Lymph node involvement is rare in mucinous cystic neoplasms of the pancreas: Role of minimally invasive surgery

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Abstract. Mucinous cystic neoplasm (MCN) is a premalignant cystic tumor of the pancreas. Resection of MCN in the distal pancreas is a standard treatment; however, at present, there is no consensus on the necessity or extent of lymph node dissection, and minimally invasive pancreatectomy is commonly the preferred surgical technique. Thus, the present study aimed to assess the efficacy of minimally invasive surgery and the extent of lymph node metastasis as factors in determining an appropriate surgical treatment for MCN. The present study retrospectively analyzed 21 consecutive patients who underwent distal pancreatectomy (DP) for MCN under general anesthesia at Chiba University Hospital (Chiba, Japan) between April 2011 and July 2019. All 21 patients were female. DP with a splenectomy was performed in all the patients. A total of 14 patients underwent laparoscopic DP (LDP). No lymph node metastasis was found in any of the patients. The minimally invasive surgery group had lower operative blood loss and a shorter hospital stay than the open surgery group. There was no significant difference in the number of dissected lymph nodes between the open surgery group and the minimally invasive surgery group. Preoperative findings of malignancy in MCN included solid components on enhanced CT and endoscopic ultrasonography, high carbohydrate antigen 19-9 values and large tumor size. In conclusion, DP with spleen preservation, which is minimally invasive, may be preferentially considered as a surgical technique for MCN without malignant findings because lymph node metastases are rare in MCN and were not observed in the present study.

Introduction

Mucinous cystic neoplasm (MCN) is defined as a mucin-producing, septate cyst having a distinctive, ovarian-type stroma and arising from an epithelial neoplasm in the pancreas. Because MCN is also a premalignant cystic tumor, resection is routinely considered (1,2).

The invasive carcinoma incidence in MCN varies between 6 and 36% (3-8). This fact raises the question of whether a surgical resection with a splenectomy should be done for lymph node dissection, considering the high risk of surgical morbidity and mortality (9). In the European consensus statement, a pancreas- and/or spleen-preserving procedure for MCN without signs of malignancy may be performed by experienced surgeons because lymph node metastases are rare in MCN (10). The International Association of Pancreatology (IAP) guidelines recommend parenchyma-sparing resection (i.e., middle pancreatectomy) and distal pancreatectomy (DP) with spleen preservation as options in patients with MCN without malignant findings, such as tumor size <4 cm without mural nodules (1). In addition, laparoscopic pancreatectomies have come to be widely performed as a minimally invasive form of surgery. The IAP guidelines also recommend laparoscopic pancreatectomy for MCN (1).

Previous studies have reported factors predictive of malignancy in MCN. Park *et al* (11) reported that tumor size >30 mm, mural nodules on enhanced computed tomography (CT), and an elevated serum carbohydrate antigen 19-9 (CA19-9) concentration were significant predictors of malignancy. Le Baleur *et al* (12) also revealed that preoperative CT detection of a mural nodule within a cystic pancreatic neoplasm and a tumor diameter >40 mm strongly suggested malignancy.

The relationship between these predictors and lymph node metastasis in MCN has not been examined. Several studies reported that MCN involved no lymph node metastases (13,14). Moreover, other studies reported no recurrence besides invasive cystadenocarcinoma in patients with MCN (15,16). Thus, lymphadenectomy may not be necessary in cases of MCN without any of these predictors.

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Abbreviations: LDP, laparoscopic distal pancreatectomy; MCN, mucinous cystic neoplasm; IAP, International Association of Pancreatology; DP, distal pancreatectomy; CT, computed tomography; CA19-9, carbohydrate antigen 19-9; EUS, endoscopic ultrasonography; MRI, magnetic resonance imaging; POPF, postoperative pancreatic fistula; IQR, interquartile range; HALS, hand-assisted laparoscopic surgery

Key words: MCN, minimally invasive surgery, DP

We aimed herein to assess the benefits of minimally invasive surgery for MCN. We also tried to identify the preoperative radiological indicators of malignancy and lymph node involvement based on our experience.

Materials and methods

Patients and data collection. Twenty-one, consecutive patients who underwent DP for MCN at Chiba University Hospital between April 2011 and July 2019 were included. The patients' data were retrieved from prospectively maintained databases and included baseline patient characteristics, such as demographic data, preoperative risk factors, co-morbidities, intraoperative characteristics, and postoperative outcomes.

Preoperative assessment and treatment and pathological analysis. All the patients were routinely examined with enhanced CT and endoscopic ultrasonography (EUS) except one patient who was pregnant and received only plain CT and magnetic resonance imaging (MRI). Tumors were categorized according to the WHO classification (17). The preoperative enhanced CT and EUS images were assessed for evidence of wall calcification, multilobular findings, mural nodules, wall thickness, dilatation of the main pancreatic duct, communication with the main pancreatic duct, signs of pancreatitis, regional lymph node swelling, increased fat weave concentration, and vascular invasion. Wall calcification was defined as a high attenuation lesion in the cyst wall on non-contrast CT; multilobularity was defined by the contours of the cyst; mural nodules were defined as solid nodules ≥5 mm on CT or EUS; wall thickness was defined by the thickest point on CT or EUS; pancreatic duct dilatation was defined as a duct diameter >3 mm on CT and EUS; pancreatic duct communication was defined as continuity between the cyst and the main pancreatic duct on endoscopic retrograde cholangiopancreatography, magnetic resonance cholangiopancreatography or CT; pancreatitis was defined as peripancreatic infiltration or fluid collection on CT; and regional lymph node swelling was defined as a swelling >10 mm on CT, MRI or EUS.

Postoperative pancreatic fistulas (POPF) were assessed using the International Study Group for Pancreatic Fistula definition (18).

Experienced pathologists reviewed all the surgical specimens and slides to confirm the presence of a mucin-producing, columnar epithelium supported by an ovarian stroma. The 7th Union for International Cancer Control classification was used for the pathologic evaluation of the specimens.

All the surgical procedures were performed after obtaining the patients' informed consent. The study was conducted in accordance with the guidelines of the Helsinki Declaration and was approved by the Chiba University Human Research Committee.

Statistical analysis. Categorical variables were expressed as a number (%) and were compared using Fisher's exact test. Continuous variables were expressed as the median (interquartile range [IQR]]) and were compared using Wilcoxon's rank sum test P<0.05 was considered statistically significant. All statistical analyses were performed using the commercially available software JMP® 13 (SAS Institute Inc., Cary, NC, USA).

Results

Patient demographics and clinical presentations. Twenty-one patients were enrolled. Table I summarizes their demographic and clinical characteristics. All the patients were female, with a median age of 47 years (IQR: 38-62 years). The operative procedures included ODP in six patients, ODP with celiac axis resection in one patient, hand-assisted laparoscopic DP (HALS) in three patients, LDP in nine patients, and robot-assisted DP (RDP) in two patients. A splenectomy was performed in all the patients. The surgical procedures did not differ significantly between the benign and malignant groups. There were no operative deaths, and no patient required re-operation while hospitalized. Five patients had POPF grade B or higher. Lymph node dissection was performed in all patients, with a median number of lymph nodes dissected of 15.0 (IQR: 12.0-24.5). None of the patients had a lymph node metastasis.

The pathological findings demonstrated a mucinous cystic adenoma in 17 patients (81.0%), a mucinous cystadenocarcinoma (non-invasive) in three patients (13.6%), and a mucinous carcinoma (invasive) in one patient (4.5%).

Comparison of clinical features between the open and minimally invasive surgery groups. The demographic data were compared between the open and the minimally invasive surgery groups, including the patients who underwent laparoscopic DP, robot-assisted DP or HALS-DP. The minimally invasive surgery group showed a lower malignancy rate (0% vs. 57.1%; P=0.006) and lower operative blood loss (82.5 ml vs. 525.0 ml; P=0.044) than the open surgery group. Additionally, the minimally invasive surgery group tended to have a lower preoperative CA19-9 level, smaller tumor size, and shorter hospital stay. There was no significant difference in the number of dissected lymph nodes between the open surgery group and the minimally invasive surgery group (16.0 vs. 15.0; P=0.708) (Table II).

Comparison of clinical features between the benign and malignant tumor groups. Table III compares the clinical features of the benign and malignant tumor groups. Patients with benign postoperative pathological findings had a lower preoperative CA19-9 value (8.4 U/ml vs. 241.8 U/ml, P=0.008 and smaller tumor size (45.0 mm vs. 95.0 mm, P=0.009) than the patients with malignant postoperative pathological findings.

The malignant group had a significantly higher frequency of solid components on EUS and enhanced CT than the benign group. The malignant group also had a higher frequency of increased fat weave concentration and vascular invasion findings on CT. There was no significant difference between the groups in terms of preoperative symptoms, wall calcification, multilobular findings, mucin balls, wall thickness, dilatation of the main pancreatic duct, communication with the main pancreatic duct or pancreatitis. There was also no significant difference in the number of dissected lymph nodes between the malignant and the benign groups (22.0 vs. 15.0; P=0.324). In comparison to the benign group, the malignant group showed significantly more median intraoperative bleeding, a higher POPF rate, and a longer median length of hospital stay (1,102.5 ml vs. 50.0 ml, P<0.001; 75.0% vs. 11.8%, P=0.008; 36.0 days vs. 14.0 days, P=0.007, respectively) (Table III).

Table I. Patient demographics and clinical presentations (n=21).

Variables	Value
Median age, years (range)	47.0 (37.5-62.0)
Sex, n (female/male)	21/0
Median preoperative CEA level, ng/ml (range)	1.3 (1.0-2.1)
Median preoperative CA19-9 level, U/ml (range)	11.5 (6.6-79.1)
Median tumor size, mm (range)	47.0 (32.5-77.5)
Surgical method, n (ODP/DP-CAR/HALS DP/LDP/RDP)	6/1/3/9/2
Median operative time, min (range)	292.0 (241.5-340.5)
Median blood loss, ml (range)	130.0 (0.0-477.5)
POPF, n (no POPF or BL/Grade B or C POPF)	16/5
Median length of hospital stay, days (range)	19.0 (12.0-28.0)
Histological grade, n (adenoma/malignancy)	17/4
Median number of dissected lymph nodes (range)	15.0 (12.0-24.5)
Pathological lymph node metastasis, n (positive/negative)	0/21

No POPF, BL, Grade B POPF and Grade C POPF were classified according to the International Study Group of Pancreatic Surgery 2016 pancreatic fistula criteria. CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; ODP, open distal pancreatectomy; DP-CAR, ODP with celiac axis resection; LDP, laparoscopic distal pancreatectomy; HALS DP, hand-assisted laparoscopic surgery distal pancreatectomy; RDP, robot-assisted DP; POPF, postoperative pancreatic fistula; BL, biochemical leak.

Table II. Comparison of clinical features between the open and minimally invasive surgery groups.

Variables	LDP/RDP (n=14)	ODP (n=7)	P-value
Median age, years (range)	44.0 (35.3-58.8)	60.0 (44.0-76.0)	0.073
Median preoperative CEA level, ng/ml (range)	1.2 (1.0-2.0)	1.6 (1.3-2.3)	0.287
Median preoperative CA19-9 levels, U/ml (range)	8.2 (4.7-28.4)	114.9 (18.4-245.1)	0.079
Median tumor size, mm (range)	42.5 (20.0-73.8)	60.0 (45.0-130.0)	0.065
Median operative time, min (range)	296.5 (264.3-337.3)	240.0 (183.0-423.0)	0.382
Median blood loss, ml (range)	82.5 (0.0-225.0)	525.0 (40.0-1260.0)	0.044
POPF, n (no POPF or BL/Grade B or C POPF)	12/2	4/3	0.280
Median length of hospital stay, days (range)	13.5 (11.8-24.3)	22.0 (20.0-41.0)	0.105
Histological grade, n (adenoma/malignancy)	14/0	3/4	0.006
Median number of dissected lymph nodes (range)	15.0 (12.5-24.3)	16.0 (10.0-29.0)	0.708
Pathological lymph node metastasis, n (positive/negative)	0/14	0/7	-

Categorical variables are presented as a number and were compared using Fisher's exact test. Continuous variables are presented as the median (interquartile range) and were compared using Wilcoxon's rank sum test. $P<0.05$ was considered to indicate a statistically significant difference. No POPF, BL, Grade B POPF and Grade C POPF were classified according to the International Study Group of Pancreatic Surgery 2016 pancreatic fistula criteria. LDP, laparoscopic distal pancreatectomy; RDP, robot-assisted distal pancreatectomy; ODP, open distal pancreatectomy; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; POPF, postoperative pancreatic fistula; BL, biochemical leak.

Follow-up and survival. The median postoperative follow-up duration of the 21 MCN patients was 77.6 months (IQR: 50.2-90.1 months). During the follow-up, one patient experienced a recurrence. The patient had diarrhea as a preoperative symptom and high CA19-9 value (238.5 U/ml). She presented a 45 mm, cystic, multilobular tumor with a solid component in the pancreatic tail, increased fat weave concentration, vascular invasion findings, and lymph node swelling on enhanced CT. A liver metastasis and local recurrence developed one year after the primary resection, and the patient died 27.7 months after the primary resection. Histological examination found no lymph node metastasis, suggesting that lymph node dissection would not have prevented tumor recurrence. The five-year overall survival rate of all the patients was 95.2%.

Discussion

In the present series, none of the patients had lymph node metastasis. The IAP guidelines recommend DP with spleen preservation for patients with MCN <4 cm without mural nodules (1). Interestingly, ovarian mucinous neoplasms show similar biological behavior as MCN and have clearly different

Table III. Comparison of clinical features between the benign and malignant tumor groups.

Variables	Benign (n=17)	Malignant (n=4)	P-value
Median age, years (IQR)	47.0 (37.5-60.5)	60.0 (37.3-79.0)	0.228
Symptoms, n (%)			0.146
Asymptomatic	10 (58.8)	1 (25.0)	
Nonspecific abdominal pain	6 (35.3)	2 (50.0)	
Abdominal mass	1 (5.9)	0 (0.0)	
Diarrhea	0 (0.0)	1 (25.0)	
Median preoperative CEA level, ng/ml (range)	1.2 (0.9-2.0)	2.0 (1.4-3.1)	0.084
Median preoperative CA19-9 level, U/ml (range)	8.4 (6.4-32.8)	241.8 (145.8-1958.8)	0.008
Median tumor size, mm (range)	45.0 (25.0-70.0)	95.0 (48.8-212.5)	0.009
Solid component on EUS, n (presence/absence)	5/12	3/1	0.021
Solid component on enhanced CT, n (presence/absence)	0/17	3/1	0.003
Wall calcification on enhanced CT and/or EUS, n (presence/absence)	5/12	2/2	0.574
Multilobularity on enhanced CT and/or EUS, n (presence/absence)	13/4	4/0	0.546
Mucin balls on enhanced CT and/or EUS, n (presence/absence)	3/14	0/4	>0.999
Wall thickness on enhanced CT and/or EUS, n (presence/absence)	12/5	3/1	>0.999
Dilatation of main pancreatic duct on enhanced CT and/or EUS, n (presence/absence)	3/14	1/3	>0.999
Communication with main pancreatic duct on enhanced CT and/or EUS, n (presence/absence)	2/15	1/3	0.489
Pancreatitis on enhanced CT, n (%)	0/17	1/3	0.191
Increased fat weave concentration on enhanced CT, n (%)	0/17	2/2	0.029
Vascular invasion on enhanced CT and/or EUS, n (%)	0/17	2/2	0.029
Median operative time, min (range)	292.0 (238.5-324.0)	333.0 (240.8-430.5)	0.235
Median blood loss, ml (range)	50.0 (0.0-210.0)	1102.5 (630.0-3817.5)	<0.001
POPF, n (no POPF or BL/Grade B or C POPF)	15/2	1/3	0.008
Median length of hospital stay, days (range)	14.0 (11.5-23.0)	36.0 (22.8-71.8)	0.007
Median number of dissected lymph nodes (range)	15.0 (12.0-22.5)	22.0 (11.3-38.0)	0.324
Pathological lymph node metastasis, n (positive/negative)	0/17	0/4	-

Categorical variables are presented as the number (%) and were compared using Fisher's exact test. Continuous variables are presented as the median (IQR) and were compared using Wilcoxon's rank sum test. $P<0.05$ was considered to indicate a statistically significant difference. No POPF, BL, Grade B POPF and Grade C POPF were classified according to the International Study Group of Pancreatic Surgery 2016 pancreatic fistula criteria. IQR, interquartile range; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; EUS, endoscopic ultrasonography; CT, computed tomography; POPF, postoperative pancreatic fistula; BL, biochemical leak.

clinicopathologic characteristics to other ovarian histo-types (19-21). Ovarian mucinous carcinomas usually spread to the peritoneum and other organs via the bloodstream, but lymph node metastases were reported in fewer than 10% of the cases (22,23). Our experiences also suggest that a splenectomy for lymph node dissection, which may cause thromboembolisms or infectious complications, is unnecessary for MCN. Post-splenectomy infections are potentially severe, and post-splenectomy thrombosis causes complications involving both the vena cava system (deep-vein thrombophlebitis, pulmonary embolism) and the portal system, both of which have the potential to become life-threatening. For these reasons, we suggest avoiding a splenectomy for MCN except in cases where the tumor is near the splenic vessels or has invaded them. Although SPDP is technically more difficult than DP, previous reports have proven the safety and usefulness of SPDP, at least in the facilities familiar with this technique (24). Therefore, SPDP in a high-volume center is recommended for MCN.

Our study identified three, independent indicators of malignancy in MCN: preoperative CA19-9, tumor size, and a solid component on enhanced CT and/or EUS. Compared to the benign group, the malignant group had a significantly higher frequency of solid component on CT and/or EUS. Previous studies revealed that the sensitivity and specificity of CT in detecting mural nodules was 60.0-90.9 and 94.8-98.0%, respectively (11,12). EUS has a sensitivity and specificity of 70 and 100%, respectively, in detecting a solid component, invasion outside the pancreas, and a pancreatic duct obstruction that is highly indicative of malignancy (25). However, in the absence of these findings, the ability of EUS to diagnose a malignancy is limited, at an overall sensitivity and specificity of 56 and 45%, respectively (26). On the other hand, Postlewait *et al* (27) showed a relatively high lymph node metastasis rate of 34.1%, especially for cases with predictive factors for malignancy. In cases with those malignant factors, such as high preoperative CA19-9 level or large tumor size, DP with splenectomy is recommended.

In the present study, minimally invasive surgery, including laparoscopic and robot-assisted surgery, resulted in less operative blood loss and a shorter hospital stay than open surgery in DP for MCN, in line with previous findings. Some previous studies revealed that laparoscopic surgery provided short- and long-term, oncologic outcomes equivalent to those of open surgery, including a potentially shorter hospital stay and less operative blood loss (28-30). Moreover, Daouadi et al (31) demonstrated that patients in a robot-assisted surgery group did not require conversion to open surgery and had a lower risk of excessive blood loss than a laparoscopic surgery group. Therefore, endoscopic procedures and DP with spleen preservation should be considered preferentially for the treatment of MCN.

Postlewait et al (32) reported that minimally invasive surgery was associated with smaller MCN size. However, as with LDP and RDP, HALS-DP had lower operative blood loss and a shorter hospital stay than open surgery, with no increase in the complication rate (32). Shinchi et al (33) demonstrated that HALS-DP might have the advantages of laparotomy and laparoscopy in the handling of the splenic artery and vein just below the mini-laparotomy site, suggesting that it is more accessible and safer than a purely laparoscopic procedure. Thus, HALS may be helpful if the tumor is too large for a purely laparoscopic operation.

The present study had several limitations: it was retrospective, and the relatively small number of MCN patients may have weakened the analyses. Therefore, further research enrolling a larger cohort is warranted.

In conclusion, endoscopic procedures and DP with spleen preservation may be considered preferentially for the surgical treatment of MCN without signs of malignancy and the presence of a solid component because lymph node metastases are generally rare in such pancreatic MCN. Moreover, minimally invasive DP should be considered because of its superior operative and oncologic outcomes.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

KK and HY designed the study. KK analyzed and interpreted the patient data. KK was involved in the acquisition of data. KK was a major contributor in writing the manuscript. HY revised the manuscript. KF, TT, SKu, ST, SKa and MO confirmed the authenticity of all the raw data, and made substantial contributions to conception and design, and acquisition of data, and analysis and interpretation of data. All authors gave their final approval of the version to be published and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study protocol was reviewed and approved by Chiba University Human Research Committee (approval no. 3302; Chiba, Japan). The present study was performed in compliance with the regulations and carried out in accordance with the relevant guidelines. Data collection and analysis followed the ethical guidelines of the World Medical Association Declaration of Helsinki. Written informed consent was obtained for participation in the present study.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Tanaka M, Fernández-del Castillo C, Adsay V, Chari S, Falconi M, Jang JY, Kimura W, Levy P, Pitman MB, Schmidt CM, et al: International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas. Pancreatology 12: 183-197, 2012.
2. Thompson LD, Becker RC, Przygodzki RM, Adair CF and Heffess CS: Mucinous cystic neoplasm (mucinous cystadenocarcinoma of low-grade malignant potential) of the pancreas: A clinicopathologic study of 130 cases. Am J Surg Pathol 23: 1-16, 1999.
3. Campbell F and Azadeh B: Cystic neoplasms of the exocrine pancreas. Histopathology 52: 539-551, 2008.
4. Crippa S, Salvia R, Warshaw AL, Domínguez I, Bassi C, Falconi M, Thayer SP, Zamboni G, Lauwers GY, Mino-Kenudson M, et al: Mucinous cystic neoplasm of the pancreas is not an aggressive entity: lessons from 163 resected patients. Ann Surg 247: 571, 2008.
5. Reddy RP, Smyrk TC, Zapiach M, Levy MJ, Pearson RK, Clain JE, Farnell MB, Sarr MG and Chari ST: Pancreatic mucinous cystic neoplasm defined by ovarian stroma: Demographics, clinical features, and prevalence of cancer. Clin Gastroenterol Hepatol 2: 1026-1031, 2004.
6. Tanaka M, Chari S, Adsay V, Fernandez-del Castillo C, Falconi M, Shimizu M, Yamaguchi K, Yamao K, Matsuno S and International Association of Pancreatology: International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas. Pancreatology 6: 17-32, 2006.
7. Visser B, Muthusamy V, Yeh B, Coakley F and Way L: Diagnostic evaluation of cystic pancreatic lesions. HPB (Oxford) 10: 63-69, 2008.
8. Zamboni G, Scarpa A, Bogina G, Iacono C, Bassi C, Talamini G, Sessa F, Capella C, Solcia E, Rickaert F, et al: Mucinous cystic tumors of the pancreas: clinicopathological features, prognosis, and relationship to other mucinous cystic tumors. Am J Surg Pathol 23: 410-422, 1999.
9. Nathan H, Cameron JL, Goodwin CR, Seth AK, Edil BH, Wolfgang CL, Pawlik TM, Schulick RD and Choti MA: Risk factors for pancreatic leak after distal pancreatectomy. Ann Surg 250: 277-281, 2009.
10. Del Chiaro M, Verbeke C, Salvia R, Klöppel G, Werner J, McKay C, Friess H, Manfredi R, Van Cutsem E, Löhr M, et al: European experts consensus statement on cystic tumours of the pancreas. Dig Liver Dis 45: 703-711, 2013.

11. Park JW, Jang JY, Kang MJ, Kwon W, Chang YR and Kim SW: Mucinous cystic neoplasm of the pancreas: Is surgical resection recommended for all surgically fit patients? Pancreatology 14: 131-136, 2014.
12. Le Baleur Y, Couvelard A, Vullierme MP, Sauvanet A, Hammel P, Rebours V, Maire F, Hentic O, Aubert A, Ruszniewski P and Lévy P: Mucinous cystic neoplasms of the pancreas: definition of preoperative imaging criteria for high-risk lesions. Pancreatology 11: 495-499, 2011.
13. Crippa S, Fernández-Del Castillo C, Salvia R, Finkelstein D, Bassi C, Domínguez I, Muzikansky A, Thayer SP, Falconi M, Mino-Kenudson M, *et al*: Mucin-producing neoplasms of the pancreas: An analysis of distinguishing clinical and epidemiologic characteristics. Clin Gastroenterol Hepatol 8: 213-219. e214, 2010.
14. Fernández-del Castillo C: Mucinous cystic neoplasms. J Gastrointest Surg 12: 411-413, 2008.
15. Sarr MG, Carpenter HA, Prabhakar LP, Orchard TF, Hughes S, van Heerden JA and DiMagno EP: Clinical and pathologic correlation of 84 mucinous cystic neoplasms of the pancreas: Can one reliably differentiate benign from malignant (or premalignant) neoplasms? Ann Surg 231: 205, 2000.
16. Wilentz RE, Albores-Saavedra J, Zahurak M, Talamini MA, Yeo CJ, Cameron JL and Hruban RH: Pathologic examination accurately predicts prognosis in mucinous cystic neoplasms of the pancreas. Am J Surg Pathol 23: 1320-1327, 1999.
17. Bosman FT, Carneiro F, Hruban RH and Theise ND: WHO classification of tumours of the digestive system. World Health Organization, 2010.
18. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, Allen P, Andersson R, Asbun HJ, Besselink MG, *et al*: The 2016 update of the international study group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. Surgery 161: 584-591, 2017.
19. Hart WR: Mucinous tumors of the ovary: A review. Int J Gynecol Pathol 24: 4-25, 2005.
20. Heinzelmann-Schwarz VA, Gardiner-Garden M, Henshall SM, Scurry JP, Scolyer RA, Smith AN, Bali A, Vanden Bergh P, Baron-Hay S, Scott C, *et al*: A distinct molecular profile associated with mucinous epithelial ovarian cancer. Br J Cancer 94: 904-913, 2006.
21. Hess V, A'Hern R, Nasiri N, King DM, Blake PR, Barton DP, Shepherd JH, Ind T, Bridges J, Harrington K, *et al*: Mucinous epithelial ovarian cancer: A separate entity requiring specific treatment. J Clin Oncol 22: 1040-1044, 2004.
22. Morice P, Joulie F, Camatte S, Atallah D, Rouzier R, Pautier P, Pomel C, Lhommé C, Duvillard P and Castaigne D: Lymph node involvement in epithelial ovarian cancer: Analysis of 276 pelvic and paraaortic lymphadenectomies and surgical implications. J Am Coll Surg197: 198-205, 2003.
23. Rodríguez IM and Prat J: Mucinous tumors of the ovary: A clinicopathologic analysis of 75 borderline tumors (of intestinal type) and carcinomas. Am J Surg Pathol 26: 139-152, 2002.
24. Kimura W, Yano M, Sugawara S, Okazaki S, Sato T, Moriya T, Watanabe T, Fujimoto H, Tezuka K, Takeshita A and Hirai I: Spleen-preserving distal pancreatectomy with conservation of the splenic artery and vein: techniques and its significance. J Hepatobiliary Pancreat Sci 17: 813-823, 2010.
25. Sahani DV, Kadavigere R, Saokar A, Fernandez-del Castillo C, Brugge WR and Hahn PF: Cystic pancreatic lesions: A simple imaging-based classification system for guiding management. Radiographics 25: 1471-1484, 2005.
26. Brugge WR, Lewandrowski K, Lee-Lewandrowski E, Centeno BA, Szydlo T, Regan S, del Castillo CF and Warshaw AL: Diagnosis of pancreatic cystic neoplasms: A report of the cooperative pancreatic cyst study. Gastroenterology 126: 1330-1336, 2004.
27. Postlewait LM, Ethun CG, McInnis MR, Merchant N, Parikh A, Idrees K, Isom CA, Hawkins W, Fields RC, Strand M, *et al*: Association of preoperative risk factors with malignancy in pancreatic mucinous cystic neoplasms: A multicenter study. JAMA Surg 152: 19-25, 2017.
28. Eom B, Jang JY, Lee S, Han HS, Yoon YS and Kim SW: Clinical outcomes compared between laparoscopic and open distal pancreatectomy. Surg Endosc 22: 1334-1338, 2008.
29. Kooby DA, Hawkins WG, Schmidt CM, Weber SM, Bentrem DJ, Gillespie TW, Sellers JB, Merchant NB, Scoggins CR, Martin RC 3rd, *et al*: A multicenter analysis of distal pancreatectomy for adenocarcinoma: Is laparoscopic resection appropriate? J Am Coll Surg 210: 779-785, 2010.
30. Venkat R, Edil BH, Schulick RD, Lidor AO, Makary MA and Wolfgang CL: Laparoscopic distal pancreatectomy is associated with significantly less overall morbidity compared to the open technique: A systematic review and meta-analysis. Ann Surg 255: 1048-1059, 2012.
31. Daouadi M, Zureikat AH, Zenati MS, Choudry H, Tsung A, Bartlett DL, Hughes SJ, Lee KK, Moser AJ and Zeh HJ: Robot-assisted minimally invasive distal pancreatectomy is superior to the laparoscopic technique. Ann Surg 257: 128-132, 2013.
32. Postlewait LM, Ethun CG, McInnis MR, Merchant N, Parikh A, Idrees K, Isom CA, Hawkins W, Fields RC, Strand M, *et al*: The hand-assisted laparoscopic approach to resection of pancreatic mucinous cystic neoplasms: An underused technique? Am Surg 84: 56-62, 2018.
33. Shinchi H, Takao S, Noma H, Mataki Y, Iino S and Aikou T: Hand-assisted laparoscopic distal pancreatectomy with mini-laparotomy for distal pancreatic cystadenoma. Surg Laparosc Endosc Percutan Tech 11: 139-143, 2001.