Grade C in 2 patients (1.4%). Overall, 50 patients (34.7%) experienced medical or surgical complications, and three patients died during hospitalization. Fifty-two patients (36.1%) underwent classical Whipple resection, whereas 92 (63.9%) underwent pylorus-preserving pancreaticoduodenectomy. Demographic and clinical characteristics are summarized in Table 1.

Table 1
Demographic and Clinical Characteristics of Patients

Age (mean ± SD) (year)		**62.2 ± 12.7**
Gender (n,%)	Female (n, %)	52 (%36.1)
	Male (n, %)	92 (%63.9)
Tumor localization (n,%)	Head of pancreas (n, %)	71 (%49.3.)
	Common bile duct (n, %)	14 (%9.7)
	Ampulla (n, %)	46 (%32)
	Duodenum (n, %)	13 (%9)
Pancreatic fistula grade (n,%)	No (n, %)	76(%52.8)
	Grade A (n, %)	51 (%35.4)
	Grade B (n, %)	15(%10.4)
	Grade C (n, %)	2(%1.4)
Anycomplication	Yes (n, %)	50 (%34.7)
	No (n, %)	94 (%65.3))
Mortality	Yes (n, %)	3 (%2.1)
	No (n, %)	141 (%97.9a)
Treatment (n,%)	Whipple (n,%)	52 (%36.1)
	Pylorus protective whipple (n,%)	92 (%63.9)
Stage	Stage 1 (n,%)	17 (%11.8)
	Stage 2 (n,%)	102 (%70.8)
	Stage 3 (n,%)	23 (%16)
	Stage 4 (n,%)	2 (%1.4)
Hospitalization duration (days)	12.95 ± 6.49	

Drain amylase measurements were available on postoperative days 1 through 5. Because measurement frequency varied among patients, the highest recorded amylase value within the first 5 postoperative days was used for analysis, and patients were categorized according to the postoperative day on which this value was obtained. An elevated amylase level was defined as > 3 times the upper limit of normal (ISGPS threshold). The association between the day of elevated amylase measurement and the presence of clinically relevant POPF (Grades B–C) was evaluated.

Elevated drain amylase values detected on postoperative day 3 demonstrated high diagnostic performance for identifying clinically relevant POPF, with a sensitivity of 90.5% and specificity of 85%. The corresponding AUC was 0.886 (95% CI: 0.780–0.991). While the highest AUC value was observed on postoperative day 4 (AUC 0.904, 95% CI: 0.774–1.000), the difference in diagnostic performance between POD3 and POD4 was modest. Notably, POD3 demonstrated higher sensitivity and specificity compared to POD4, and represents an earlier clinically actionable time point. Detailed diagnostic performance metrics for each postoperative day are presented in Table 2.

Table 2
Diagnostic performance of drain amylase levels according to postoperative day for predicting clinically relevant pancreatic fistula

Day of drainage fluid test	Cut-off value (U/L)	Sensivity	Specificity	AUC(%95 C.I)	p-value
Postop 1.day (n = 29)	208	%84.6	75%	0.788 (0.618–0.959)	0.020
Postop 2.day (n = 24)	100	90%	73%	0.867 (0.725-1.000)	0.006
Postop 3.day (n = 38)	118.5	%90.5	85%	0.886 (0.780–0.991)	< 0.001
Postop 4.day (n = 23)	126.0	%84.6	%80.0	0.904 (0.774-1.000)	0.005
Postop 5.day (n = 30)	21.0	%82.4	%66.7	0.867 (0.745–0.989)	0.004

Discussion

Pancreaticoduodenectomy remains the standard treatment for periampullary tumors but continues to carry a substantial risk of postoperative morbidity, with postoperative pancreatic fistula (POPF) being the most clinically significant complication **[7]**. Early recognition of clinically relevant POPF is essential for initiating timely interventions and reducing associated morbidity. Measurement of drain amylase is widely used for this purpose; however, there is no consensus on the optimal postoperative day on which it provides the highest diagnostic value. In this study, we evaluated the association between the day of postoperative drain amylase assessment and the development of clinically relevant POPF. Our findings demonstrate that amylase measurements obtained on postoperative day 3 offered high diagnostic accuracy, suggesting that this time point represents an early and clinically actionable assessment point rather than a definitively superior time point based solely on diagnostic accuracy.

Despite notable advances in operative techniques, perioperative care, and centralization of pancreatic surgery, pancreaticoduodenectomy continues to be associated with substantial postoperative morbidity. Although mortality rates in high-volume centers have declined to below 2%, largely due to improvements in anesthesia, critical care, and enhanced recovery protocols, morbidity rates remain persistently high,

ranging from 30% to 65% in contemporary series [9–11]. This high morbidity burden reflects the complexity of the procedure and the inherent vulnerability of the pancreatoenteric anastomosis.

In our cohort, the overall complication rate was 34.7%, which aligns with the lower range of values reported in the literature, indicating that our outcomes are comparable to those of established pancreatic surgery centers. Additionally, the in-hospital mortality rate of 2.1% mirrors the rates observed in high-volume international studies, suggesting that perioperative management and postoperative care at our institution meet current global standards. These findings further support the reliability of our dataset and provide a robust foundation for evaluating diagnostic indicators such as drain amylase levels.

Clinically, postoperative pancreatic fistula (POPF) is defined by the International Study Group of Pancreatic Fistula (ISGPF) as drainage fluid with an amylase concentration exceeding three times the upper limit of normal serum values, obtained from either surgically placed or subsequently inserted percutaneous drains [4]. Differentiating between parenchymal leaks and anastomotic leaks in the early postoperative period can be challenging. Parenchymal leaks are characterized by persistently elevated drain amylase levels without radiologic contrast extravasation and typically resolve spontaneously, whereas anastomotic leaks usually demonstrate contrast extravasation at the pancreaticojejunostomy and often require prolonged intervention or reoperation [12–13].

The reported incidence of POPF varies widely in the literature—from 2% to 51%—reflecting differences in surgical technique, fistula definitions, and institutional protocols [14–16]. In the study by Vladimir Dugalič et al. [17], evaluating drain amylase dynamics after pancreaticoduodenectomy, the overall POPF rate was 37.7% (Grade A: 22.8%, Grade B: 11.0%, Grade C: 3.9%). In our study, adopting the ISGPF threshold of three times the upper limit of normal, we observed a POPF rate of 47.2%, comprising 35.4% Grade A, 10.4% Grade B, and 1.4% Grade C fistulas. The rate of clinically relevant (Grade B–C) POPF was 11.8%, which is consistent with the mid-range of values reported in high-volume centers.

Two separate studies evaluating the relationship between elevated drain amylase levels on postoperative day 1 reported a significant association between early high amylase values and the development of Grade B and C POPF [18,19]. However, neither of these studies compared day-1 values with measurements obtained on subsequent postoperative days, leaving uncertainty regarding the most informative time point for clinical decision-making.

A review by Tsetsegdemberel Bat-Ulzii Davidson et al. [20] examined amylase levels in drainage fluid at 48 hours and later, concluding that measurements obtained on postoperative day 5 were more reliable for diagnosing POPF. In contrast, a study of 117 patients by Sung Ryol Lee et al. [21], which analyzed amylase measurements on postoperative days 1, 3, and 5, found that postoperative day 3 demonstrated the highest diagnostic accuracy, with a sensitivity of 92% and specificity of 82% for clinically relevant fistulas.

Our findings are consistent with this observation. In our cohort, elevated drain amylase levels measured on postoperative day 3 demonstrated a robust association with Grade B and C POPF, supporting the growing evidence that postoperative day 3 may serve as a clinically actionable time point for detecting symptomatic pancreatic fistulas. Unlike prior studies focusing on fixed daily measurements, our analysis reflects real-world variability in postoperative monitoring, thereby providing complementary insight into clinically actionable timing. Importantly, although POD4 demonstrated a slightly higher AUC, the marginal gain in diagnostic performance does not outweigh the clinical advantage of earlier detection on POD3, which may facilitate timely clinical decision-making and intervention.

In a study by Damiano Caputo et al. [22], which evaluated the utility of drain amylase testing and abdominal CT on postoperative day 3 to guide drain management after pancreaticoduodenectomy, the authors suggested that drains could be safely removed when the POD3 amylase level was < 252 U/L. Although our study does not directly address optimal timing for drain removal, our findings reinforce the clinical relevance of postoperative day 3 as a key assessment point. Specifically, a POD3 amylase value > 118.5 U/L was significantly associated with clinically relevant POPF in our cohort, supporting the concept that amylase assessment on this day may offer meaningful guidance for postoperative monitoring and decision-making.

The role of prophylactic intra-abdominal drains following pancreaticoduodenectomy (PD) remains a subject of ongoing debate, particularly regarding their impact on postoperative morbidity and the optimal timing of drain removal [23]. In a large cohort study by Zaghal et al. [24], which included 6,858 patients who underwent PD, routine placement of prophylactic drains was associated with higher postoperative complication rates and longer hospital stays. Similarly, other studies have suggested that prolonged retention of surgical drains may increase the risk of intra-abdominal infections and contribute to higher rates of POPF [25]. These findings highlight a critical clinical dilemma: while elevated drain amylase levels can be a valuable indicator of POPF, early differentiation between Grade A and clinically relevant Grade B/C fistulas is essential to avoid unnecessary interventions. Taken together, the literature underscores that inappropriate or prolonged drain use may contribute to increased morbidity, extended hospitalization, and higher healthcare costs, emphasizing the need for evidence-based strategies to guide both placement and timing of drain removal.

Limitations

This study has several limitations that should be acknowledged. First, the number of patients with available drain amylase measurements differed across postoperative days, which may have affected statistical power. Second, drain amylase levels were not obtained according to a strictly standardized daily protocol in all patients, and the analysis therefore relied on the highest available value, introducing potential measurement-related bias. In addition, the lack of continuous longitudinal monitoring and the inclusion of procedures performed by different surgeons may have limited standardization in perioperative management. Despite these limitations, the observed associations were internally consistent. Postoperative day 3 should be considered an early and clinically relevant assessment point

rather than a definitive or prescriptive threshold. Further prospective studies with standardized measurement protocols are warranted to refine these findings.

Conclusion

Our study demonstrates that measuring drain amylase levels on postoperative day 3 offers high diagnostic accuracy and may provide clinically useful guidance for early identification of patients at increased risk of clinically relevant pancreatic fistula. This finding may support postoperative decision-making by helping clinicians identify patients at increased risk and optimize the timing of drain management. Monitoring drain amylase is a simple and minimally invasive tool that can assist in evaluating postoperative status and guiding drain removal within the context of postoperative risk stratification. Further prospective studies with standardized measurement protocols are needed to clarify which postoperative days and threshold values provide the most reliable diagnostic performance.

Declarations

Conflict of interest: All authors are in agreement with the contents of a manuscript and confirm that the paper is not being published or under consideration elsewhere.

There is no conflict of interest in our article.

Funding: There is no funding institution or person in our article

Acknowledgments: There is no organization or person that funded our study. All of the authors reported no biomedical financial interests or potential conflicts of interest.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Author Contributions:

- Critical Review: Cihad Tatar, Ufuk Oguz idiz

- Study concepts and design: Omer Akay, Ufuk Oguz idiz, Mert Guler

- Literature research: Omer Akay, Muhammed Gurluk, Husnu Ozan Sevik,

- Clinical studies: Furkan Turkoglu, Mert Mahsuni Sevinc, Mert Guler, Husnu Ozan Sevik, Cihad Tatar

- Data collection and analysis: Omer Akay, Muhammed Gurluk, Mert Guler, Cihad Tatar

- Statistical analysis: Omer Akay, Mert Guler, Cihad Tatar, Mert Mahsuni Sevinc, Husnu Ozan Sevik,

- Writing Manuscript: Omer Akay, Cihad Tatar

- Final approval of the manuscript: Omer Akay, Mert Guler, Mert Mahsuni Sevinc, Husnu Ozan Sevik, Muhammed Gurluk, Ufuk Oguz Idiz, Cihad Tatar

Ethics approval: The study was approved by the Ethics Committee of Health Sciences University Istanbul Training and Research Hospital (Decision No: 182, Date: 21 July 2023).

Consent to participate: Informed consent was waived by the institutional ethics committee due to the retrospective nature of the study.

References

1. Schneider M, Hackert T, Strobel O, Büchler MW. Technical advances in surgery for pancreatic cancer. Br J Surg. 2021;108(8):952-60. doi:10.1093/bjs/znab133.
2. Mungroop TH, Klompmaker S, Wellner UF, Steyerberg EW, Coratti A, D'Hondt M, et al. Updated Alternative Fistula Risk Score (ua-FRS) to include minimally invasive pancreatoduodenectomy: Pan-European validation. Ann Surg. 2021;273(2):334-40. doi:10.1097/SLA.0000000000003234.
3. Giuliano K, Ejaz A, He J. Technical aspects of pancreaticoduodenectomy and their outcomes. Chin Clin Oncol. 2017;6:64. doi:10.21037/cco.2017.09.01.
4. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, et al. The 2016 update of the International Study Group definition and grading of postoperative pancreatic fistula. Surgery. 2017;161(3):584-91. doi:10.1016/j.surg.2016.11.014.
5. Yang F, Jin C, Li J, Di Y, Zhang J, Fu D. Clinical significance of drainage fluid culture after pancreaticoduodenectomy. J Hepatobiliary Pancreat Sci. 2018;25:508-17. doi:10.1002/jhbp.589.
6. Chong E, Ratnayake B, Lee S, French JJ, Wilson C, Roberts KJ, et al. Risk factors for postoperative pancreatic fistula following distal pancreatectomy: systematic review and meta-analysis. HPB (Oxford). 2021;23:1139-51. doi:10.1016/j.hpb.2021.02.015.
7. Cai J, Ramanathan R, Zenati MS, Al Abbas A, Hogg ME, Zeh HJ, et al. Robotic pancreaticoduodenectomy is associated with decreased clinically relevant pancreatic fistulas: A propensity-matched analysis. J Gastrointest Surg. 2020;24:1111–1118. doi: 10.1007/s11605-019-04274-1
8. McMillan MT, Zureikat AH, Hogg ME, Kowalsky SJ, Zeh HJ, Sprys MH, et al. A propensity score-matched analysis of robotic vs open pancreaticoduodenectomy on incidence of pancreatic fistula. JAMA Surg. 2017;152:327–335. doi: 10.1001/jamasurg.2016.4755.
9. Schuh F, Mihaljevic AL, Probst P, Trudeau MT, Müller PC, Marchegiani G, et al. A simple classification of pancreatic duct size and texture predicts postoperative pancreatic fistula. Ann Surg. 2023;277:e597–e608. doi: 10.1097/SLA.0000000000004855.
10. Suurmeijer JA, Emmen AM, Bonsing BA, Busch OR, Daams F, van Eijck CH, et al. Nationwide validation of the ISGPS risk classification for postoperative pancreatic fistula after

pancreatoduodenectomy: "less is more". Surgery. 2023;173:1248–1253. doi: 10.1016/j.surg.2023.01.004.

11. Emmen AMLH, Ali M, Groot Koerkamp B, Boggi U, Molenaar IQ, Busch OR, et al. Predicting postoperative pancreatic fistula after robotic pancreatoduodenectomy. BJS Open. 2025;9(3):zraf036. doi:10.1093/bjsopen/zraf036.
12. Nguyen JH. Distinguishing between parenchymal and anastomotic leakage in pancreatic reconstruction. World J Gastroenterol. 2008;14:6648-54. doi:10.3748/wjg.14.6648.
13. Mahvi D. Defining, controlling, and treating a pancreatic fistula. J Gastrointest Surg. 2009;**13**:1187–1188. doi: 10.1007/s11605-009-0867-x.
14. Zureikat AH, Beane JD, Zenati MS, Al Abbas AI, Boone BA, Moser AJ, et al. 500 minimally invasive robotic pancreaticoduodenectomies: a decade of optimizing performance. Ann Surg. 2021;273:966–972. doi: 10.1097/SLA.0000000000003550
15. Ingwersen EW, Stam WT, Meijs BJV, Roor J, Besselink MG, Groot Koerkamp B, et al. Machine learning vs logistic regression for predicting complications after pancreaticoduodenectomy. Surgery. 2023;174:435-40. doi:10.1016/j.surg.2023.03.012.
16. Gu Z, Du Y, Wang P, Zheng X, He J, Wang C, et al. Nomogram for predicting pancreatic fistula after PD using Lasso-logistic regression. Int J Surg. 2023;109:4027-40. doi:10.1097/JS9.0000000000000695.
17. Dugalic VD, Knezevic DM, Obradovic VN, et al. Drain amylase value as an early predictor of pancreatic fistula after cephalic duodenopancreatectomy. World J Gastroenterol. 2014;20(26):8691-9. doi:10.3748/wjg.v20.i26.8691.
18. Giglio MC, Spalding DR, Giakoustidis A, Zarzavadjian Le Bian A, Jiao LR, Habib NA, et al. Meta-analysis of drain amylase POD1 and pancreatic fistula. Br J Surg. 2016;103(4):328-36. doi:10.1002/bjs.10090.
19. Lu X, Wang X, Fang Y, Chen H, Peng C, Li H, et al. POD1 drain amylase after pancreatic resection to predict fistula: meta-analysis. Medicine (Baltimore). 2016;95(5):e2569. doi:10.1097/MD.0000000000002569.
20. Bat-Ulzii T, Yaghoobi M, Davidson BR, Gurusamy KS. Amylase in drain fluid for diagnosis of pancreatic leak after surgery. Cochrane Database Syst Rev. 2017;4:CD012009. doi: 10.1002/14651858.CD012009.pub2.
21. Lee SR, Kim HO, Shin JH. Significance of drain amylase check on day 3 after pancreatectomy. ANZ J Surg. 2019;89(5):497-502. doi:10.1111/ans.15025.
22. Caputo D, Angeletti S, Ciccozzi M, Cartillone M, Cascone C, La Vaccara V, et al. Role of drain amylase and routine POD3 CT after pancreaticoduodenectomy. Updates Surg. 2020;72(3):727-41. doi:10.1007/s13304-020-00784-9.
23. Anderson RJ, Dunki-Jacobs E, Callender GG, Burnett N, Scoggins CR, McMasters KM, et al. Clinical evaluation of somatostatin use in pancreatic resections. Surgery. 2013;154(4):755-60. doi:10.1016/j.surg.2013.07.001.

24. Zaghal A, Tamim H, Habib S, Jaafar R, Mukherji D, Khalife M, et al. Drain or no drain after pancreaticoduodenectomy: unresolved dilemma. Scand J Surg. 2020;109(3):228-37. doi:10.1177/1457496919840960.
25. Bassi C, Molinari E, Malleo G, Crippa S, Butturini G, Salvia R, et al. Early vs late drain removal after pancreatic resections: randomized trial. Ann Surg. 2010;252(2):207-14. doi:10.1097/SLA.0b013e3181e61e88.