Overview of Pancreatic Head Tumor Resectability at Haji Adam Malik General Hospital Medan.

Febrian Parlangga[1], Budi Irwan[2], Safruddin Nasution[3]

[1] Department of Surgery, Faculty of Medicine, University of Sumatera Utara, Medan, Indonesia
Corresponding author: Febrian Parlangga M, Email: Febryan_parlangga@yahoo.com

Abstract

Pancreatic head carcinoma is the 4th leading cause of death from cancer. The diagnosis of this tumor is difficult to make using a standard diagnostic modality, especially in an early stage, and the treatment approach is usually based on the assumptive of clinicians. The International Association of Pancreatology (IAP) in 2016 recommends resectability criteria for pancreatic head tumors based on the results of a CT scan. Tumor detection and staging with resectability assessment and diagnostic imaging are important in planning treatment management, both conservative and non-conservative. **Objective:** To describe the resectability of pancreatic head tumors according to IAP criteria. **Methods:** This is an observational descriptive study with a case series design which was conducted at Rumah Sakit Umum Pusat Haji Adam Malik Medan from July to December 2021. The study sample consisted of patients diagnosed with pancreatic head tumors who met the inclusion and exclusion criteria. Furthermore, data were collected and data analysis was carried out. **Results:** Of the 14 patients, 2 patients aged 36-45 years (14.29%), 8 patients aged 46-55 years (57.14%), and 4 patients aged >56 years (28.57%), with a male predominance of 11 people (78.57%). Patients with resectable criteria were found in 3 people (21.43%), borderline resectable criteria in 11 people (78.57%), and no unresectable criteria. There was 1 patient (7.14%) with stage IB criteria, 2 patients with stage IIA (14.29%), and 11 patients with stage III (78.57%). There were no patients with the criteria for stage IA, stage IIB, and stage IV. Conclusion: Stage III criteria dominated this study with a total of 11 people.

Keywords: resectability, pancreatic head tumor, IAP.

INTRODUCTION

Pancreatic tumor is a type of tumor that affect the pancreas, both the exocrine and endocrine tissues of the pancreas, as well as its supporting tissues, which can become a benign or malignant.[1] Most pancreatic carcinomas occur in the head of the pancreas (75%), and the rest are found in the corpus (15%). Pancreatic cancer is very difficult to diagnose at an early stage, because it is asymptomatic, and has rapid growth so it is called a silent killer.[2]

Pancreatic head carcinoma is the 4th leading cause of death from cancer. According to the American Cancer Society in 2020, this cancer is the fourth largest cause of death from cancer in men and the third largest in women. In England, it is estimated that there are 6.000 new cases of pancreatic head carcinoma per year.[2] Data from the US National Institutes of Health and the National Cancer Institute state that new cases in Indonesia are 1.6 per 100,000 population/year and are the 3rd rank malignancy in men after lung carcinoma and colon.[1]

Diagnosing pancreatic head carcinoma, especially at an early stage is very difficult using a standard diagnostic modality. Therefore, therapy from clinicians is often carried out assumptively. Several modalities used to detect pancreatic head carcinoma include conventional radiography, ultrasonography (USG), and magnetic resonance imaging (MRI). CT scanning has become the initial imaging modality of choice for the evaluation of pancreatic head pathology. Improvements in CT scan technology over the

last decade have increased the accuracy of CT scans for the detection and characterization of pancreatic head lesions.[3] A pancreatic CT scan can help diagnose and determine the characteristics of the lesion, as well as determine the stage of malignancy in the head of the pancreas.[4]

The International Association of Pancreatology (IAP) in 2016 recommends resectability criteria for pancreatic head tumors based on the results of a CT scan, which is an examination modality that can be performed in almost all public health service centers (hospitals), especially in Indonesia. Tumor detection and staging with resectability assessment with diagnostic imaging are important in planning treatment management, whether analytical or non-animated. This imaging is also important for monitoring the handling of the response.[5] Based on this background, this study aims to look at the description of tumor resectability and its grade based on IAP criteria at Haji Adam Malik General Hospital Medan.

METHODS

This research is an observational descriptive study with a case series design, which was conducted at Rumah Sakit Umum Pusat Haji Adam Malik Medan from July 2021 to December 2021. The study sample was patients diagnosed with a pancreatic head tumor from July 2021 to December 2021 and registered in medical records. The inclusion criteria were patients with pancreatic head tumors who had CT scan data, while the exclusion criteria were patients with CT scans who had artifacts; and patients whose CT scan did not show celiac artery, common hepatic artery, superior mesenteric artery, superior mesenteric vein, and portal vein. Data were collected and then analyzed descriptively using statistical software. Data on a ratio scale will be calculated by mean and standard deviation, while data on a category scale will be displayed in percentage form.

RESULTS

This study obtained 18 research subject candidates, but only 14 research subjects met the inclusion and exclusion criteria. Based on table 1, it was found that the majority of patients were aged 46-55 years (57.14%), and the majority were male (78.57%).

Table 1 Characteristics of Sample

Characteristics	Total (n)	Frequency (%)
Age (years)		
- 36-45	2	14.29
- 46-55	8	57.14
- ≥ 56	4	28.57
Sex		
- Male	11	78.57
- Female	3	21.43

The resectability criteria based on IAP are divided into three categories, resectable, borderline resectable, and unresectable/locally advanced (Table 2). The results of this study were dominated by borderline resectable criteria, namely 11 people (78.57%), followed by resectable criteria.

Table 2 Resectability Criteria Based on IAP

IAP Resectability Criteria	Total (n)	Frequency (%)
Resectable	3	21.43
Borderline Resectable	11	78.57
Unresectable/Locally Advanced	0	0

Table 4.3 Resectability of the Superior Mesenteric Artery, Celiac Axis or Hepatic Artery, and Superior Mesenteric Vein or Portal Vein

Overview of Resectability	Total (n)	Frequency (%)
Superior Mesenteric Artery		
Absence of tumor contact	12	85.71
Tumor contact <180° without deformity or stenosis	2	14.29

Tumor contact >180°	0	0
Celiac Axis or Hepatic Artery		
Absence of tumor contact	8	57.14
Tumor contact with hepatic artery without contact with proper hepatic artery or celiac artery	6	42.86
Tumor contact or invasion >180° or contact with proper hepatic artery	0	0
Superior Mesenteric Vein or Portal Vein		
Absence of tumor contact or unilateral narrowing	4	28.57
Tumor contact >180° or bilateral narrowing or occlusion, but not exceeding the inferior border of the duodenum	10	71.43
Bilateral narrowing or occlusion beyond the inferior border of the duodenum	0	0

The resectability criteria based on IAP are divided into six categories, namely, stage IA, IB, IIA, IIB, III, and IV (Table 4). The results of this study were dominated by 11 (78.57%) stage III criteria, followed by stage IIA and stage IB.

Table 4.6 Sample Distribution Based on AJCC Staging

AJCC Staging	Total (n)	Frequency (%)
Stage IA	0	0
Stage IB	1	7.14
Stage IIA	2	14.29
Stage IIB	0	0
Stage III	11	78.57
Stage IV	0	0

DISCUSSION

The incidence of pancreatic heads tumor is not as high as other tumors, but this tumor has a significant mortality rate worldwide due to its poor prognosis. In 2018 GLOBOCAN reported that pancreatic cancer was ranked the 11th most common cancer in the world.[6] Several epidemiological studies in Indonesia showed the incidence of pancreatic cancer in Dr. Mohammad Hoesin Palembang by 0.05%, at Dr. Wahidin Sudirohusodo Makassar by 1.4%, and at Rumah Sakit Umum Dr. Soedarso Pontianak by 7.9%.[7-9] Although the incidence tends to be low, the mortality is quite high, namely being the 7th highest cause of death worldwide in men and women.[6] In this study, there were a total of 14 patients with pancreatic head tumors who were registered at the Rumah Sakit Umum Pusat Haji Adam Malik in Medan and were then included in the study for a total duration of 6 months.

In our study, subjects for pancreatic head tumors were dominated by patients aged 46-55 years and the least is patients aged 36-45 years. This indicates that pancreatic head cancer tends to occur in adults and the elderly, which is in line with previous epidemiological studies, namely 62.6% of pancreatic cancer patients occurred at the age of 45-64 years. Other studies also describe the age distribution of pancreatic cancer as most at the age of 45-60 years or more than 40 years and rarely diagnosed at the age of younger than 30 years.[8,9] Age is a major determinant of pancreatic cancer incidence because most patients are diagnosed at an age above >50 years.[10]

GLOBOCAN 2018 reported that the highest prevalence of pancreatic cancer was in males.[6] The same result was also shown in our study, namely, the total number of male subjects was more than female. This may be influenced by other risk factors related to sex, such as smoking and alcohol consumption. Smokers have a 2-3 times risk of developing pancreatic cancer compared to non-smokers and the proportion of pancreatic cancer cases caused by smoking is 15-30% in various populations.[6,10] Excessive alcohol consumption is also a risk factor for pancreatic cancer reported by many studies. The correlation between alcohol consumption and pancreatic cancer is thought to be associated with an increased risk of recurrent acute pancreatitis and chronic pancreatitis.[11]

The IAP resectability criteria were divided into three categories, namely resectable, borderline resectable, and unresectable/locally advanced. In this study, almost all subjects met the borderline resectable criteria, which is in line with the

theoretical basis, where almost all patients with pancreatic head tumors, around 80-90%, will have borderline resectable tumors because the tumor is diagnosed at an advanced stage after the patient has symptoms. In fact, pancreatic cancer is the most frequently detected cancer in autopsy studies.[12,13]

Previous studies showed that the rate of resectable pancreatic cancer was 29.9%, borderline resectable was 7.8%, locally advanced was 23.3%, and the rest had metastatic disease. However, this study used the NCCN classification which has high variability in grouping resectability, thereby it reduced the reliability of therapy recommendations and clinical trial evidence that classifies patients based on their resectability.[14,15] In addition, the study was also conducted in South Korea, which has a high screening rate, and a much larger number of samples, thus allowing more patients to be detected at an early stage, so most of the samples were found to be in the resectable category.

Another study showed that there were 39.3% of patients with borderline resectable criteria and 60.7% of patients with locally advanced PDAC and 23.9% of patients underwent surgical exploration, then 15.1% of them underwent tumor resection. Then the resection rate was 24.1% for borderline resectable patients and 9% for locally advanced patients after chemotherapy. Patient survival after resection was 35.4 months for borderline patients and 41.8 months for locally advanced patients.[16] This suggests that appropriate resectability grouping can help clinicians provide more specific therapy and improve patient survival.

The resectability criteria defined by the IAP include important factors for considering resectability. The previous criteria were only defined based on the anatomical location of the tumor and often did not provide a good prognosis in patients undergoing resection.[17]

Previous studies that examined the prognostic effect of resectability defined by IAP compared to the NCCN guidelines (2016) showed that using IAP criteria, there was a significant difference in overall survival between borderline resectable and locally-advanced unresectable criteria, and this difference was not found with NCCN criteria.[18] This may be due to the IAP criteria changing patients who have biologically more active tumors from the resectable NCCN group to the borderline resectable group. So this shows that IAP criteria can define resectability in terms of selecting pre-operative patient therapy.

Based on IAP criteria, patients who enter the biologically borderline classification have significantly worse overall survival than patients who are resectable criteria, which shows that even though biological borderline patients include patients that have no contact with arteries or SMV-PV, it still has a poor outcome and can be indicated to receive a neoadjuvant strategy.[18]

The benefit of objective resectability grouping is that patients can receive more specific therapy at the time of diagnosis. The borderline resectable criterion is used for patients with arterial involvement and short venous segment occlusion (superior mesenteric-portal vein [SM-PV]). However, following administration of adjuvant therapy, patients who respond (clinical improvement, improved imaging features, and decreased tumor markers) may potentially undergo surgery. Patients with borderline resectable cancer differ from resectables because: (1) they have the highest risk for positive margins of resection due to tumor bordering arteries, (2) require surgery that is more complex and involves vascular resection and reconstruction, and (3) are at high risk of having Distant metastases that are not radiologically visible. Therefore, borderline resectable patients receive induction therapy for a longer period, including chemotherapy followed by chemoradiation.[19]

The treatment of choice for resectable borderline pancreatic cancer is pancreoduodenectomy with resection, but only 10-20% of cases are selected as candidates for surgery. This is because most pancreatic cancer patients are diagnosed at an advanced stage or an inoperable condition. Palliative management is usually the best approach for patients.[20] In a study conducted by Renaldi, et al. In 2018 at RSCM, pancreatic cancer patients were treated with endoscopic drainage, 10 cases (83.4%) with the help of ERCP, 1 case underwent Endoscopic Ultrasound Biliary Drainage with EUS-guided choledocoduodenostomy (EUS-CDS) and 1 case underwent percutaneous transhepatic. biliary drainage (PTBD).[21]

Nowadays, vein resection and reconstruction have become routine when the pancreatic tumor cannot be separated from the adjacent superior mesenteric or portal vein. However, many authors consider the invasion of the hepatic artery, the celiac axis of the superior mesenteric artery, to be a contraindication to surgery, because of the high morbidity and mortality associated with arterial resection and reconstruction.[22]

The AJCC TNM staging system is useful for predicting prognosis and collecting epidemiological data related to cancer.[23] In our study, only patients with stages IB, IIA, and III were found, there were no patients with stages IA, IIB, and IV. Based on cohort data from SEER using the AJCC grouping system, there were 2.3% of patients with stage I, 18.8% of patients with stage II, and 12.4% of patients with stage III tumors.[23] From other studies it was found that 8% of patients with stage IA, 22% of patients with stage IB, 4% of patients with stage IIA, 40% of patients with stage IIB, and 26% of patients with stage III.[24] The difference in percentages may be due to the different basic characteristics of patients and the selection bias that occurs in the study. Cohort data from SEER showed that the median overall survival (OS) of stage IA patients was significantly longer, namely 38 months, then 24 months for stage IB, 18 months for stage IIA, 17 months for stage IIB, and 14 months for stage III (p< 0.0001).[25] Another large retrospective cohort study from the United States reported 41.78% of patients with stage I, 50.7% with stage II, and 6.22% with stage III.[26]

Based on previous studies, the use of AJCC staging is a valid tool for stratifying pancreatic adenocarcinoma patients and can increase the reproducibility of staging because it eliminates extra-pancreatic invasion as a staging criterion and provides better prognostic stratification because of the description status of lymph nodes.[25] In the 8th AJCC staging system, there is a change from the previous edition, namely category T is grouped by size regardless of extra-pancreatic invasion with pT4 including locally unresectable tumors due to major arterial involvement, and category N1 is grouped again into pN1 and pN2 (≥4 lymph node metastases) and pN2 is classified as stage III regardless of tumor size.[23]

Although the TNM staging is valid in stratifying patients and helping to determine prognosis, still most studies did not include stage IV or unresectable pancreatic cancer or sample with unknown staging. In patients with stage III, borderline resectable and locally advanced cancer cannot be distinguished.[14] So it is less helpful in providing specific and effective therapy for patients. Most classification systems focus on anatomic findings and are retrospective studies. Guidelines that also incorporate biological features such as tumor markers for classification are needed to predict early recurrence, even in resectable pancreatic cancer patients, and to support indications for neoadjuvant therapy in certain resectable patients.

The limitations of this study include the fact that this study was a descriptive study in that this study could not identify the relationship between tumor resectability, the incidence of tumors in the head of the pancreas, and the staging of tumors in the head of the pancreas. This study also has a limited sample and a narrow duration, namely six months, so it is prone to selection bias.

CONCLUSION

Based on the results of this study, it can be concluded that the majority of male patients suffer from pancreatic head tumors. In addition, the majority of cases have stage III criteria, and borderline resectable criteria where this case needs to be managed with pancreaticoduodenectomy, resection, and vascular reconstruction procedures.

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