**Cukurova Medical Journal**
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2019;44(2):594-601
DOI: 10.17826/cumj.450246

**ARAŞTIRMA / RESEARCH**

# Impact of high amylase level in drainage fluid after gastric cancer surgery: Is it a complication or suspicious biochemical measurement?

## Mide kanser cerrahisi sonrası dren sıvısındaki yüksek amilaz değerinin etkisi: Bu bir komplikasyon mu yoksa sadece şüpheli biyokimyasal bir ölçüm mü?

Mustafa Hasbahçeci[1], Merve Büşra Cengiz[2], Adem Akçakaya[3], Fatma Ümit Malya[3], Enver Kunduz[3], Hüseyin Kazım Bektaşoğlu[3]

[1]Medical Park Fatih Hastanesi Genel Cerrahi Kliniği, İstanbul, Turkey
[2]Yozgat Devlet Hastanesi Genel Cerrahi Kliniği, Yozgat, Turkey
[3]Bezmialem Vakıf Üniversitesi Tıp Fakültesi, Genel Cerrahi Anabilim Dalı, İstanbul, Turkey

*Cukurova Medical Journal 2019;44(2):594-601*

**Abstract**

**Purpose:** Pancreatic fistula is a potential postoperative complication with variable definitions, incidences and risk factors. We intended to evaluate its impact after gastric surgery.

**Materials and Methods:** A total of 28 consecutive patients who underwent curative open gastrectomy with lymphadenectomy for gastric adenocarcinoma were retrospectively analyzed. Patients' demographics, peri-operative and pathological data were collected. Pancreatic fistula that was diagnosed and graded according to International Study Group of Pancreatic Fistula's system was identified as main variable.

**Results:** Mean age of patients was 58.8±10.1 years with a female to male ratio of 9/19. Grade A pancreatic fistula was diagnosed in six patients (21.4%). There was no grade B and C pancreatic fistula. Drain amylase level was significantly higher in patients with pancreatic fistula. There was no significant difference with regard to amount of drainage, length of hospital stay and duration of drains in patients with and without fistula. No significant association was shown between development of fistula and patients' demographics, peri-operative and pathological data.

**Conclusion:** The development of grade A pancreatic fistula after gastric surgery does not appear to be a major complication with clinical consequences. High amylase level in the drainage fluid can be considered as a biochemical measure only.

**Keywords:** Gastrectomy, gastric cancer, amylase level, drainage fluid, pancreatic fistula.

**Öz**

**Amaç:** Pankreatik fistülün, olası bir postoperatif komplikasyon olarak, değişkenlik gösteren tanım, görülme sıklığı ve risk faktörleri vardır. Bu çalışmada, mide cerrahisi sonrası pankreatik fistülün etkisini değerlendirmeyi amaçladık.

**Gereç ve Yöntem:** Mide adenokarsinomu için tedavi edici amaçlı lenfadenektomi ile açık gastrektomi uygulanan toplam 28 ardışık hasta retrospektif olarak incelendi. Hastaların demografik, peri-operatif ve patolojik verileri toplandı. Uluslararası Pankreatik Fistül Sistemi çalışma grubuna göre teşhis ve derecelendirilen pankreas fistülü ana değişken olarak tanımlandı.

**Bulgular:** Hastaların yaş ortalaması 58,8 ± 10,1yıl idi ve kadın / erkek oranı 9 / 19'du. Altı hastada (% 21.4) grade A pankreatik fistül saptandı. Grade B ve C pankreatik fistül yoktu. Dren amilaz düzeyi pankreas fistülü olan hastalarda anlamlı olarak daha yüksekti. Fistüllü ve fistülsüz hastalarda drenaj miktarı, hastanede kalış süresi ve dren süreleri açısından anlamlı fark yoktu. Fistül gelişimi ile hastaların demografik özellikleri, peri-operatif ve patolojik veriler arasında anlamlı ilişki bulunmadı.

**Sonuç:** Mide cerrahisi sonrası grade A pankreatik fistül gelişimi klinik sonuçları olan majör bir komplikasyon olarak görünmemektedir. Dren sıvısındaki yüksek amilaz seviyesi, sadece biyokimyasal bir ölçü olarak düşünülebilir.

**Anahtar kelimeler**: Gastrektomi, gastrik kanser, amilaz seviyesi, dren sıvısı, pankreas fistülü

Yazışma Adresi/Address for Correspondence: Dr. Mustafa Hasbahçeci, [1]Medical Park Fatih Hastanesi Genel Cerrahi Kliniği, İstanbul, Turkey E-mail: hasbahceci@yahoo.com
Geliş tarihi/Received: 01.08.2018 Kabul tarihi/Accepted: 21.11.2018 Çevrimiçi yayın/Published online: 23.03.2019

## INTRODUCTION

Gastric cancer remains the second-leading cause of the death, although its incidence has shown to decline in recent years[1]. Gastrectomy with radical lymph node dissection has been still considered as the standard treatment and it offers a better survival for gastric cancer compared with chemotherapy and radiotherapy[2]. D2 lymphadenectomy alone or in combination with splenectomy, or distal pancreatectomy has been regarded to be responsible for several complications including anastomotic leakage and postoperative pancreatic fistula (POPF)[3-5]. Intraabdominal abscess, sepsis, and severe pseudoaneurysmal bleedings may also develop as consequences of POPF[4]. Therefore, due to the possibility of POPF after gastrectomy in association with lymphadenectomy even without pancreatic resection, surgeons should give maximum attention to prevent these complications.

POPF is still one of the most serious potential complications after radical lymph node dissection associated with gastrectomy[3]. However, even in high-volume centers with experienced surgeons, the incidence of pancreatic fistula has been reported ranging from 5.8% to 49.7 %[6, 7]. It has been thought that these highly variable rates are due to the use of different definitions. Therefore, use of the same definition and diagnostic criteria may help to clarify the incidence of POPF.

It has been speculated that the development of POPF might be associated with several surgery- and host-related factors. It has been shown that higher incidence of POPF might be seen in the presence of radical lymph node dissection and pancreaticosplenectomy[8, 9]. In previous studies, higher body mass index (BMI), higher visceral fatty area, male gender, hyperlipidemia and comorbidities have been shown to be significantly correlated with the occurrence of POPF[4, 7].Therefore, prediction of POPF following gastric surgery using several clinical and biochemical indicators may have positive impact on early diagnosis and prevention of consequences of POPF.

Beside there have been many classification systems for postoperative complications i.e. Clavien and Dindo, the International Study Group of Pancreatic Fistula (ISGPF) developed a universal definition for pancreatic fistula as drain output of any measurable volume of fluid on or after postoperative day 3 with an amylase content >3 times the upper normal serum amylase activity and divided POPF into three degrees of severity[4, 5, 10]. Although there is a general consensus on the use of this definition and grading system for POPF after pancreatic and gastric surgery, the impact on gastric surgery may be questioned due to the lack of clinical relevance of Grade A POPF[4]. Additionally, there have been several studies with variable timing of amylase measurement starting from the postoperative first day[11].

The aim of the present study was to detect the incidence of POPF after gastrectomy with radical lymph node dissection according to ISGPF classification based on the postoperative second day and to evaluate the risk factors to predict the grades of POPF in relation to the treatment modalities within the postoperative first month.

## MATERIALS AND METHODS

From April 2015 to December 2015, 51 consecutive patients who underwent curative open gastrectomy with lymphadenectomy for histologically proven gastric adenocarcinoma were included. All data were prospectively collected and retrospectively analyzed. The study was performed according to the declaration of Helsinki, and approved by the local ethical committee. Signed informed consent was taken from all patients. The study was registered to "researchregistry" with an ID number of 2022.

Patients with metastatic disease (n=12), gastroesophageal junction tumors (n=4) and emergent admission (n=2) and with missing laboratory data (n = 5) were excluded. Therefore, a total of 28 patients were included in the study.

A worksheet including patients' demographics (age, gender, BMI), peri-operative data (type of operation, length of hospital stay, development of postoperative complications) and pathological data (tumor size, tumor grade, TNM classification, number of total and metastatic lymph nodes) was used. The amount of drainage was measured until the drain was removed. Drain and serum amylase values were detected at the second postoperative day.

### Surgical procedures

All patients were operated through laparotomy. The peritoneal cavity was washed with 200 ml of saline, and at least one third of this washing was sampled for histopathological examination. Based on the pre-

operative and intra-operative evaluation, total or subtotal gastrectomy with D2 lymphadenectomy was performed according to the Japanese guidelines for the treatment of gastric cancer by the same surgical team (MH, AA)[12]. For D2 lymphadenectomy, all perigastric lymph nodes and the lymph nodes associated with major vascular structures (for distal subtotal and total gastrectomy, numbers 7-9, 11p, 12a and numbers 7-11, 12a, respectively) were completely dissected. After distal subtotal or total gastrectomy, reconstruction was performed via retrocolic Roux-en-Y gastro- or esophagojejunostomy. During bursectomy, the entire posterior leaf of the peritoneum covering the lesser sac over the transverse mesocolon with the pancreatic capsule was excised en bloc.

Before closing the abdomen, two drainage silicone tubes were placed in the left subphrenic cavity and Winslow's cavity for total gastrectomy and only one in Winslow's cavity for distal gastrectomy. Depending on the clinical evaluation, the drainage tubes were removed on the 5th or 6th postoperative day.

### Definition of POPF

The level of amylase in the drainage fluid and serum of the patients were measured on the 2nd postoperative day. The ISGPF classification, except for the amylase drain measurement schedule, was used to define and record POPF: drain output of any measurable volume on or after postoperative day 2, with amylase content more than 3 times higher than the upper limit of institutional normal serum amylase activity (>381 IU/ml)[2, 10]. Other diagnostic criteria including clinical findings, laboratory data, and imaging findings were not used. The presence of a biochemical leakage, classified as grade A (formerly transient fistula), was defined as a pancreatic amylase output from the drain placed during the surgery higher than three times the upper normal serum level on the second postoperative day or later, without any clinical impact. A clinically significant grade B pancreatic fistula was present if there was any change in the postoperative management, for example if drains were either left in place more than 3 weeks or repositioned through endoscopic or percutaneous procedures. A grade C fistula corresponded to the occurrence of severe clinical repercussions requiring reoperation or lead to single or multiple organ failure and/or mortality attributable to the pancreatic fistula[1, 5, 10]. Severe POPF were regarded as the cases with grade B or C pancreatic fistula.

### Statistical analysis

Development of postoperative pancreatic fistula was identified as the main variable. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 22.0 (IBM SPSS, New York, USA). Kolmogorov-Smirnov test and histograms were used to assess normal distributions of the variables. Normally-distributed continuous variables were expressed as mean ± standard deviation. Continuous variables without normal distribution and categorical variables were expressed as median with minimum and maximum values and frequencies with percentages, respectively. Characteristics of the study and control groups were compared using the t-test and Mann-Whitney U test for normally distributed continuous variables and continuous variables without normal distribution, respectively. For comparison of categorical variables, Fisher's exact and Pearson chi square tests were used. The statistical results were presented at a 95% confidence interval. The differences were considered statistically significant if the p value was less than 0.05.

## RESULTS

There were a total of 28 patients with gastrectomy plus lymphadenectomy with a mean age of 58.8±10.1 years. Female to male ratio was 9/19. The mean BMI was 26.6±4.2 kg/m$^2$. Distal and total gastrectomy was performed in 13 (46.4%) and 15 patients (53.6%), respectively. Simultaneous splenectomy and cholecystectomy were performed in two patients and one patient, respectively. The length of hospital stay was 6.7±1.0 days. There was no complication during the first postoperative month, except for superficial surgical site infection in two patients. No mortality was seen.

Grade A POPF was seen in six patients (21.4%). The level of drain amylase in patients with and without POPF was 1,463.3±938.5 IU/ml (522-2,764 IU7ml) and 121.8±81.2 IU/ml (range 29-356 IU/ml) (p=0.0001) (Table 1). Serum amylase levels in patients with and without POPF were similar (62.6±35.2 IU/ml and 41.3±22.6 IU/ml, respectively) (p=0.194). Severe POPF (Grade B or Grade C) didn't occur. The mean amount of drainage per day for all patients and the mean duration of the drains were 103.7±75.7 ml and 5.5±1.2 days, respectively. However, there was no significant difference with regard to the amount of drainage,

length of hospital stay and the duration of the drains in patients with and without POPF (Table 1).

The mean diameter of the tumors was 52.9±26.4 mm. Stage III was the most common stage (50%) (Table 2). With regard to T and N stages, T3 and N3 were seen in 14 (50%) and 9 patients (32.1%), respectively. Mean numbers for total and metastatic lymph nodes were 29.9±10.6 and 6.5±7.2, respectively. R0 resection was accomplished in all except three patients (89.3%) whom peritoneal washing cytology was positive (10.7%).

There was no impact of the patients' demographics (age, gender, BMI), tumor size and the lymph node numbers on the development of POPF (Table1). There was also no association between POPF and tumor grade, T, N and TNM stages (p=0.775, p=0.774, p=0.274 and p=0.260, respectively)

**Table 1. Clinicopathological features of the patients with and without POPF.**

| Variable | Patients with POPF (n=6) | Patients without POPF (n=22) | p |
|---|---|---|---|
| Age (year) [α] | 60.3±10.9 | 58.4±10.4 | 0.686 |
| Gender (Male/Female) | 4/2 | 15/7 | 0.944 |
| BMI (kg/m$^2$) [α] | 26.2±3.1 | 26.7±4.5 | 0.814 |
| Drain amylase (IU/ml) [β] | 1,463.3±938.5<br>1,138 (522-2,764) | 121.8±81.2<br>90 (29-356) | 0.0001 |
| Serum amylase (IU/ml) [β] | 41.33±22.5<br>48 (15-74) | 62.6±35.2<br>46 (21-161) | 0.179 |
| Amount of drainage/day (ml) | 96.0±30.3<br>96.1 (66-149.3) | 105.8±82.8<br>72.5 (19.1-357) | 0.823 |
| Duration of drain/s (day) [α] | 5.7±1.0 | 5.5±1.3 | 0.769 |
| Length of hospital stay (day) [α] | 7.0±1.3 | 6.7±1.3 | 0.727 |
| Tumor diameter (mm) [α] | 55.8±32.6 | 52.1±25.9 | 0.771 |
| Total lymph node number [β] | 32.7±10.1<br>31 (19-31) | 29.1±11.0<br>26 (0-61) | 0.281 |
| Metastatic lymph node number [β] | 6.2±11.5<br>1 (0-29) | 6.7±6.2<br>4 (0-19) | 0.261 |

[α]: mean±standard deviation; [β]: mean±standard deviation, median (min-max)

**Table 2. Pathological features of the patients.**

| Feature | | N (%) |
|---|---|---|
| Tumor grade | Well differentiated | 1 (3.6) |
| | Moderate differentiated | 7 (25.0) |
| | Undifferentiated/signet ring cell | 20 (71.4) |
| T stage | 1a | 2 (7.1) |
| | 1b | 1 (3.6) |
| | 2 | 2 (7.1) |
| | 3 | 14 (50.0) |
| | 4a | 9 (32.2) |
| N stage | 0 | 6 (21.4) |
| | 1 | 5 (17.85) |
| | 2 | 8 (28.6) |
| | 3a | 5 (17.85) |
| | 3b | 4 (14.3) |
| TNM stage | 1a | 2 (7.1) |
| | 1b | 0 (0) |
| | 2a | 5 (17.9) |
| | 2b | 4 (14.3) |
| | 3a | 6 (21.4) |
| | 3b | 5 (17.9) |
| | 3c | 3 (10.7) |
| | 4 | 3 (10.7) |

## DISCUSSION

Gastrectomy with D2 lymph node dissection is the standard procedure for the treatment of gastric cancer worldwide[13, 14]. Although radical lymphadenectomy for surgical treatment of gastric cancer has not been performed routinely in Western countries up to the recent years, it has been referred as the standard treatment for advanced gastric cancer according to the clinical guidelines of European Society of Medical Oncology in 2010[15]. While D2 lymphadenectomy has an important role for local control of gastric cancer, it is important to comprehend complications following lymph node dissection[15]. Surgical complications cannot be completely avoided even in the presence of meticulous care during surgery[4]. The morbidity of open total gastrectomy ranges from 5.4 to 37.2% and its mortality rate is approximately 1%[2, 16]. When extended lymph node dissection beyond D2 is added, the incidence of complications after gastrectomy increases[17, 18]. Therefore, it has been shown that the incidence of complications after gastrectomy is directly related with the extent of the surgery. Additionally, pancreatic resection in association with gastrectomy has been shown to be an important and inevitable risk factor for POPF[5, 7]. During the evaluation of POPF after gastrectomy, exclusion of these cases may help physicians to predict more accurate risk factors. Although small study group and absence of concurrent pancreatic resection in the present study prevent to perform detailed analysis, future studies are needed to clarify the exact incidence and risk factors of POPF after gastrectomy alone.

The complications after gastrectomy mostly resolved with conservative treatment[2]. But, some major complications need active interventions including reoperation. One of the most frequent major complications after D2 or more extended lymphadenectomy is the development of pancreatic fistula[17]. Because POPF are potentially lethal, early detection and appropriate management are essential[15]. In Yu's study[2], it has been reported that the incidence of POPF ranges from 13% to 22.1% depending on the type of surgery and stage of the disease following open gastrectomy based on the previous studies. Authors also mentioned their POPF rates as 6.86% in open gastrectomy, and 13.8% in total gastrectomy[2]. The incidence of POPF is highest when the distal pancreas is co-resected with the spleen[17, 18]. The Italian Gastric Cancer Study Group study showed that D2 dissection could be performed safely without splenectomy and distal pancreatectomy[19]. The inadequacy of pretrial training in D2 dissection might explain higher complication rates in the South African, Dutch, UK, and Hong Kong trials, compared with their Italian and Taiwanese counterparts[19]. In the present study, the incidence of POPF was detected as 21.4% and all of them were grade A. Although the incidence was thought to be higher than the rates published previously, all of them were Grade A. Therefore, definition and clinical significance of this complication should be questioned by future prospective studies with inclusion of larger number of patients from both Eastern and Western countries.

Classification of ISGPF consists of three severity groups from grade A to Grade C[3,6,10,14,17]. Sano et al.[6] described an amylase level in the drain ≥ 4000 IU / L on the first postoperative day after gastrectomy as the best threshold value for developing pancreatic fistula. In Miki's study[15], it was shown that high drain level of amylase at the first postoperative day (≥3398 IU / L) revealed the best threshold value for predicting grade B or higher POPF. They also studied the drain amylase level on the first postoperative day[15]. In a recent study, it has been believed that drain amylase levels higher than 2000 IU/L on the first postoperative day would serve as a warning sign to predict POPF[4]. In Taniguchi's study[20], it has been shown that splenectomy is an independent risk factor for POPF and an amylase level of 2100 U/L on POD 3 may be regarded as an early indicator for severe POPF. As opposed to those studies, the measurement of drain amylase level was performed on the second postoperative day in the present study and none of our patients have had drain amylase level more than 2800 IU/L. Although it may be expected to see some degree of correlation between drain amylase levels and severity of POPF, s significant variation from the first to the fifth postoperative days during the measurement of drain amylase levels has been shown in Kobayashi's study[4]. Use of only drain amylase level to predict the severity of POPF has been questioned by the authors. Therefore, a combination of several predictive markers i.e. drain amylase and C-reactive protein, enables the physicians to select more accurately the postoperative management of their patients, in other words to decide timing of insertion of drains or prolonged delivery of antibiotics[4, 21]. Our study could not solve the controversy about the timing of drain amylase

measurements; this question will necessitate future studies to be answered.

In accordance with these controversial issues, 2005 version of ISGPF definition of pancreatic fistula after pancreatectomy has been currently revised[10, 22]. According to this new classification, grade A POPF has been re-named as biochemical leak only. It has been mentioned that although high amylase level in drainage fluid only cannot be regarded as fistula, it also cannot be ignored due to its possible clinical implications. Another striking point that was reported in this study is that the great differences with regard to the rates of grade A POPF from zero to 50 %[10]. It has been thought that this difference was originated from the different approaches of usage of drains and sampling of drain fluid for amylase.

It has been recommended that it is eligible to remove the drains early in the absence of elevation of these parameters from the point of avoidance of retrograde infection[4]. In Kung's study[5], it has been reported that the prophylactic drain is used in only 71% of the cases. In this study, placement of the drains was performed in all patients, and the drains were placed in their localizations up to the exclusion of POPF and anastomotic problems. So, prophylactic use of drainage tubes may be recommended to diagnose and treat future POPF following gastrectomy with D2 lymphadenectomy in all patients[17]. So, it has been concluded that grade A POPF was redefined as biochemical leak without clinical importance and is no longer referred to a true pancreatic fistula.

In our study, it was observed that the POPF was seen in 6 out of 28 patients with the severity of grade A. In a recent study, POPF diagnosis of ISGPF grades A and B was found to be 33.7% and 22.1%, respectively[15]. Considering ISGPF classification, grade A is not clinically important because they have only abnormal laboratory data and any further treatment is not needed[10, 15]. On the other hand, the origin of high drain amylase level cannot be specified exactly if it is related to disrupted lymphatic vessels or from the damaged pancreas itself[15]. Therefore, a new subclassification of grade A i.e. grade A- high amylase level in drainage fluid as a biochemical measurement only, may be needed to define the situations in which only high drain amylase level is detected without any clinical signs in accordance with the new definition of ISGPF[10].

We did not demonstrate a relation between the development of POPF and other related factors. In some studies, it has been proposed that the risk of pancreatic fistula formation is influenced by the patient's BMI and the extent of the surgical procedures[6]. In addition, no significant association has been detected between BMI and abdominal shape indexes and postoperative complications including POPF in another study performed by the same surgical team[23]. After total gastrectomy, Katai et al. [24] reported the risk factors for POPF as the age, BMI, and the dissection of the lymph nodes along the distal splenic artery. On the other hand, Nobuoka et al. [9] analyzed causes of POPF on 740 gastric cancer patients who underwent total gastrectomy, and they found that obesity and pancreatic transection (due to pancreatosplenectomy) were correlated with development of POPF. Tanaka et al. [2] identified visceral fat area and splenectomy as the significant predictors of POPF. In another study, it was found that the proportion of the patients who develop POPF after total gastrectomy alone was considerably low, whereas the rate was relatively higher in patients who underwent more aggressive surgery. Additionally, they also reported that calculated visceral fat area was a significant risk factor for POPF[25]. Bursectomy may be another potential risk factor for pancreatic fistula formation due to the increased risk of damaging the pancreatic tissue, but this was not demonstrated in a recent randomized study from Japan comparing gastrectomy with and without bursectomy[5, 26]. Although it has been also speculated that low blood lymphocyte counts and upper abdominal body shape may be regarded as risk factors for POPF, more studies from both Western and Eastern countries are needed to clarify the risk factors for POPF[7, 13].

Although a prospectively held database was used for this study, retrospective design of the study with inclusion of small number of the cases was a major limitation. In this study, we aimed to evaluate the use of drain amylase level for the diagnosis of POPF. For this reason, we used drain amylase level only at the postoperative second day besides widespread use of the definition of pancreatic fistula diagnosed via drain amylase level at the postoperative third day. However, prospective studies comparing the diagnostic efficiency of measurement of drain amylase levels at the postoperative second, third and fourth days are needed. Furthermore, the findings obtained in this study may be considered to be the same as ISGPF. Considering the time period for the present study, it can been seen that similar hypothesis were taken into account. However, due to antecedent

publication of ISPGF, our findings have been regarded as only supportive.

In conclusion, although development of POPF after gastric surgery is not a rare event, it does not seem to be a major complication with clinical consequences due to the domination of Grade A POPF on the most severe types. High amylase level in drainage fluid without clinical consequences may not be considered a grade A POPF complication. Instead, it can be regarded as a biochemical measurement only.

**Yazar Katkıları:** Çalışma konsepti/Tasarımı: MH, AA, MBC, FÜM; Veri toplama: MBC, FÜM, EK, HKB; Veri analizi ve yorumlama: MH, MBC; Yazı taslağı: MH, MBC; İçeriğin eleştirel incelenmesi: FÜM, EK, HKB; Son onay ve sorumluluk: MH, MBC, AA, FÜM, EK, HKB; Teknik ve malzeme desteği: FÜM, EK, HKB; Süpervizyon: MH, AA; Fon sağlama (mevcut ise): yok.
**Bilgilendirilmiş Onam:** Katılımcılardan yazılı onam alınmıştır.
**Hakem Değerlendirmesi:** Dış bağımsız.
**Çıkar Çatışması:** Yazarlar çıkar çatışması beyan etmemişlerdir.
**Finansal Destek:** Yazarlar finansal destek beyan etmemişlerdir.

**Author Contributions:** Concept/Design :MH, AA, MBC, FÜM; Data acquisition: MBC, FÜM, EK, HKB; Data analysis and interpretation: MH, MBC; Drafting manuscript: MH, MBC; Critical revision of manuscript: FÜM, EK, HKB; Final approval and accountability: MH, MBC, AA, FÜM, EK, HKB; Technical or material support: FÜM, EK, HKB; Supervision: MH, AA; Securing funding (if available): n/a.
**Informed Consent:** Written consent was obtained from the participants.
**Peer-review:** Externally peer-reviewed.
**Conflict of Interest:** Authors declared no conflict of interest.
**Financial Disclosure:** Authors declared no financial support

## REFERENCES

1. Seo HS, Shim JH, Jeon HM, Park CH, Song KY. Postoperative pancreatic fistula after robot distal gastrectomy. J Surg Res. 2015;194:361-6.
2. Yu HW, Jung DH, Son SY, Lee CM, Lee JH, Ahn SH et al. Risk factors of postoperative pancreatic fistula in curative gastric cancer surgery. J Gastric Cancer. 2013;13:179-84.
3. De Sol A, Cirocchi R, Di Patrizi MS, Boccolini A, Barillaro I, Cacurri A et al. The measurement of amylase in drain fluid for the detection of pancreatic fistula after gastric cancer surgery: an interim analysis. World J Surg Oncol. 2015;13:65.
4. Kobayashi D, Iwata N, Tanaka C, Kanda M, Yamada S, Nakayama G et al. Factors related to occurrence and aggravation of pancreatic fistula after radical gastrectomy for gastric cancer. J Surg Oncol. 2015;112:381-6.
5. Kung CH, Lindblad M, Nilsson M, Rouvelas I, Kumagai K, Lundell L et al. Postoperative pancreatic fistula formation according to ISGPF criteria after D2 gastrectomy in Western patients. Gastric Cancer. 2014;17:571-7.
6. Hiura Y, Takiguchi S, Yamamoto K, Kurokawa Y, Yamasaki M, Nakajima K et al. Use of fibrin glue sealant with polyglycolic acid sheets to prevent pancreatic fistula formation after laparoscopic-assisted gastrectomy. Surg Today. 2013;43:527-33.
7. Komatsu S, Ichikawa D, Kashimoto K, Kubota T, Okamoto K, Konishi H et al. Risk factors to predict severe postoperative pancreatic fistula following gastrectomy for gastric cancer. World J Gastroenterol. 2013;19:8696-702.
8. Bonenkamp JJ, Songun I, Hermans J, Sasako M, Welvaart K, Plukker JT et al. Randomised comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. Lancet. 1995;345:745-8.
9. Nobuoka D, Gotohda N, Konishi M, Nakagohri T, Takahashi S, Kinoshita T. Prevention of postoperative pancreatic fistula after total gastrectomy. World J Surg. 2008;32:2261-6.
10. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. Surgery. 2017;161:584-91.
11. Miyai H, Hara M, Hayakawa T, Takeyama H. Establishment of a simple predictive scoring system for pancreatic fistula after laparoscopy-assisted gastrectomy. Dig Endosc. 2013;25:585-92.
12. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. Gastric Cancer. 2011;14:101-12.
13. Yamamoto N, Oshima T, Sato T, Makino H, Nagano Y, Fujii S et al. Upper abdominal body shape is the risk factor for postoperative pancreatic fistula after splenectomy for advanced gastric cancer: a retrospective study. World J Surg Oncol. 2008;6:109.
14. Kodera Y, Sasako M, Yamamoto S, Sano T, Nashimoto A, Kurita A. Gastric Cancer Surgery Study Group of Japan Clinical Oncology Group. Identification of risk factors for the development of complications following extended and superextended lymphadenectomies for gastric cancer. Br J Surg. 2005;92:1103-9.
15. Miki Y, Tokunaga M, Bando E, Tanizawa Y, Kawamura T, Terashima M. Evaluation of postoperative pancreatic fistula after total gastrectomy with D2 lymphadenectomy by ISGPF classification. J Gastrointest Surg. 2011,15:1969-76.
16. Nakauchi M, Suda K, Kadoya S, Inaba K, Ishida Y, Uyama I. Technical aspects and short- and long-term outcomes of totally laparoscopic total gastrectomy for advanced gastric cancer: a single-institution retrospective study. Surg Endosc. 2016;30:4632-9.
17. Sasako M, Katai H, Sano T, Maruyama K. Management of complications after gastrectomy with extended lymphadenectomy. Surg Oncol. 2000;9:31-4.
18. Jiang X, Hiki N, Nunobe S, Kumagai K, Nohara K, Sano T et al. Postoperative pancreatic fistula and the risk factors of laparoscopy-assisted distal gastrectomy for early gastric cancer. Ann Surg Oncol. 2012;19:115-21.

19. Jiang L, Yang KH, Chen Y, Guan QL, Zhao P, Tian JH et al. Systematic review and meta-analysis of the effectiveness and safety of extended lymphadenectomy in patients with resectable gastric cancer. Br J Surg. 2014;101:595-604.
20. Taniguchi Y, Kurokawa Y, Mikami J, Tanaka K, Miyazaki Y, Makino T et al. Amylase concentration in drainage fluid as a predictive factor for severe postoperative pancreatic fistula in patients with gastric cancer. Surg Today. 2017;47:1378-83.
21. Matsunaga T, Saito H, Murakami Y, Kuroda H, Fukumoto Y, Osaki T. Serum level of C-reactive protein on postoperative day 3 is a predictive indicator of postoperative pancreatic fistula after laparoscopic gastrectomy for gastric cancer. Asian J Endosc Surg. 2017;10:382-7.
22. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery. 2005;138:8-13.
23. Hasbahceci M, Mehdi E, Malya FU, Kunduz E, MemmI N, YIgman S et al. Role of obesity and abdominal shape morphometric features to predict postoperative complications and quality of lymph node dissection of gastrectomy for gastric cancer. Neoplasma. 2017;64:922-32.
24. Katai H, Yoshimura K, Fukagawa T, Sano T, Sasako M. Risk factors for pancreas-related abscess after total gastrectomy. Gastric Cancer. 2005;8:137-41.
25. Tomimaru Y, Miyashiro I, Kishi K, Motoori M, Yano M, Shingai T et al. Is routine measurement of amylase concentration in drainage fluid necessary after total gastrectomy for gastric cancer? J Surg Oncol. 2011,104:274-7.
26. Imamura H, Kurokawa Y, Kawada J, Tsujinaka T, Takiguchi S, Fujiwara Y, et al. Influence of bursectomy on operative morbidity and mortality after radical gastrectomy for gastric cancer: results of a randomized controlled trial. World J Surg. 2011;35:625-30.