

Effect of Covid-19 pandemic on pancreatic cancer surgery

Covid-19 pandemisinin pankreas kanseri cerrahisine etkisi

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ÖZET

AMAÇ: Covid-19 salgını sırasında yaşanan kaos, yeni tanı konulan ve tedavi altındaki pankreas kanseri hastalarının tedavilerinde aksamalara neden olmuştur. Ayrıca pankreas tümörlerinin tanısının gecikmesine ve dolayısıyla planlanacak tedavilerin de değişmesine neden oldu. Bu nedenlerden dolayı bu dönemde pankreas ameliyatı geçiren hastalarda daha fazla sorun ortaya çıkabilmektedir. Bu çalışmada, kanser tanısı veya şüphesi nedeniyle pankreas ameliyatı geçiren hastaların, Covid-19 salgını öncesinde ve sırasında ameliyat sonrası morbidite ve mortalitelerini karşılamayı amaçladık.

GEREÇ VE YÖNTEM: 2017-2022 yılları arasında pankreas kanseri nedeniyle pankreas ameliyatı geçiren hastaların verileri prospektif olarak kaydedildi. Ameliyat sırasında inoperabl kabul edilen veya palyatif cerrahi uygulanan hastalar çalışma dışı bırakıldı. Toplam 226 hasta çalışmaya dahil edildi. Covid öncesi grupta 142, Covid sonrası grupta ise 84 pankreas kanseri hastası yer aldı.

BULGULAR: Covid-19 pandemi döneminde pankreas kanserli hastalarda ameliyat öncesi biliyer stent veya perkütan safra drenajı işlemlerinin Covid öncesi gruba göre daha sık uygulandı. Covid öncesi grupta 31 (%28,1) hastaya, Covid sonrası grupta ise 32 (%46,3) hastaya safra drenaj işlemi uygulandı (p=0,013). Covid öncesi grupta 5 hastaya (%3,5), Covid sonrası grupta 15 hastaya (%17,8) neoadjuvan tedavi uygulandı (p=0,000). Post-Covid grubundaki hastaların istatistiksel olarak da anlamlı ölçüde daha fazla neoadjuvan kemoterapi gördü. Covid öncesi grupta 14 (%9,8) hastaya, Covid sonrası grupta ise 16 (%19) hastaya intraoperatif vasküler rezeksiyon uygulandı. Post-Covid grubunda vasküler rezeksiyon oranı istatistiksel olarak anlamlı derecede yüksekti (p=0,049). Covid öncesi grupta 9 (%6,3) hastaya, Covid sonrası grupta ise 12 (%14,2) hastaya ekstra-organ rezeksiyonu yapıldı. Ekstra-organ rezeksiyonu, Covid sonrası grupta, Covid öncesi gruba göre anlamlı derecede yüksekti (p=0,047).

SONUÇ: Çalışmamızda pankreas tümörlü hastalarda Covid-19 pandemisinde, biliyer stent yerleştirilmesi, perkütan safra drenajı, neoadjuvan tedavi uygulaması ve vasküler/ekstraorgan rezeksiyonu yapılan hasta sayısında artış gözlemlendi.

Anahtar kelimeler: Covid-19 pandemisi, pankreas kanseri, neoadjuvan kemoterapi

ABSTRACT

AIM: The chaos experienced during the Covid-19 pandemic caused disruptions in the treatments of pancreatic cancer patients; both the ones who were newly diagnosed and the ones who had ongoing treatments. In this study, we aim to compare postoperative morbidity and mortality of patients who had pancreatic surgery due to diagnosis or suspect of cancer before and during Covid-19 pandemic.

MATERIAL AND METHOD: Data of patients who had pancreatic surgery due to pancreas cancer between 2017-2022 were recorded prospectively. A total of 226 patients were included. There were 142 patients in Pre-Covid group, and 84 patients with pancreas cancer in the Post-Covid group. Patients who were accepted as inoperative during surgery or the ones who had palliative surgery were excluded.

RESULTS: Preoperative biliary stent or percutaneous biliary drainage procedures were compared in patients with pancreatic cancers and these were performed more often in Post-Covid group than in Pre-Covid group during pandemic period. Biliary drainage was performed to 31 patients in Pre-Covid group (28.1%), and 32 (46.3%) patients in Post-Covid group (p=0.013). Five patients (3.5%) in Pre-Covid group, 15 patients (17.8%) in Post-Covid group had neoadjuvant therapy (p=0.000). Patients in Post-Covid group had significantly more neoadjuvant chemotherapy. Vascular resection was performed for 14 patients (9.8%) in Pre-Covid group, and 16 (19%) patients in Post-Covid group. Rate of vascular resection was significantly higher in Post-Covid group (p=0.049). Nine (6.3%) patients in Pre-Covid group, and 12 (14.2%) patients in Post-Covid group had extra-organ resection. Extra-organ resection was significantly higher in Post-Covid group than in Pre-Covid group (p=0.047).

CONCLUSION: In our study, an increase was observed in the number of patients who underwent biliary stent implantation, percutaneous biliary drainage, neoadjuvant treatment and vascular/extraorgan resection in patients with pancreatic tumors during the Covid-19 pandemic.

Keywords: Covid-19 pandemic, pancreas cancer, neoadjuvant chemotherapy

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INTRODUCTION

Periampullary region refers to the area including head of pancreas, duodenum, ampulla of Vater, and distal bile duct. Pancreatic cancers constitute the majority of malignant tumors of this region.¹ Pancreatic cancer is the 7th most common cause of cancer-related death in the world.^{1,2} It is expected to be one of the leading causes of cancer-related death until 2030.^{1,3,4} Incidence and mortality of pancreas cancer increase with age. Adenocarcinomas consist of more than 85% of pancreatic malignant tumors. More than 80% of these tumors are in the advanced or metastatic stage when diagnosed in which surgery cannot be performed.⁴⁻⁶ The prognosis of pancreatic cancer is poor; 1-year mortality is 24% whereas 5-year mortality is 9% after diagnosis.^{2,3} Total survival was improved to 10% in 2021 literature.¹ Advances in surgical techniques, and their contributions in neoadjuvant and adjuvant therapies were mostly responsible for this improvement. However, prognosis still remains poor.

Potentially curative treatment of pancreatic cancer is surgery. The most important factor in surgical treatment is to obtain negative surgical margins with adequate lymph node dissection. Preoperative and postoperative adjuvant therapies prolong survival.^{4,7}

The chaos experienced during the Covid-19 pandemic caused disruptions in the treatments of pancreatic cancer patients; both the ones who were newly diagnosed and the ones who had ongoing treatments. It also caused delays in the diagnosis of pancreas tumors and thus changes in the treatments which would be planned. For these reasons, more problems might arise in patients who had pancreatic surgeries during this interval.

In this study, we aim to compare postoperative morbidity and mortality of patients who had pancreatic surgery due to diagnosis or suspect of cancer before and during Covid-19 pandemic.

MATERIAL AND METHOD

Data of patients who had pancreatic surgery due to pancreas cancer between 2017-2022 were recorded prospectively.

First patient with Covid-19 was diagnosed on 11th March 2020 in our country; and this date was accepted as the initiation of pandemic. Patients who had the surgery before Covid-19 pandemic were evaluated in Pre-Covid group; and the ones who had the surgery after this date until 09.04.2022 which normalization was initiated in our country were evaluated in the 'Post-Covid group'.

A total of 226 patients were included. There were 142 patients in Pre-Covid group, and 84 patients with pancreas cancer in the Post-Covid group. Patients who were accepted as inoperative during surgery or the ones who had palliative surgery were excluded.

Patients were evaluated according to vascular or extra-organ resection. Early (T1-2, N0, M0) and late stages (T3-4, N1-2, M0-1) according to pathological evaluation were compared in terms of preoperative endoscopic interventions or biliary drainage, and neoadjuvant treatment.

SPSS 20.0 software (SPSS Inc., Chicago, IL, ABD) was used for statistical analysis. Categorical measurements were described as numbers and percentages, whereas continuous measurements were described as mean±standard deviation and interval. Chi-square test and Independent-samples T-Test were used to compare groups. P<0.05 was accepted as statistical significance.

This study received approval from the ethics committee of Gülhane Training and Research Hospital in accordance with decision number 2022/26.

RESULTS

A total of 226 patients were included to the study. In Pre-Covid group (142 patients); distal pancreatectomy was performed in 32 (22.5%), and whipple procedure was performed in 110 (77.5%) patients. In Post-Covid group (84 patients); distal pancreatectomy was performed in 15 (17.9%), and whipple procedure was performed in 69 (82.1%) patients.

Demographic data including age, sex, body mass index (BMI),

comorbidities, and surgical procedures were shown on Table 1.

Table 1. Demographical features of patients and surgical procedures performed

| | Pre-Covid Group (%) n=142 | Post-Covid Group (%) n=84 | p |
|-----------------------------|------------------------------|------------------------------|------|
| Age | 60.5±11.4 | 61.9±9.2 | 0.31 |
| Sex (Male/Female) | | | 0.19 |
| • Male | 77 (54.2) | 53 (63) | |
| • Female | 65 (45.8) | 31 (37) | |
| Body mass index | 27.6±4 | 26.7±4.4 | 0.24 |
| Patients with comorbidities | 66 (46.4) | 46 (54.7) | 0.27 |
| Distal pancreatectomy | 32 (22.5) | 15 (17.9) | 0.49 |
| Whipple procedure | 110 (77.5) | 69 (82.1) | 0.49 |

Preoperative biliary stent or percutaneous biliary drainage procedures were compared in patients with pancreatic cancers and these were performed more often in Post-Covid group than in Pre-Covid group during pandemic period. Biliary drainage was performed to 31 patients in Pre-Covid group (28.1%), and 32 (46.3%) patients in Post-Covid group (p=0.013, Table 2).

Table 2. Procedures performed preoperatively

| | Pre-Covid Group n=110 | Post-Covid Group n=69 | p |
|---|--------------------------|--------------------------|-------|
| Percutaneous biliary drainage /stent implantation | 31 (28.1) | 32 (46.3) | 0.013 |
| Percutaneous biliary drainage | 15 (13.6) | 12 (17.3) | 0.49 |
| Stent implantation | 16 (14.5) | 20 (29) | 0.019 |

Five patients (3.5%) in Pre-Covid group, 15 patients (17.8%) in Post-Covid group had neoadjuvant therapy (p=0.000). Patients in Post-Covid group had significantly more neoadjuvant chemotherapy.

Pancreatic fistula developed in 32 (22.5%) patients of Pre-Covid group, and 20 patients (23.8%) of Post-Covid group. There was no statistical significance (p=0.82). When patients with hepaticojejunostomy surgery were compared 7 (6.3%) patients in Pre-Covid group, 4 (5.7%) patients in Post-Covid group had bile leak, and there was no statistical significance (p=0.87). Delayed gastric emptying was present in 4 (2.8%) patients of Pre-Covid group, and 2 (2.3%) patients in Post-Covid group (p=0.84). Intraabdominal collection or hematoma developed in 28 (19.7%) patients in Pre-Covid group, 14 (16.6%) patients in Post-Covid group; there was no statistical significance between two groups (p=0.56). Data about postoperative pancreatic fistula, bile leak, delayed gastric emptying, intraabdominal collection were summarized in Table 3.

Table 3. Postoperative complications

| | Pre-Covid Group (%) n=142 | Post-Covid Group (%) n=84 | p |
|-------------------------------------|------------------------------|------------------------------|------|
| Pancreatic fistula | 32 (22.5) | 20 (23.8) | 0.82 |
| Grade B | 29 (20.4) | 18 (21.4) | 0.85 |
| Grade C | 3 (2.1) | 2 (2.4) | 0.89 |
| Bile leakage | 7 (6.3) | 4 (5.7) | 0.63 |
| Delayed gastric emptying | 4 (2.8) | 2 (2.3) | 0.84 |
| Intra-abdominal collection/Hematoma | 28 (19.7) | 14 (16.6) | 0.56 |
| Collection | 24 (16.9) | 12 (14.2) | 0.60 |
| Hematoma | 4 (2.8) | 2 (2.4) | 0.84 |

Modified Clavien-Dindo classification and comparison of groups were shown on Table 4 and Table 5.

Table 4. Modified Clavien-Dindo Classification

| | |
|----------|--|
| Grade 1 | Any deviation from the normal postoperative changes without need for pharmacological treatment, surgical or radiological interventions |
| Grade 2 | Requiring pharmacological treatment with drugs other than used for Grade 1 |
| Grade 3A | Requiring surgical, endoscopic or radiological intervention without need for general anesthesia |
| Grade 3B | Requiring surgical, endoscopic or radiological intervention in general anesthesia |
| Grade 4A | Single-organ dysfunction |
| Grade 4B | Multi-organ dysfunction |
| Grade 5 | Death |

Table 5. Evaluation of patients due to Modified Clavien-Dindo Classification.

| | Grade 1 | Grade 2 | Grade 3A | Grade 3B | Grade 4A | Grade 4B | Grade 5 |
|------------------------------|-------------|------------|----------|----------|----------|----------|----------|
| Pre-Covid Group (%) n=142 | 104 (73.2%) | 27 (19%) | 4 (2.8%) | 3 (2.1%) | 1 (0.7%) | 0 (0%) | 3 (2.1%) |
| Post-Covid Group (%) n=84 | 61 (72.6%) | 15 (17.8%) | 5 (5.9%) | 1 (1.1%) | 0 (0%) | 0 (0%) | 2 (2.3%) |
| P value | 0.91 | 0.82 | 0.24 | 0.61 | 0.44 | - | 0.89 |

There was no statistical significance in Clavien-Dindo classification between groups (p values were as follows; grade1=0.91; grade2=0.82; grade3A=0.24; grade3B=0.61; grade4A=0.44; grade4B=0.89; grade5=0.89).

Vascular resection was performed for 14 patients (9.8%) in Pre-Covid group, and 16 (19%) patients in Post-Covid group. Rate of vascular resection was significantly higher in Post-Covid group (p=0.049, Figure 1, Table 6).

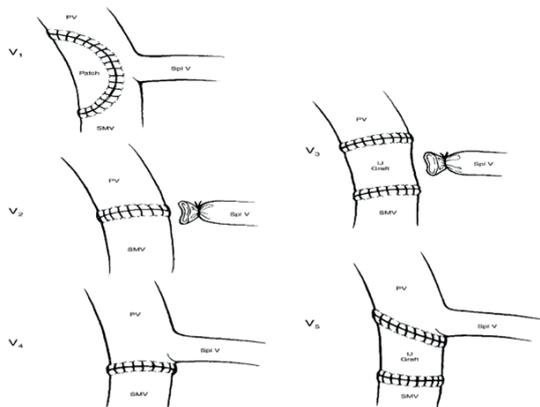


Figure 1. Mesentericoportal venous resection and reconstruction types.¹³

Table 6. Vascular resections and reconstructions performed to patients

| | Pre-Covid Group n=142 (%) | Post-Covid Group n=84 (%) | p |
|--|------------------------------|------------------------------|-------|
| Vascular resection and reconstruction | 14 (9.8) | 16 (19) | 0.049 |
| Type 1 | 2 (1.4) | 1 (1.2) | |
| Type 2 | 10 (7) | 7 (8.3) | |
| Type 3 | 1 (0.7) | 5 (5.9) | |
| Type 4 | 1 (0.7) | 1 (1.2) | |
| Type 5 | 0 (0) | 2 (2.4) | |

Nine (6.3%) patients in Pre-Covid group, and 12 (14.2%) patients in Post-Covid group had extra-organ resection. Extra-organ resection was significantly higher in Post-Covid group than in Pre-Covid group (p=0.047, Table 7).

Table 7. Extra-organ resections performed

| | Pre-Covid Group n (%) | Post-Covid Group n (%) | P |
|-------------------------------|--------------------------|---------------------------|-------|
| Extra-Organ Resections | 9 (6.3) | 12 (14.2) | 0.047 |
| Stomach | 3 (2.1) | 3 (3.5) | 0.51 |
| Liver | 2 (1.4) | 6 (7.1) | 0.02 |
| Transvers colon | 3 (2.1) | 2 (2.4) | 0.89 |
| Right adrenal gland | 1 (0.7) | 1 (1.2) | 0.70 |

According to pathological evaluation, 29 (20.4%) patients in Pre-Covid

group and 9 (10.7%) patients in Post-Covid group were diagnosed in early stage; there was no statistical significance between them (p=0.059).

Metastatic lymph nodes were present in 78 (54.9%) patients in Pre-Covid group and 52 (61.9%) patients in Post-Covid group. Statistical significance was not present between two groups (p=0.30).

Length of hospital stay was 9±7.5 days for Pre-Covid group, and 8.7±9.1days for Post-Covid group (p=0.79).

Survival analysis results which might not be reliable due to short follow-up period revealed median survival as 27.6 months for Pre-Covid group, and 24.9 months for Post-Covid group. One year survival was found 68% for Pre-Covid group, and 77% for patient group. There was no statistically significance for survival between two groups (p=0.25).

DISCUSSION

In early period of Covid-19 pandemic, doctors and all health care professions had anxiety and fear in evaluation of patients due to unavailability of fast and reliable diagnostic tests. This anxiety caused delays in elective procedures and trends to seek alternative solutions other than invasive procedures which require closer contact with the patients. Increased cleaning duration of rooms where invasive procedures took place for Covid-19, and high rate of occupied critical care beds lead some changes in elective cancer patients.⁸⁻¹¹

Disruptions occurred in the treatments of patients with pancreatic cancer. Delays were observed for most of the patients with a new diagnosis. We aim to evaluate the effects of pandemic on pancreas surgery.

As most of the other patients, our patient group delayed their admissions to hospital in pandemic period. In our clinical practice, preoperative biliary drainage is not performed unless bilirubin level is above 15 mg/ml or acute cholangitis is present. In our study, biliary stent implantation or percutaneous biliary drainage due to jaundice and itching symptoms was more common than Pre-Covid group.

Importance of neoadjuvant therapy especially for borderline resectable pancreatic adenocarcinomas were emphasized recently.^{1,3,4} Our study results reveal the increase in neoadjuvant therapy in pandemic, especially for the patients whose decisions of treatment -to chose first to perform surgery or neoadjuvant therapy- are difficult. As shown in our series, this approach did not have a negative effect on postoperative morbidity and mortality.

There was no statistical significance for postoperative complications in this study. Absence of significant difference for pancreatic fistula between groups may be due to multifactorial factors (eg; pancreatic stiffness/ stump closure techniques) that affect the development of pancreatic fistula.¹² Bile leak was highly prevalent in 2 groups due to frequent biliary drainage and biliary stent implantation. Other than these, absence of significant difference for delayed gastric emptying between groups may be due to similar postoperative complications in two groups. No difference for postoperative intraabdominal collection or hematoma between groups may be explained by similar postoperative complications and similar cancer staging in two groups.

In our study, significant difference for vascular or extra-organ resection may be due to late diagnosis or late referral for surgery. More vascular and extra-organ resections performed in the Post-Covid group did not seem to contribute morbidity and mortality. This might be the consequence of the local experience with cancer surgery since we perform numerous cancer surgery in our center.⁴ Performing advanced cancers in experienced centers can make a significant contribution to reducing mortality and morbidity.

Incidence of patients with early stage pancreatic tumors was not decreased in Covid-19 pandemic. Absence of difference for metastatic lymph nodes between Post-Covid and Pre-Covid group supported this. No difference for metastatic lymph nodes and staging between groups suggest that pancreatic cancer patients are not early diagnosed outside of Covid-19 pandemic. Similar survival between groups may be explained by the absence of difference for metastatic lymph nodes, and staging, and late diagnosis of patients.

CONCLUSION

In our study, an increase was observed in the number of patients who underwent biliary stent implantation, percutaneous biliary drainage, neoadjuvant treatment and vascular/extraorgan resection in patients with pancreatic tumors during the Covid-19 pandemic.

Presence of biliary stent and locally invasive tumors made surgical practice difficult. In this view, effect of Covid-19 on long term survival of cancer patients may be investigated in another study.

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Conflicts of Interest: The authors declare that they have no conflicts of interest.

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