to-mucosa anastomosis against conventional dunking method [21, 22]. It was reported that pancreaticogastrostomy was not superior to pancreaticojejunostomy in a randomized trial performed in a high-volume center [23]. Up to now, the best reconstruction method for the pancreatic duct during pancreaticoduodenectomy remains unclear.

Conclusion

Our multivariate analysis revealed that bile juice infection on day I was a significant and independent risk factor for POPF. As bile juice infection on day 1 was strongly associated with retrograde biliary drainage, not with percutaneous drainage, PTCD might be or would be recommended for patients undergoing biliary drainage before pancreaticoduodenectomy.

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References

- 1. Yeo CJ, Cameron JL, Sohn TA, Lillemoe KD, Pitt HA, Talamini MA et al (1997) Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. Ann Surg 226:248-257
- 2. Adam U, Makowiec F, Riediger H, Schareck WD, Benz S, Hopt UT (2004) Risk factors for complications after pancreatic head resection. Am J Surg 187:201-208
- 3. Muscari F, Suc B, Kirzin S, Hay JM, Fourtanier G, Fingerhut A, French Associations for Surgical Research et al (2006) Risk factors for mortality and intraabdominal complications after pancreatoduodenectomy: multivariate analysis in 300 patients. Surgery 139:591-598
- 4. Kazanjian KK, Hines OJ, Eibl G, Reber HA (2005) Management of pancreatic fistulas after pancreaticoduodenectomy: results in 437 consecutive patients. Arch Surg 140:849-854
- 5. Payne RF, Pain JA (2006) Duct-to-mucosa pancreaticogastrostomy is a safe anastomosis flowing pancreaticoduodenectomy. Br J Surg 93:73-77
- 6. Veillette G, Dominguez I, Ferrone C, Thayer SP, McGrath D, Warshaw AL et al (2008) Implications and management of pancreatic fistulas following pancreaticoduodenectomy: the Massachusetts General Hospital experience. Arch Surg 143:476-481
- 7. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, International Study Group on Pancreatic Fistula Definition et al (2005) Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 138:8-13 8. Pedrazzoli S, Liessi G, Pasquali C, Ragazzi R, Berselli M, Sperti
- C (2009) Postoperative pancreatic fistulas: preventing severe

- complications and reducing reoperation and mortality rate. Ann Surg 249:97-104
- Shimada K, Sano T, Sakamoto Y, Kosuge T (2006) Clinical implications of combined portal vein resection as a palliative procedure in patients undergoing pancreaticoduodenectomy for pancreatic head carcinoma. Ann Surg Oncol 13:1569-1578
- 10. Sakamoto Y, Shimada K, Esaki M, Kajiwara T, Sano T, Kosuge T (2007) Wrapping the stump of the gastroduodenal artery using the falciform ligament during pancreaticoduodenectomy. J Am Coll Surg 204:334-336
- 11. Sakamoto Y, Kajiwara T, Esaki M, Shimada K, Nara S, Kosuge T (2009) Roux-en-Y reconstruction using staplers during pancreaticoduodenectomy: results of a prospective preliminary study. Surg Today 39:32-37
- 12. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR et al (2007) Delayed gastric emptying (DGE) after pancreatic surgery: definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 142:761-768
- 13. Kawai M, Tani M, Terasawa H, Ina S, Hirono S, Nishioka R et al (2006) Early removal of prophylactic drains reduced the risk of intraabdominal infections in patients with pancreatic head resection. Prospective study for 104 consecutive patients. Ann Surg 244:1-7
- 14. de Castro SM, Busch OR, van Gulik TM, Obertop H, Gouma DJ (2005) Incidence and management of pancreatic leakage after pancreaticoduodenectomy. Br J Surg 92:1117-1123
- 15. Povoski SP, Karpeh MS Jr, Conlon KC, Blumgart LH, Brennan MF (1999) Association of preoperative biliary drainage with postoperative outcome following pancreaticoduodenectomy. Ann Surg 230:131-142
- 16. Sohn TA, Yeo CJ, Cameron JL, Pitt HA, Lillemoe KD (2000) Do preoperative biliary stents increase postpancreaticoduodenectomy complications? J Gastrointest Surg 4:258-267
- 17. Sewnath ME, Birjmohun RS, Rauws EA, Huibregtse K, Obertop H, Gouma DJ (2001) The effect of preoperative biliary drainage on postoperative complications after pancreaticoduodenectomy. J Am Coll Surg 192:726-734
- 18. Pisters PW, Hudec WA, Hess KR, Lee JE, Vauthey JN, Lahoti S et al (2001) Effect of preoperative biliary decompression on pancreaticoduodenectomy-associated morbidity in 300 consecutive patients. Ann Surg 234:47-55
- 19. Martignoni ME, Wagner M, Krähenbühl L, Redaelli CA, Friess H, Büchler MW (2001) Effect of preoperative biliary drainage on surgical outcome after pancreatoduodenectomy. Am J Surg 181:52-59
- 20. Nagino M, Takada T, Miyazaki M, Miyakawa S, Tsukada K, Kondo S et al (2008) Preoperative biliary drainage for biliary tract and ampullary carcinomas. J Hepatobiliary Pancreat Surg 15:25-30
- 21. Bassi C, Falconi M, Molinari E, Mantovani W, Butturini G, Gumbs AA et al (2003) Duct-to-mucosa versus end-to-side pancreaticojejunostomy reconstruction after pancreaticoduodenectomy: results of a prospective randomized trial. Surgery 134:766-771
- 22. Langrehr JM, Bahra M, Jacob D, Glanemann M, Neuhaus P (2005) Prospective randomized comparison between a new mattress technique and Cattell (duct-to-mucosa) pancreaticojejunostomy for pancreatic resection. World J Surg 29:1111-1119
- 23. Yeo CJ, Cameron JL, Maher MM, Sauter PK, Zahurak ML, Talamini MA et al (1995) A prospective randomized trial of pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy. Ann Surg 222:580-592





Original Article

Can the Physiologic Ability and Surgical Stress (E-PASS) Scoring System Predict Operative Morbidity After Distal Pancreatectomy?

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Abstract

Purpose. Mortality rates after pancreatic resection are now lower than 5% in high-volume centers; however, morbidity remains high. This stresses the importance of identifying accurate predictors of operative morbidity after pancreatic resection. The Estimation of Physiologic Ability and Surgical Stress (E-PASS) scoring system was developed for a comparative audit of general surgical patients. Our previous study confirmed its usefulness for predicting morbidity after pancreaticoduodenectomy. In the present study, we evaluated whether the E-PASS scoring system can predict the occurrence of complications after distal pancreatectomy (DP).

Methods. The subjects were 46 patients who underwent DP for pancreatic disease. We studied correlations between the incidence of postoperative complications and the preoperative risk score (PRS), surgical stress score (SSS), and comprehensive risk score (CRS) of the E-PASS scoring system.

Results. A collective total of 20 postoperative complications developed in 13 (28.3%) of the 46 patients. All E-PASS scores, particularly PRS and CRS, were significantly higher in the patients with postoperative complications than in those without complications. The complication rate increased with increasing PRS, SSS, and CRS scores.

Conclusion. The E-PASS scoring system is useful for predicting morbidity after DP.

Key words E-PASS scoring system · Distal pancreatectomy · Complication

Introduction

Advances in surgical techniques and perioperative management have reduced the operative mortality rate after pancreatic resection to less than 5% in high-volume centers; however, morbidity rates have changed little and range from 30% to 40%. The majority of perioperative complications are not life-threatening, but they can prolong the hospital stay, increase costs, necessitate readmission, and delay adjuvant therapy. Thus, it is important to identify the predictive and intraoperative risk factors associated with operative morbidity after distal pancreatectomy (DP).

Haga et al. devised and validated the Estimation of Physiologic Ability and Surgical Stress (E-PASS) scoring system for risk stratification of patients undergoing elective general gastrointestinal (GI) surgery.¹⁷ It has been externally validated in a different geographical setting from where it was originally developed, and is reproducible for accurately predicting outcomes after elective GI surgery. 18 We previously reported its usefulness for predicting morbidity after pancreaticoduodenectomy (PD). 19 This system comprises a preoperative risk score (PRS), a surgical stress score (SSS), and a comprehensive risk score (CRS), calculated from the PRS and SSS. The E-PASS was based on the premise that morbidity and mortality rates are correlated with the patient's physiological risk and anticipated surgical stress. The aim of this study was to evaluate whether the E-PASS scoring system could predict postoperative complications in patients undergoing DP.

Patients and Methods

Patients and Treatments

Between April 2005 and December 2007, 46 consecutive patients underwent DP for malignant or benign pancre-

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Table 1. Equations for Estimation of Physiologic Ability and Surgical Stress (E-PASS) scoring system

Preoperative risk score (PRS)

 $= -0.0686 + 0.00345X_1 + 0.323X_2 + 0.205X_3 + 0.153X_4 + 0.148X_5 + 0.0666X_6$

Where X_1 is age, X_2 is presence (1) or absence (0) of severe heart-disease⁶, X_3 is presence (1) or absence (0) of severe pulmonary disease⁶, X_4 is presence (1) or absence (0) of diabetes mellitus, X_5 is performance status index⁶ (0-4), X_6 is American Society of Anesthesiologists physiological status classification

Surgical stress score (SSS)

 $= -0.342 + 0.0139X_1 + 0.0392X_2 + 0.353X_3$

Where X_1 is blood loss/body weight (ml/kg), X_2 is operation time (h), X_3 is extent of skin incision (0 = minor incision for laparoscopic or thoracoscopic surgery, 1 = laparotomy or thoracotomy alone, 2 = both laparotomy and thoracotomy)

Comprehensive risk score (CRS) = -0.328 + 0.936 (PRS) + 0.976 (SSS)

atic diseases at Kumamoto University Hospital. Written informed consent was obtained from all patients before the treatment. The same three surgeons performed the operations using almost uniform procedures. The pancreas was routinely transected with a scalpel, the pancreatic duct was ligated, and the pancreatic stump was closed with monofilament sutures. A closed-suction drain was placed in the vicinity of the pancreatic stump. D2 lymph node dissection was performed in patients with pancreatic cancer.²⁰

E-PASS Scoring System

The equations used in the E-PASS scoring system are shown in Table 1. The PRS is calculated using factors such as age, the presence or absence of severe heart disease, severe lung disease, or diabetes mellitus, American Society of Anesthesiologists (ASA) physiological status classification, and performance status index defined by the Japanese Society for Cancer Therapy,²¹ which is the same as that defined by the Eastern Cooperative Oncology Group. The performance status index is defined as follows: grade 0, conditions without symptoms that restrict social activities; grade 1, conditions with mild symptoms that restrict muscular labor but do not restrict walking or mild exertion; grade 2, conditions that require some physical assistance for daily living; grade 3, conditions that require frequent physical assistance for daily living; grade 4, conditions that require constant physical assistance. Patients in grade 2 are not restricted to bed for more than half a day, those in grade 3 are restricted to bed for more than half a day, and those in grade 4 are restricted to bed all day. According to a previous study,22 the expected in-hospital mortality rate was estimated as Y = -0.465 + 1.192(CRS) +10.91(CRS)².

Postoperative Complications

The postoperative complications, apart from pancreatic fistula (POPF), were assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0 (NCI CTCAE v.3.0). 23,24 In this study, adverse events of grade 2-5 occurring within 30 days after surgery were considered to be postoperative complications. Adverse events corresponding to grade 1 were excluded because medical treatment was not required. Postoperative pancreatic fistula was assessed according to an international study group (ISGPF) definition, that is a as drainage output of any measurable volume of fluid on or after postoperative day (POD) 3 with amylase content greater than three times the serum amylase activity.25 Three different grades of POPF (grades A, B, C) are defined according to the clinical impact on the patient's hospital course. Grade B and grade C were considered to be postoperative complications in this study. Grade A was excluded because it had no clinical impact. The overall complication rate was defined as the proportion of patients with at least one complication. Operative and hospital mortality was defined as death within 30 days after surgery or during hospitalization, respectively.

Statistical Analysis

We used the chi-squared test, Fisher's exact test and the Mann-Whitney U-test for statistical analysis, as appropriate. Receiver operator characteristic (ROC) curves were plotted to assess the extent to which CRS, PRS, and SSS could accurately predict morbidity. The area under the ROC curve (AUC) was used as a measure of overall diagnostic accuracy. Statistical significance was considered at P < 0.05.

^{*}Severe heart disease was defined as heart failure of New York Heart Association Class III or IV or severe arrhythmia requiring mechanical support

Severe pulmonary disease was defined as a condition with a % vital capacity <60% or a % forced expiratory volume in 1.0 second <50%

^ePerformance status index was based on the definition by the Japanese Society for Cancer Therapy

Results

Patients' Characteristics

The patients comprised 27 women and 19 men, with a median age of 63.5 years (range, 22–87 years). Malignant diseases were diagnosed in 26 (56.5%) patients, including pancreatic cancer in 19, a malignant islet cell tumor in 4, and malignant intraductal papillary mucinous neoplasm (IPMN) in 3. The remaining 20 (43.5%) patients had benign diseases, including a benign islet cell tumor in 8 and chronic pancreatitis in 5, and benign IPMN, a solid-pseudopapillary tumor, serous cyst adenoma, mucinous cyst adenoma, schwannoma, an accessory spleen, and a pancreatic cyst in 1 patient each. The pancreatic texture at the stump of pancreatic remnant was soft and the main pancreatic duct was not dilated in all except one patient.

Morbidity Associated with Distal Pancreatectomy

A collective total of 20 postoperative complications developed in 13 (28.3%) of the 46 patients (Table 2). There were no operative or hospital deaths, nor were there any cases of intraperitoneal fluid collection or abscess. Postoperative pancreatic fistula grade B, which requires a change in management or adjustment in the clinical pathway, was observed in all patients with post-

operative complications. Postoperative pancreatic fistula grade C, in which a major change in clinical management or deviation from the normal clinical pathway occurs, was not observed.

Correlations Between E-PASS Scores and Postoperative Complications

Postoperative complications were correlated significantly with performance status, ASA classification, and blood loss, but not with the other variables (Table 3). The E-PASS scores, particularly PRS and CRS, were significantly higher in patients with postoperative complications than in those without complication (Fig. 1).

Table 2. Postoperative complications

Complications	17
Pancreatic fistula (ISGPF grade B)	13
Delayed gastric emptying	1
Intra-abdominal bleeding	1
Cerebral hemorrhage	1
Pneumonia	1
Pleural effusion	1
Sepsis	1
Duodenal ulcer	1
Total	20

Table 3. E-PASS variables and postoperative complications

		Complication		
Variable	Total (n = 46)	Presence $(n = 13)$	Absence $(n = 33)$	P value
Mean age (years)	63.5 ± 13.4	65.1 ± 12.5	62.9 ± 13.9	NS
Severe heart-disease				NS
Presence	0	0	0	
Absence	46	13	33	
Severe pulmonary disease				NS
Presence	2	1	1	
Absence	44	12	32	
Diabetes mellitus				NS
Presence	11	4	7	
Absence	33	8	26	
Performance status				0.029
0	27	3	24	
1	13	6	7	
2	6	4	2	
ASA classification				0.023
1	15	2	13	
2	25	6	19	
3	6	5	1	
Blood loss (ml)	476.5 ± 602.7	982.9 ± 878.9	277.0 ± 275.6	0.001
Body weight (kg)	56.0 ± 11.5	60.6 ± 13.3	54.2 ± 10.4	NS
Operation time (min)	362.2 ± 98.7	430.2 ± 119.6	335.4 ± 75.6	NS

NS, not significant

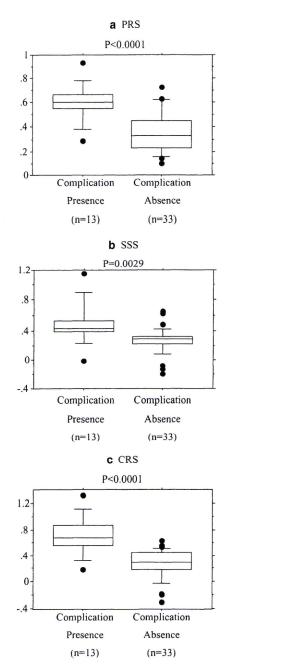
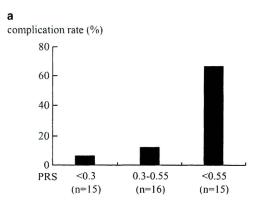
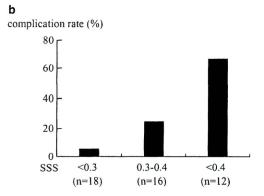


Fig. 1. Association between postoperative complications and the Estimation of Physiologic Ability and Surgical Stress (E-PASS) scores. **a** Preoperative risk score (*PRS*); **b** surgical stress score (*SSS*); **c** comprehensive risk score (*CRS*). *Boxes* show the 95% confidence intervals

The mortality rate estimated using the E-PASS scoring system was 3.4% for patients with postoperative complications. The associations between the PRS, SSS, and CRS and the complication rate are shown in Fig. 2. The complication rate tended to increase as the PRS, SSS, and CRS increased.





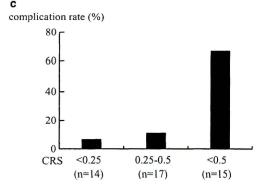
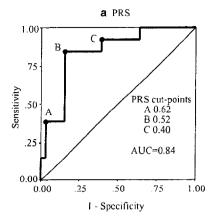
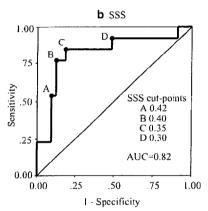


Fig. 2. Estimation of the proportion of patients with postoperative morbidity, calculated using the Estimation of Physiologic Ability and Surgical Stress (E-PASS) scores. a Preoperative risk score (PRS); b surgical stress score (SSS); c comprehensive risk score (CRS)

Receiver Operating Characteristic Analysis of the E-PASS Scores for Morbidity

The E-PASS scores showed good predictive power for morbidity associated with DP, demonstrated by the wide areas under the ROC curve in Fig. 3. The AUC was 0.84 for PRS (95% confidence interval [CI] 0.72–0.97), 0.82 for SSS (95% CI 0.67–0.97), and 0.89 for CRS (95% CI 0.77–1.01). The ROC curves show the strong associa-





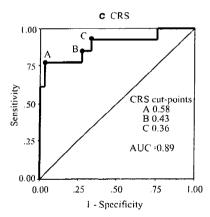


Fig. 3. Receiver operator characteristic curves for morbidity based on the Estimation of Physiologic Ability and Surgical Stress (E-PASS) scores. **a** Preoperative risk score (*PRS*): **b** surgical stress score (*SSS*): **c** comprehensive risk score (*CRS*). *AUC*, area under the curve

tion between morbidity and the PRS, SSS, and CRS individually. Fig. 3 shows various cutoff points for each graph. For CRS, a cutoff point of 0.43 would give a decision rule with sensitivity of 84.6% and specificity of 72.7% for the prediction of morbidity (Fig. 3c).

Discussion

In this series, the morbidity rate after DP was 28.3%. which is comparable with reported morbidity rates ranging from 30% to 40% in previous studies. 1-14 The E-PASS scoring system, which was developed for a general surgical audit, has been applied to various subspecialties. 18,22,24,26,27 The system is easy to use because the required information can be retrieved from preanesthetic sheets and operation notes. Kaneko et al. assessed the outcomes of laparoscopic hepatectomy (L-Hr) compared with open hepatectomy (O-Hr) for hepatocellular carcinoma (HCC), using the E-PASS scoring system.²⁸ They found that the SSS and CRS of the L-Hr group were significantly lower than those of the O-Hr group, although there was no difference in PRS between the two operations. In fact, the L-Hr group had a 10% complication rate, whereas the O-Hr group had a complication rate of 18%, demonstrating that the E-PASS scoring system is useful for assessing the outcome of hepatectomy for HCC.

We previously reported the good predictive power of E-PASS scores for both mortality and morbidity, as demonstrated by the large areas under the ROC curve, in patients undergoing PD.19 In this study, we used the E-PASS scoring system to predict operative morbidity after DP and found a strong correlation between E-PASS scores and the incidence of postoperative complications. The ROC analysis in this study indicates that E-PASS scores are useful predictors of postoperative complications after DP. The E-PASS system can be used to predict operative morbidity after DP for each patient before surgery, not only by the PRS, but also the SSS and CRS, which are calculated by expected operating times and blood loss. This allows surgeons, anesthesiologists, and medical staff to evaluate high-risk patients before surgery. Although there was no mortality in this series, the E-PASS system might help surgeons consider the indications for DP in each patient and avoid performing this operation if the risks are too high. The E-PASS system can also be used to inform patients about the risks of complications before surgery. In this series, the CRS had the best predictive utility for postoperative complications. Moreover, because the SSS and CRS can be calculated immediately after DP using actual operating time and blood loss, surgeons can identify the risk of morbidity shortly after surgery, enabling the initiation of appropriate perioperative care for each patient.

The most frequent complication in this series was POPF grade B. Previous investigators have reported that pancreatic characteristics, such as soft pancreatic texture and pancreatic duct size, are predictors of POPF, including grade A. The pancreatic texture at the stump of the pancreatic remnant was soft and the main pancreatic duct was not dilated in all but one of our patients.

Most patients undergoing DP have a soft pancreas and a normal-sized main pancreatic duct, unlike patients undergoing PD. Therefore complications after DP, including POPF, would possibly reflect the patient's own general condition and surgical stress, such as performance status, ASA classification, and blood loss, rather than pancreatic characteristics. In fact, several studies have indicated that the patient's condition, such as ASA classification, obesity, and nutritional status, and indicators of surgical stress, such as blood loss and operating time, affect the rate of postoperative complications, including POPF, after DP. 3.11.29.30 E-PASS, especially the PRS, is easy to calculate before DP. Systemic complications such as pneumonia would tend to occur in patients with high E-PASS scores, reinforcing its value before surgery. In conclusion, the E-PASS scoring system is useful for predicting operative morbidity, including POPF, in patients undergoing DP for malignant or benign pancreatic disease.

References

- Benzoni E, Saccomano E, Zompicchiatti A, Lorenzin D, Baccarani U, Adani G, et al. The role of pancreatic leakage on rising of postoperative complications following pancreatic surgery. J Surg Res 2008;149:272-7.
- Kooby D, Gillespie T, Bentrem D, Nakeeb A, Schmidt M, Merchant N, et al. Left-sided pancreatectomy. A multicenter comparison of laparoscopic and open approaches. Ann Surg 2008;248: 438–46.
- 3. Kleeff J, Diener M, Z'graggen K, Hinz U, Wagner M, Bachmann J, et al. Distal Pancreatectomy. Risk factors for surgical failure in 302 consecutive cases. Ann Surg 2007;245:573–82.
- Mohebati A, Schwarz R. Extended left-sided pancreatectomy with spleen preservation. J Surg Oncol 2008;97:150–5.
- Abe N, Sugiyama M, Suzuki Y, Yamaguchi T, Mori T, Atomi Y. Preoperative endoscopic pancreatic stenting: a novel prophylactic measure against pancreatic fistula after distal pancreatectomy. J Hepatobiliary Pancreat Surg 2008;15:373-6.
- Kawai M, Tani M, Yamaue H. Transection using bipolar scissors reduces pancreatic fistula after distal pancreatectomy. J Hepatobiliary Pancreat Surg 2008;15:366–72.
- Okano K, Kakinoki K, Yachida S, Izushi K, Wakabayashi H, Suzuki Y. A simple and safe pancreas transection using a stapling device for a distal pancreatectomy. J Hepatobiliary Pancreat Surg 2008:15:353–8.
- 8. Kitagawa H, Ohta T, Tani T, Tajima H, Nakagawara H, Ohnishi I, et al. Nonclosure technique with saline-coupled bipolar electrocautery in management of the cut surface after distal pancreatectomy. J Hepatobiliary Pancreat Surg 2008;15:377–83.
- Diener M, Knaebel H, Witte S, Rossion I, Kieser M, Buchler M, et al. DISPACT trial: a randomized controlled trial to compare two different surgical techniques of DIStal PAnCreaTectomy study rationale and design. Clinical Trials 2008;5:534-45.
- Irani J, Ashley S, Brooks D, Osteen R, Raut C, Russell S, et al. Distal pancreatectomy is not associated with increased perioperative morbidity when performed as part of a multivisceral resection. J Gastrointest Surg 2008;12:2177–82.
- Ferrone C, Warshaw A, Rattner D, Berger D, Zheng H, Rawal B, et al. Pancreatic fistula rates after 462 distal pancreatectomies: staplers do not decrease fistula rates. J Gastrointest Surg 2008; 12:1691-7.

- Truty M, Sawyer M, Que F. Decreasing pancreatic leak after distal pancreatectomy: saline-coupled radiofrequency ablation in a porcine model. J Gastrointest Surg 2008;11:998–1007.
- Koukoutsis I, Tamijmarane A, Bellagamba R, Bramhall S, Buckels J, Mirza D. The impact of splenectomy on outcomes after distal and total pancreatectomy. World J Surg Oncol 2007;5:61.
- Carrere N, Abid S, Julio C, Bloom E, Pradere B. Spleen-preserving distal pancreatectomy with excision of splenic artery and vein: a case-matched comparison with conventional distal pancreatectomy with splenectomy. World J Surg 2007;31:375–82.
- Sasaki A, Nitta H, Nakajima J, Obuchi T, Baba S, Wakabayashi G. Laparoscopic spleen-preserving distal pancreatectomy with conservation of the splenic artery and vein: report of three cases. Surg Today 2008;38:955–8.
- Iso Y, Sawada T, Tagaya N, Kato M, Rokkaku K, Shimoda M, et al. Pancreatic juice leakage is a risk factor for deep mycosis after pancreatic surgery. Surg Today 2009;39:326-31.
- Haga Y, Ikei S, Ogawa M. Estimation of physiologic ability and surgical stress (E-PASS) as a new prediction scoring system for postoperative morbidity and mortality following elective gastrointestinal surgery. Surg Today 1999;29:219-25.
- Oka Y, Nishijima J, Oku K, Azuma T, Inada K, Miyazaki S, et al. Usefulness of an estimation of physiologic ability and surgical stress (E-PASS) scoring system to predict the incidence of postoperative complications in gastrointestinal surgery. World J Surg 2005;29:1029–33.
- Hashimoto D, Takamori H, Sakamoto Y, Ikuta Y, Nakahara O, Furuhashi S, et al. Is Estimation of physiologic ability and surgical stress (E-PASS) able to predict operative morbidity after pancreaticoduodenectomy? J Hepatobiliary Pancreat Surg 2009; Online First. DOI: 10.1007/s00534-009-0116-4.
- Japan Pancreas Society. General rules for the study of pancreatic cancer. 5th ed. April 2002.
- Furue H. Criteria for the direct effect of chemotherapy against solid cancer by Japanese Society for Cancer Therapy (in Japanese). J Jpn Soc Cancer Ther 1986;21:931

 –42.
- Haga Y, Wada Y, Takeuchi H, Kimura O, Furuya T, Sameshima H, et al. Estimation of physiologic ability and surgical stress (E-PASS) for a surgical audit in elective digestive surgery. Surgery 2004; 135:586-94.
- http://ctep.cancer.gov/protocolDevelopment/electronic_ applications/ctc.htm#ctc_v30
- 24. Baba Y, Haga Y, Hiyoshi Y, Imamura Y, Nagai Y, Yoshida N, et al. Estimation of physiologic ability and surgical stress (E-PASS system) in patients with esophageal squamous cell carcinoma undergoing resection. Esophagus 2008;5:81-6.
- 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.
- 26. Tang T, Walsh S, Fanshawe T, Seppi V, Sadat U, Hayes P, et al. Comparison of risk-scoring methods in predicting the immediate outcome after elective open abdominal aortic aneurysm surgery. Eur J Vasc Endovasc Surg 2007;34:505–13.
- 27. Tang T, Walsh S, Fanshawe T, Gillard J, Sadat U, Varty K, et al. Estimation of physiologic ability and surgical stress (E-PASS) as a predictor of immediate outcome after elective abdominal aortic aneurysm surgery. Am J Surg 2007;194:176–82.
- Kaneko H, Takagi S, Otsuka Y, Tsuchiya M, Tamura A, Katagiri T, et al. Laparoscopic liver resection of hepatocellular carcinoma. Am J Surg 2005;189:190–4.
- Goh B, Tan Y, Chung Y, Cheow P, Ong H, Chan W, et al. Critical appraisal of 232 consecutive distal pancreatectomies with emphasis on risk factors, outcome, and management of the postoperative pancreatic fistula: a 21-year experience at a single institution. Arch Surg 2008;143:956–65.
- Sierzega M, Niekowal B, Kulig J, Popiela T. Nutritional status affects the rate of pancreatic fistula after distal pancreatectomy: a multivariate analysis of 132 patients. J Am Coll Surg 2007; 205:52-9.

ORIGINAL ARTICLE

Risk factors for postoperative infectious complications after hepatectomy

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Abstract

Background/purpose This study aimed to clarify the incidence of surgical site infections (SSIs) after hepatectomy.

Methods The database records of three hundred and eight patients who underwent elective surgical treatment for hepatolithiasis, hepatocellular carcinoma (HCC), and metastatic carcinoma were retrospectively analyzed to determine the occurrence of postoperative infectious complications. The incidences of SSIs, classified as superficial or deep incisional SSIs and organ or space SSIs, and all other infectious complications within 30 days after hepatectomy were evaluated.

Results The incidences of SSIs after a hepatectomy for hepatolithiasis (23.8%) were higher than those after a hepatectomy for HCC (11.3%) (p=0.034) and after a hepatectomy for metastatic carcinoma (2.7%) (p<0.001), and the incidence of SSIs after a hepatectomy for HCC was higher than that after a hepatectomy for metastatic carcinoma (p=0.028). However, there was no significant difference in the incidence of remote site infections between the three groups. The incidence of superficial or deep incisional SSIs after a hepatectomy for hepatolithiasis (11.9%) was higher than that after a hepatectomy for metastatic carcinoma (1.4%) (p<0.001) and the incidence of superficial or deep incisional SSIs after a hepatectomy for HCC (7.8%) was higher than that after a hepatectomy for metastatic carcinoma (1.4%) (p=0.050). There was a

significant difference in the incidence of space/organ SSIs between the patients with hepatolithiasis (11.9%) and HCC patients (3.6%) (p=0.029), and between the patients with hepatolithiasis and metastatic carcinoma patients (1.4%) (p<0.001). The rate of positive bile culture was 36.2% in all patients in this study, and the rates were 83.3, 7.8, and 10.0% for patients with hepatolithiasis, HCC, and metastatic carcinoma, respectively. A significantly higher (p<0.001) positive bile culture rate was observed in patients with hepatolithiasis as compared with HCC or metastatic carcinoma patients.

Conclusions Our study suggests the existence of a relationship between postoperative SSIs and bile infection, thus supporting the proposed relationship between post-hepatectomy infection and such variables as liver function, blood sugar control, and nutritional status.

Keywords Surgical site infections (SSIs) · Bile infection · Hyperglycemia · Nutrition

Introduction

Despite improvements in surgical techniques and refinements in perioperative care, the high incidence of postoperative infectious complications remains a major problem in patients undergoing hepatectomy for benign liver disease or hepato-biliary carcinoma [1]. Surgical site infections (SSIs) are a potentially morbid and costly complication following hepato-biliary surgery [2]. In recent years, there has been growing attention placed on the accurate identification and monitoring of such surgical complications, as measured in terms of increased patient morbidity [3]. In regard to hospital-acquired infections, the Centers for Disease Control and Prevention (CDC)

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National Nosocomial Infection Surveillance (NNIS) system serves in part to provide a comprehensive monitoring system that reports SSI trends. The purpose of this nationwide surveillance is to establish benchmarks for interhospital and intrahospital comparisons. According to the NNIS system report [4], the incidence of SSI following bowel surgery was high and ranged from 1 to 13.5% (median) during the period from January 1992 through June 2003; however, the risk factors of SSI after a hepatectomy under the CDC guidelines have not yet been closely examined.

Biliary stone disease such as hepatolithiasis is associated with bile stasis and bacterial infection. Biliary stones contain large amounts of calcium bilirubinate and exist in the intra- and/or extrahepatic bile ducts, and the presence of stones may be closely related to the presence of bacteria [5, 6]. High infectious morbidity rates are associated with surgical treatment for this condition, and the appropriate administration of antibiotics is important in preventing postoperative complications [7]. Postoperative complications after hepatectomy for neoplasms such as hepatocellular carcinoma (HCC) and metastatic carcinoma have been well studied [8]. However, the risk factors and management of infectious complications after hepatectomy for hepatolithiasis have not been fully investigated. Our specific objectives were to determine the rates of incisional and space/organ SSIs following elective hepatectomy in patients with hepatolithiasis, HCC, and metastatic carcinomas.

Patients and methods

Patient population

We analyzed the database records of 308 patients who underwent a hepatectomy without reconstruction of the intestine or the biliary tract between 1995 and 2009 at Wakayama Medical University Hospital (WMUH). The records of 42 patients with hepatolithiasis, 193 with hepatocellular carcinoma, and 73 with metastatic carcinoma were evaluated to assess the postoperative infectious complications. We examined the prevalence of pathogenic bacteria in the bile and the correlations between the presence of bacteria, postoperative complications, and SSIs. Demographic and clinical variables were recorded on admission. The data for the 308 hepatectomy patients included sex, age, body mass index (BMI), history of biliary tract treatment and previous operation except for biliary tract surgery, type of operation, additional surgical procedures, bacteria isolated in the bile from the bile duct, and administration of perioperative antibiotics. The indocyanine green (ICG) clearance test was conducted by

intravenous injection of the ICG reagent at a dose of 0.5 mg/kg body weight and collection of blood at 0, 5, 10, and 15 min to determine the blood clearance rate (K value). The serum total bilirubin, albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and hemoglobin A1c (HbA1c) were measured at the Central Laboratories of WMUH. The outcome variables included early-stage postoperative complications, incisional SSI (superficial or deep), space/organ SSI (intraabdominal abscess, peritonitis), remote site infections such as respiratory or urinary tract infections, and the distribution of bacterial flora in the bile.

Hepatectomy procedures

At WMUH, anatomic hepatectomy is the standard treatment, as previously described [9]. An anatomic resection was defined as the complete removal of at least one Couinaud segment [10]. Right hepatectomy (V + VI + VIII + VIII), right trisectionectomy (I + IV + V + VI + VII + VIII), left hepatectomy (II + III + IV), left trisectionectomy (I + II + III + IV + V + VIII), middle bisectionectomy (IV + V + VIII), right posterior hepatectomy (VI + VII), and right anterior hepatectomy (V + VIII) have all been defined as a major hepatectomies according to Couinaud's classification. Hepatic inflow occlusion to control blood loss by clamping the portal pedicle (20-min clamping followed by 5-min unclamping) was utilized during the hepatic parenchyma transection. No patients underwent regional lymph node dissection in the hepatic hilum. Intraoperative ultrasonography was routinely used to evaluate the remnant liver tumors or residual stones. Closed-circle drains were placed routinely in the subphrenic space or in Winslow's foramen for 1-3 days. Abdominal incisions were closed with polydioxanone (PDS) monofilament absorbable sutures for the fascia and absorbable or nonabsorbable sutures for the skin. The skin was closed primarily in all cases. Antibiotics were not applied to the wound, and subcutaneous drains were not used. All the patients were followed up for at least 30 days after surgery in order to monitor for the development of an SSI or other postoperative complications. Antibiotics were injected intravenously (i.v.) within 30 min prior to skin incision. In the patients who underwent operations that lasted longer than 3 h, additional antimicrobial agents were intravenously injected every 3 h, as recommended by the CDC guidelines, [4] and these agents were also administered on the day after surgery.

The evaluation of SSIs

SSIs were defined according to the CDC's NNIS system [4]. By these criteria, SSIs are classified as being either incisional (superficial or deep) or organ/space. Criteria for



a superficial incisional SSI included an infection occurring at the incision site within 30 days after surgery that involved only the skin and subcutaneous tissue and at least one of the following: pus discharge from the incision; bacteria isolated from a sample culture from the superficial incision: localized pain, tenderness, swelling, redness, or heat; and wound dehiscence. Criteria for a deep incisional SSI included an infection of the fascia or muscle related to the surgical procedure occurring within 30 days after surgery and at least one of the following: pus drainage from the deep incision; spontaneous dehiscence of the incision; or deliberate opening of the incision when the patient had the previously described signs and symptoms of infection. In this study, organ/space SSI was categorized as either intraabdominal abscess without evidence of clinical anastomotic leakage (an intraperitoneal collection of pus diagnosed by ultrasonography, computed tomography, or laparotomy) or clinical bile leakage. An intraabdominal abscess near the leakage site was reported as clinical bile leakage.

The evaluation of remote site infections

The criteria for respiratory infection were defined as a fever greater than 38°C; chest pain; dyspnea; and cough and expectoration developing within 30 days after surgery, in addition to a shadow, thus indicating an abnormality on the chest X-ray, regardless of the presence/absence of bacteria in the sputum [11]. The criteria for urinary tract infection included the development of clinical symptoms, such as urinary frequency, miction pain, low back pain, and fever after removal of a urethral balloon catheter, in addition to at least 10/high power field (HF) leucocytes/bacteria in the urinary sediment [12].

The data are presented as the means \pm standard deviation. For statistical analyses, an unpaired *t*-test and the χ^2 test were used to evaluate the differences in surgical

parameters by the StatView program (version 5; Hulinks, Tokyo, Japan). Statistical significance was defined as a p value of <0.05.

Results

Background of patients with hepatectomy

The mean age of the 42 patients with hepatolithiasis was 56.5 ± 12.5 years, whereas the mean age of the 193 patients with HCC was 63.7 \pm 10.2 years (p < 0.0001) and that of the 73 patients with metastatic carcinoma was 60.8 \pm 11.9 years (p < 0.0001). A past history of biliary treatment was found in 20 of the 42 patients with hepatolithiasis (47.6%), whereas 34 of the 193 patients with HCC (17.6%) (p < 0.0001) and 7 of the 73 patients with metastatic carcinoma (9.6%) (p < 0.0001) had a previous history of surgical or endoscopic treatment for cholelithiasis. A past history of previous operations other than biliary surgery was found in all patients with metastatic carcinoma, whereas only 3 of the 42 patients with hepatolithiasis (7.1%) (p < 0.0001) and 12 of the 193 patients with HCC (6.2%) (p < 0.0001) had a history of other surgeries (Table 1). Body mass index (BMI) was not significantly different between the 3 groups; likewise, the type of liver resection was distributed homogeneously between the 3 groups. There were no intraoperative complications related to the surgical techniques and there were no significant differences between the 3 groups regarding either the type of liver resection performed or the associated surgical procedures (Table 2).

Preoperative blood examination data and postoperative complications in hepatectomy patients

The preoperative blood examination data of the patients who underwent hepatectomy is shown in Table 3.

Table 1 Background of the patients with hepatectomy

	Hepatolithiasis	Hepatocellular carcinoma	Metastatic carcinoma
No. of patients	42	193	73
Gender (male/female)	24/18	114/79*	33/40
Age, years (mean \pm SD)	56.5 ± 12.5**	63.7 ± 10.2	60.8 ± 11.9
Body mass index (BMI)	23.1 ± 0.6	23.4 ± 0.7	24.3 ± 0.8
History of biliary treatment yes/no (rate)	20/22 (47.6%)***	34/159 (11.6%)	7/66 (9.0%)
History of previous operation except biliary surgery yes/no (rate)	3/42 (7.1%)	12/193 (6.2%)	73/0 (100%)****

^{*} p = 0.042 compared with metastatic carcinoma

^{**** 68} Cases were colorectal carcinoma, 3 cases were gastrointestinal stromal tumor (GIST), one case was gastric carcinoma, and another case was carcinoma of the papilla of Vater; p < 0.0001 compared with hepatolithiasis or HCC



^{**} p < 0.0001 compared with hepatocellular carcinoma (HCC)

^{***} p < 0.0001 compared with HCC or metastatic carcinoma

Table 2 Hepatectomy Hepatolithiasis Hepatocellular Metastatic procedures carcinoma (n = 193) carcinoma (n = 73)Right hepatectomy^a 2 38 10 Left hepatectomy^b 21 32 7 Middle bisegmentectomy 0 8 0 Lateral sectionectomy 18 22 11 a Including a right trisectionectomy Right anterior sectionectomy 0 4 1 b Including a left Right posterior sectionectomy 1 11 6 trisectionectomy 0 Segmentectomy or Partial resection 70 27 ^c Indicating nontypical Othersc 0 8 11 resections or multiple resections

Table 3 Preoperative blood examination data of the hepatectomy patients

	Hepatolithiasis (a)	HCC (b)	HCC (b) Metastatic carcinoma (c) $(n = 193)$ $(n = 73)$	p Value	p Value		
	(n = 42)	(n = 193)		(a) vs. (b)	(a) vs. (c)	(b) vs. (c)	
Plt (10 ⁴ /μl)	21.1 ± 8.8	17.1 ± 7.9	24.1 ± 9.4	0.004	ND	<0.001	
PT (%)	86.2 ± 15.7	84.7 ± 13.5	85.2 ± 13.7	ND	ND	ND	
AST (IU/ml)	53.4 ± 18.3	57.1 ± 29.4	30.2 ± 9.3	ND	< 0.001	< 0.001	
ALT (IU/ml)	50.5 ± 21.6	51.7 ± 32.8	31.4 ± 8.4	ND	< 0.001	< 0.001	
Total bilirubin (mg/dl)	1.3 ± 0.7	0.9 ± 0.4	0.7 ± 0.4	< 0.001	< 0.001	< 0.001	
Albumin (g/dl)	3.9 ± 0.4	3.7 ± 0.5	4.0 ± 0.5	0.007	ND	< 0.001	
ICG K value	0.15 ± 0.04	0.13 ± 0.03	0.16 ± 0.04	0.004	ND	< 0.001	
HbA1c (%)	5.3 ± 0.3	6.0 ± 0.5	5.6 ± 0.4	< 0.001	ND	< 0.001	
WBC (/μl)	$11,100 \pm 2,280$	$6,960 \pm 1,820$	$7,650 \pm 1,570$	< 0.001	< 0.001	ND	
CRP (mg/dl)	0.9 ± 0.8	0.4 ± 0.2	0.3 ± 0.2	< 0.001	< 0.001	ND	

All data are shown as means ± standard deviation

Plt platelets, AST aspartate aminotransferase, ALT alanine aminotransferase, ICG indocyanine green, CRP C-reactive protein, PT prothrombin time, WBC white blood cell count

ND not detected

The platelet count, serum albumin, and ICG K values were significantly lower in patients with HCC than in the patients with hepatolithiasis and those with metastatic carcinoma. The white blood cell (WBC) count and C-reactive protein (CRP) level were significantly higher in patients with hepatolithiasis than in patients with HCC and those with metastatic carcinoma.

Early-stage complications following surgical treatment for hepatolithiasis, HCC, and metastatic carcinoma are compared in Table 4. Surgical site infections (SSIs) within 30 days after surgery, such as wound infection and intraperitoneal abscess, were observed in 10 patients (23.8%) with hepatolithiasis, whereas SSIs were present in 22 of 193 patients with HCC (11.3%) and only 2 of 73 patients with metastatic carcinoma. A significantly higher SSI rate was observed in the patients with hepatolithiasis than in patients with HCC (p = 0.034) and those with metastatic carcinoma (p < 0.001). Furthermore, a significantly higher SSI rate was observed in the patients with HCC than in patients with metastatic carcinoma (p = 0.034). None of

the complications were life-threatening and all improved with conservative treatment after a liver resection with hepatolithiasis.

The incidences of SSIs and remote site infections within 30 days after hepatectomy for hepatolithiasis, HCC, and metastatic carcinoma are shown separately in Table 5. The incidence of superficial or deep incisional SSIs after hepatectomy for hepatolithiasis (11.9%) was higher than that for metastatic carcinoma (1.4%) (p < 0.001). In the same way, the incidence of superficial or deep incisional SSIs after hepatectomy for HCC (7.8%) was higher than that for metastatic carcinoma (1.4%) (p = 0.050). There was a significant difference in the incidence of space/organ SSIs between the patients with hepatolithiasis (11.9%) and HCC patients (3.6%) (p = 0.029), and between the patients with hepatolithiasis and metastatic carcinoma patients (1.4%) (p < 0.001). However, there was no significant difference in the incidence of remote site infections (including respiratory, urinary tract, and catheter-related infections) between patients with hepatolithiasis, HCC, and metastatic



Table 4 Early-stage
complications following
hepatectomy

	Hepatolithiasis $n = 42$	$ HCC \\ n = 193 $	Metastatic carcinoma $n = 73$
Death	0	4 (2.2%)	1 (1.4%)
Surgical site infections	10 (23.8%)*	22 (11.3)**	2 (2.7)
Remote site infections	2 (4.8)	8 (4.1)	3 (4.1)
Bile leakage	2 (4.8)	7 (3.6)	1 (1.4)
Пеus	1 (2.4)	5 (2.6)	2 (2.7)
Disturbance of liver function	4 (9.5)	8 (4.1)	4 (5.5)
Pancreatitis	3 (7.1)	5 (2.6)	2 (2.7)
Gastrointestinal bleeding	1 (2.4)	5 (2.6)	1 (1.4)
Intractable ascites	1 (2.4)	10 (5.2)	0
Intractable pleural effusion	1 (2.4)	11 (5.7)	1 (1.4)
Intraabdominal bleeding	1 (2.4)	1 (0.5)	0
Others	2 (4.8)	6 (3.1)	3 (4.1)

* p = 0.034 compared with HCC, p < 0.001 compared with metastatic carcinoma
** p = 0.028 compared with metastatic carcinoma

Table 5 Incidence of surgical site infections after hepatectomy

		HCC (b) Metastatic carcinoma (c)	p Value			
	(n = 42)	(n = 193)	(n=73)	(a) vs. (b)	(a) vs. (c)	(b) vs. (c)
Surgical site infections (SSIs)						
Superficial or deep incisional SSIs	5 (11.9%)	15 (7.8%)	1 (1.4%)	ND	< 0.001	0.050
Organ/space SSIs	5 (11.9%)	7 (3.6%)	1 (1.4%)	0.029	< 0.001	ND
Remote site infections						
Respiratory infections	1 (2.4%)	3 (1.6%)	2 (2.7%)	ND	ND	ND
Urinary tract infections	0	1 (0.5%)	0	ND	ND	ND
Catheter-related infections	1 (2.4%)	4 (2.1%)	1 (1.4%)	ND	ND	ND

Table 6 Distribution of bacterial strains isolated from bile during hepatectomy

	Hepatolithiasis $(n = 42)$	HCC (n = 51)	Metastatic carcinoma (n = 20)
No. of patients with positive culture (%)	35 (83.3%)*	4 (7.8%)	2 (10.0%)
Bacterial flora (mono/poly)	22/13	4/0	2/0

^{*} p < 0.001 compared with HCC or metastatic carcinoma

carcinomas. There was no significant difference in the incidence of SSIs in regard to the type of liver resection (i.e., major versus minor hepatectomy) including the patients with HCC and those with metastatic carcinoma.

Distribution of bacterial strains isolated from bile during the operation and those detected from SSIs

The distribution of bacterial strains isolated from bile during the operations is shown in Table 6. The overall positive culture rate in the bile in this study was 36.2%, although the rates were 83.3, 7.8, and 10.0% for hepatolithiasis, HCC, and metastatic carcinoma, respectively. A significantly higher (p < 0.001) positive bile culture rate was found for hepatolithiasis compared with HCC or metastatic carcinoma. Similarly, polymicrobial infections were not detected in the patients with HCC or metastatic carcinoma, whereas polymicrobial infections were detected in the bile of as many as 13 of the 35 patients (37.1%) with hepatolithiasis.

Relationships between bacteria isolated from bile during the operation for hepatolithasis and those detected from SSIs are shown in Table 7. Fifty-two bacterial and fungal species were isolated from bile and fourteen bacterial and fungal species were detected from SSIs. The detection rates of *Enterococcus* sp., *Escherichia coli*, and *Klebsiella* sp. in the bile were 19.2, 21.2, and 13.5%, respectively, and in a similar pattern, the detection rates of *Enterococcus* sp., *E. coli*, and *Klebsiella* sp. from SSIs were 21.4, 21.4, and 14.3%, respectively. Case-specific data of SSI-positive patients, comparing bacterial species isolated from bile during the operation for hepatolithasis and bacterial species isolated from SSIs, are shown in Table 8. In 8 of the 10



SSI-positive patients, a similar relationship was found between bacteria isolated from the bile during the operation for hepatolithasis and bacteria isolated from SSIs.

Table 7 Relationship between bacteria isolated from bile during operation for hepatolithasis and those detected from SSIs

	Isolated bacterial species in the bile	Isolated bacterial species from SSIs
Gram-positive cocci		
MRSA	0	1
MSS	0	1
S. epidermidis	1	1
CNS	2	0
Streptococcus sp.	2	0
Enterococcus sp.	10 (19.2%)	3 (21.4%)
Others	2	0
Total	17 (32.7%)	6 (42.9%)
Gram-negative bacilli		*
E. coli	11 (21.2%)	3 (21.4%)
Klebsiella sp.	7 (13.5%)	2 (14.3%)
Enterobacter sp.	3	1
Pseudomonas sp.	5	2
Serratia sp.	2	0
Bacteroides sp.	3	0
Others	3	0
Total	34 (65.4%)	8 (57.1%)
Fungi		
Candida sp.	1	0
Total (bacteria + fungi) (Number of strains)	52	14

MRSA methicillin-resistant Staphylococcus aureus, MSS methicillinsensitive Staphylococcus aureus, CNS coagulase negative Staphylococcus aureus

Discussion

Infections frequently occur after a liver resection and cause a significant proportion of postoperative complications. According to the National Nosocomical Infections Surveillance (NNIS) report, SSI rates range from 3.24 to 7.04% after hepato-pancreaticobiliary surgery [4]. Several studies suggest an important role for the liver in postoperative infection [13, 14]. Schindl et al. [15]. reported a relationship between the resected liver volume and the incidence of postoperative infection. A significant loss of hepatic phagocytes (Kupffer cells) and the decreased synthesis of hepatic proteins involved in antigen recognition, opsonisation, and phagocytosis are considered to result in impaired innate immune function following major liver resection, consequently rendering the patient more susceptible to infection [16].

Some infections may be dependent on the condition of patients, the extent of liver resection performed, and liver function; however, other infections are determined by a multitude of factors. Ten percent to 30% of patients with cirrhosis or chronic liver dysfunction developed postoperative bacterial infections after undergoing an abdominal surgical procedure [17, 18]. Pessaux et al. [19]. reported that 37 (28.4%) of 130 patients with cirrhosis developed a postoperative infection. This high prevalence of infectious complications in cirrhotic patients can be explained by impaired immune defense mechanisms [16], including reticulo-endothelial system dysfunction, granulocyte dysfunction, and disturbed blood sugar control. Changes in the digestive flora and in the intestinal barrier may also play a role in the pathophysiology of bacterial infections during cirrhosis. Cirrhosis and chronic liver dysfunction with HCC are risk factors for global infectious complications [16].

Table 8 Case-specific data of SSI-positive patients following hepatectomy for hepatolithiasis

Patient (age, y	ts rears; sex)	Hepatectomy procedure	Bacterial species in bile during hepatectomy	Bacterial species isolated from SSI	Type of SSI
1	61 F	Left hepatectomy	E. coli, Bacteroides sp.	E. coli	0
2	51 M	Left hepatectomy	Enterococcus sp., Klebsiella sp.	Enterococcus sp., MRSA	O
3	42 M	Lateral sectionectomy	Klebsiella sp., Bacteroides sp.	Klebsiella sp.	О
4	54 M	Lateral sectionectomy	E. coli	Enterobacter sp., MSSA	O
5	65 F	Right hepatectomy	Enterococcus sp., Klebsiella sp.	Enterococcus sp., Klebsiella sp.	О
6	46 F	Lateral sectionectomy	Enterococcus sp., E. coli	Enterococcus sp	S
7	55 F	Lateral sectionectomy	E. coli	E. coli, S. epidermidis	S
8	67 F	Right hepatectomy	Serratia sp.	Pseudomonas sp.	S
9	72 M	Left hepatectomy	E. coli, Bacteroides sp.	E. coli	S
10	69 F	Left hepatectomy	Pseudomonas sp.	Pseudomonas sp.	S

Species shown in boldface are isolated both in bile and from SSI at the same patient

O organ/space SSI, S superficial or deep SSI



Several recent studies have shown that antimicrobial prophylaxis during the preoperative period reduces the incidence of SSIs [7]. If prophylactic antibiotics are not used in surgery patients, the reported incidence of incisional SSIs is 30-50% [20, 21]. Our study involved the SSI data of patients receiving prophylactic antibiotics under the CDC guidelines. Although there have been no published data about the effectiveness of postoperative administration of antibiotics, an additional 1-3 days of antibiotics were administered to the patients in our study. The incidence of SSIs after hepatectomy for the patients with hepatolithiasis in our study was higher than that in the patients with HCC and those with metastatic carcinoma. The mean age of the patients with hepatolithiasis was younger than the mean age of the patients with HCC and metastatic carcinoma. No patients with hepatolithiasis had liver cirrhosis and diabetes. We found a significant relationship between bile infection and the incidence of postoperative SSIs. Our study showed a similar relationship between bacterial species isolated from the bile during the operation for hepatolithasis and bacteria isolated from SSIs. Biliary stone disease such as hepatolithiasis is the most common cause of biliary obstruction, and the common biliary pathogens, including Escherichia coli, Klebsiella sp., and Enterococcus sp., were isolated in patients with hepatolithiasis [5]. The incidence of bile infection in patients receiving elective surgery is considerable and is associated with a significant degree of mortality and morbidity. Although all of the patients in our study underwent a hepatectomy without reconstruction of the intestine or the biliary tract, the highest incidence of SSIs after hepatectomy was observed in patients with hepatolithiasis. The reason for this high rate may be due to the fact that a small amount of infectious bile contaminated the cut edge of the liver. Our study suggests the existence of a relationship between postoperative SSIs and bile infection, thus supporting the proposed relationship between post-hepatectomy infection and such variables as liver function, blood sugar control, and nutritional status.

References

- Erdogan D, Busch OR, van Delden OM, Rauws EA, Gouma DJ, van Gulik TM. Incidence and management of bile leakage after partial liver resection. Dig Surg. 2008;25:60-6.
- Togo S, Matsuo K, Tanaka K, Matsumoto C, Shimizu T, Ueda M, et al. Perioperative infection control and its effectiveness in hepatectomy patients. J Gastroenterol Hepatol. 2007;22:1942-8.
- Li SQ, Liang LJ, Peng BG, Lu MD, Lai JM, Li DM. Bile leakage after hepatectomy for hepatolithiasis: risk factors and management. Surgery. 2007;141:340-5.
- Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for prevention of surgical site infection, 1999 Centers for Disease Control and Prevention (CDC) Hospital Infection

- Control Practices Advisory Committee. Am J Infect Control. 1999:27:97–132.
- Uchiyama K, Kawai M, Ueno M, Ozawa S, Tani M, Yamaue H. Reducing residual and recurrent stones by hepatectomy for hepatolithiasis. J Gastrointest Surg. 2007;11:626-30.
- Uchiyama K, Onishi H, Tani M, Kinoshita H, Kawai M, Ueno M, et al. Long-term prognosis after treatment of patients with choledocholithiasis. Ann Surg. 2003;238:97–102.
- Uchiyama K, Kawai M, Onishi H, Tani M, Kinoshita H, Ueno M, et al. Preoperative antimicrobial administration for prevention of postoperative infection in patients with laparoscopic cholecystectomy. Dig Dis Sci. 2003;48:1955-9.
- Kobayashi S, Gotohda N, Nakagohri T, Takahashi S, Konishi M, Kinoshita T. Risk factors of surgical site infection after hepatectomy for liver cancers. World J Surg. 2009;33:312-7.
- Uchiyama K, Ueno M, Ozawa S, Hayami S, Kawai M, Tani M, et al. Half clamping of the infrahepatic inferior vena cava reduces bleeding during a hepatectomy by decreasing the central venous pressure. Langenbecks Arch Surg. 2009;394:243-7.
- Hasegawa K, Kokudo N, Imamura H, Matsuyama Y, Aoki T, Minagawa M, et al. Prognostic impact of anatomic resection for hepatocellular carcinoma. Ann Surg. 2005;242:252-9.
- Gonzales R, Bartlett JG, Besser RE, Cooper RJ, Hickner JM, Hoffman JR, et al. Principles of appropriate antibiotic use for treatment of acute respiratory tract infections in adults: background, specific aims, and methods. Ann Intern Med. 2001;134:479-86.
- Manges AR, Johnson JR, Foxman B, O'Bryan TT, Fullerton KE, Riley LW. Wide spread distribution of urinary tract infections caused by a multidrug-resistant *Escherichia coli* clonal group. N Engl J Med. 2001;345:1007-13.
- Belghiti J, Hiramatsu K, Benoist S, Massault P, Sauvanet A, Farges O. Seven hundred forty-seven hepatectomies in the 1990s: an update to evaluate the actual risk of liver resection. J Am Coll Surg. 2000;191:38-46.
- Behrns KE, Tsiotos GG, DeSouza NF, Krishna MK, Ludwig J, Nagorney DM. Hepatic steatosis as a potential risk factor for major hepatic resection. J Gastrointest Surg. 1998;2:292-8.
- Schindl MJ, Millar AM, Redhead DN, Fearon KC, Ross JA, Dejong CH, et al. The adaptive response of the reticuloendothelial system to major liver resection in humans. Ann Surg. 2006;243:507-14.
- Schindl MJ, Redhead DN, Fearon KC, Garden OJ, Wigmore SJ. Edinburgh Liver Surgery and Transplantation Experimental Research Group (eLISTER). The value of residual liver volume as a predictor of hepatic dysfunction and infection after major liver resection. Gut. 2005;54:289-96.
- Wong R, Rappaport W, Witte C, Hunter G, Jaffe P, Hall K, et al. Risk of nonshunt abdominal operation in the patient with cirrhosis. J Am Coll Surg. 1994;179:412-6.
- Mansour A, Watson W, Shayani V, Pickleman J. Abdominal operations in patients with cirrhosis: still a major surgical challenge. Surgery. 1997;122:730-5.
- Pessaux P, Msika S, Atalla D, Hay JM, Flamant Y. French Association for Surgical Research. Risk factors for postoperative infectious complications in noncolorectal abdominal surgery: a multivariate analysis based on a prospective multicenter study of 4718 patients. Arch Surg. 2003;138:314-24.
- Fujita S, Saito N, Yamada T, Takii Y, Kondo K, Ohue M, et al. Randomized, multicenter trial of antibiotic prophylaxis in elective colorectal surgery: single dose vs. 3 doses of a second-generation cephalosporin without metronidazole and oral antibiotics. Arch Surg. 2007;142:657-61.
- Mohri Y, Tonouchi H, Kobayashi M, Nakai K, Kusunoki M. Mie Surgical Infection Research Group. Randomized clinical trial of single- versus multiple-dose antimicrobial prophylaxis in gastric cancer surgery. Br J Surg. 2007;94:683-8.



特集:縫合糸と感染

トピックス

腹腔内操作における縫合糸の選択 一多施設共同 SSI サーベイランス結果より一

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要盲:【目的】多施設共同手術部位感染(以下,SSI)サーベイランスのデータから腹腔内での絹糸使用の有無と SSI について検討したので報告する。【方法】19 施設で実施された消化器外科手術を対象とした。サーベイランス方法は JHAIS に準拠した。腹腔内で絹糸を使用した症例(絹糸群)と腹腔内で絹糸を使用せず合成吸収糸を使用した症例(吸収糸群)において SSI を比較した。【成績】解析対象として 13,378 症例を集計した。絹糸群の SSI は 17.3%であったのに対し,吸収糸群は 15.3%と統計学有意に低値であった(p < 0.01)。手術手技コード別では胃手術,胆摘,小腸手術,結腸手術,直腸手術では差を認めなかったが,虫垂手術と肝胆膵手術では 16.7% vs 10.8% 、30.0% vs 18.3%と吸収糸群で有意に低値であった(p = 0.01,p < 0.01)。【考察】消化器外科手術,特に虫垂切除術と肝胆膵手術においては SSI 予防の面から合成吸収糸を使用すべきと考えられた。

【索引用語】 手術部位感染,縫合糸,合成吸収糸

はじめに

日本では伝統的に絹糸を多く用いられてきたが、 絹糸の科学的有用性を実証した研究は乏しい。われ われは関西地区で比較的詳細に多施設共同手術部位 感染サーベイランスを施行してきた¹⁾。消化器外科 における絹糸使用の有無と手術部位感染に関して検 討したので報告する。

I. 方 法

サーベイランスは関西地区の19施設(大学病院1, 国公立病院10,その他の公的病院5,私立病院3)で, 2003年7月から2008年8月の間に施行された,消 化器外科手術(胃手術GAST,胆囊摘出術CHOL, 肝胆膵手術BILI,小腸手術SB,結腸手術COLN, 直腸手術REC)(英字は手術手技コード)を対象と した。サーベイランスの方法はJapanese healthcare-associated infections surveillance (以下,JHAIS) に準拠し,調査した項目はJHAIS項目の28種類に 網糸の使用の有無などの12項目を追加した。絹糸 を使用したかどうかについては腹腔内だけでなく腹 壁縫合も含めた。絹糸を使用していない手術におい ては腹腔内だけでなく、腹壁、皮膚縫合も絹糸以外の糸を使用している。なおドレーンの逆行性感染もSSIと定義した。SSIの判定はできるだけ看護師が行い、外科医のみの判定は避けるよう各施設に依頼した¹⁾。このサーベイランスで得られた症例のうち、鏡視下手術を除いた開腹手術症例を本研究の解析対象とした。各手術で腹腔内にて絹糸を使用した症例(絹糸群)と腹腔内で絹糸を使用せず合成吸収糸を使用した症例(吸収糸群)において手術部位感染率を比較した。また施設毎に吸収糸使用頻度を算出し、高頻度使用施設とそれ以外の施設について SSI について検討した。統計解析は t 検定および x² 検定を用いて、P値 0.05 未満を有意と判定した。

Ⅱ. 結 集

解析対象として 13.378 症例を集計した。吸収糸群と絹糸群の症例数はそれぞれ 6,991 例と 6,387 例であった。背景因子を比較すると,吸収糸群が絹糸群に比べて,汚染感染手術が多くまた ASA が 3 以上の症例が多く含まれていたが,手術時間は短時間であった(表 1)。SSI の発生は吸収糸群で 1,068 例 (15.3%),絹糸群で 1,102 例 (17.3%) と吸収糸群

表 2 虫垂切除術

	吸収糸群	絹糸群	P 値
症例数	882	508	
年齢	39.8 ± 21	37.4 ± 21	0.04
(歳,平均±SD)			
性	522/360	297/211	0.79
(男 / 女)			
創分類	440/442	266/242	0.37
(2/3, 4)			
ASA スコア	837/45	489/19	0.24
(1, 2/3, 4, 5)			
手術時間	65.2 ± 35	62.8 ± 33	0.20
(分±SD)			
SSI (%)	10.8 (95/882)	16.7 (85/508)	< 0.01

表 3 肝胆膵手術

	吸収糸群	絹糸群	P 値
症例数	1,049	830	
年齢	66.1 ± 11	65.0 ± 10	0.02
(歳,平均±SD)			
性	709/340	536/294	0.17
(男 / 女)			
創分類	977/72	775/55	0.84
(2/3, 4)			
ASA スコア	927/122	748/82	0.23
(1, 2/3, 4, 5)			
手術時間	280.9 ± 157	563.6 ± 656	0.16
(分±SD)			
SSI (%)	18.3 (192/1,049)	30.0 (248/830)	< 0.01

0.69), 結腸手術 18.3% (307/1,657), 16.6% (258/1,552), (P=0.24), 直腸手術 22.2% (182/819), 23.9% (218/912), (P=0.51), 肝胆膵手術 18.4% (192/1,049), 30.0% (248/830), (P<0.01), 小腸手術 23.0% (70/305), 32.0% (66/206), (P=0.09) と虫垂切徐術と肝胆膵手術にて有意に SSI が低値であったが,他の手術では有意な差を認めなかった (図 2)。また SSI の深さについては,虫垂切徐術では臓器体腔感染が吸収糸群 23.6%,絹糸群 19.5%と差を認めなかった (P=0.52) が,肝胆膵手術ではそれぞれ 56.8%, 74.0%と吸収糸群で臓器体腔感染の頻度が有意 (P<0.01) に低率であった。

施設毎の吸収糸使用頻度は図3に示すように多くの施設で絹糸の使用頻度が高いものの6施設(施設F,H,L,M,N,Q)で75%以上吸収糸を使用していた。この高頻度吸収糸使用施設とその他の低頻度吸収糸使用頻度施設でSSIの頻度を比較したところ,15.7%(993/6,312),15.8%(1,177/7,065)と差を認めなかった。虫垂切除術と肝胆膵手術について,背景因子について検討したところ,年齢がどち

らも絹糸群で低年齢であったが、他の因子について は差を認めなかった(表 2,3)。また高頻度吸収糸 使用施設とその他の低頻度吸収糸使用頻度施設で SSI の頻度を比較したところ、11.3%、14.2%と 21.2%,25.1%と有意な差を認めなかった(P=0.16, P=0.12)。

Ⅲ. 考察

SSI を起こすのに必要な細菌数は組織 1g あたり 10⁵ 個であるが ²¹、絹糸の存在下では 10² で SSI が起こるとされている ³¹。米国では 1970 年後半すでに創閉鎖における糸の選択について、絹糸のほうが合成吸収糸より創感染や縫合糸膿瘍が有意に高率であると報告されている ⁴⁾⁵⁾。しかし腹腔内の結紮糸に関しては絹糸と合成吸収糸について比較した科学的な報告はない。われわれのデータでは吸収糸群が絹糸群に比べて有意に SSI が低値であったが背景因子に差を認めているため評価は慎重であるべきと思われた。ただし背景因子で手術時間が吸収糸群で短時間であるが、創分類、ASA の 2 項目は吸収糸群

表1 背景因子

	吸収糸群	絹糸群	P 値
症例数	6,991	6,387	
年齢	63.2 ± 16	63.2 ± 15	0.83
(歳,平均±SD)			
性	4,362/2,664	3,992/2,397	0.46
(男 / 女)			
創分類	5,915/1,075	5,638/748	< 0.01
(2/3, 4)			
ASA スコア	6,197/793	5,775/611	< 0.01
(1, 2/3, 4, 5)			
手術時間	174.9 ± 106	205.8 ± 120	< 0.01
(分±SD)			

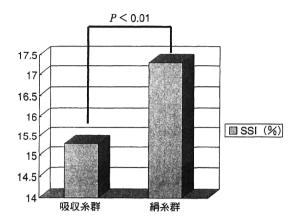


図1 腹腔内使用糸の種類とSSI

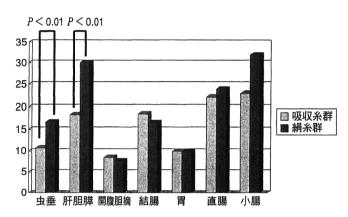


図2 手術術式別の腹腔内使用糸とSSI

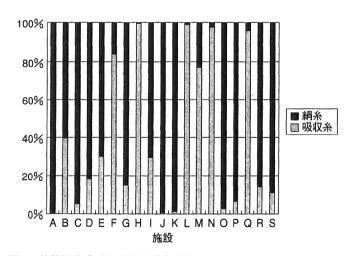


図3 施設別合成吸収糸使用手術頻度

で2ポイント SSI が統計学的有意 (P < 0.01) に低値であった (図1)。手術手技コード別では虫垂切徐術 1,390 例,肝胆膵手術 1,879 例,開腹胆嚢摘出術 728 例,結腸手術 3,209 例,胃手術 3,928 例,直腸手術 1,731 例,小腸手術 611 例であった。吸収糸群と絹糸群の症例数はそれぞれ,虫垂切徐術 882 例,508 例,肝胆膵手術 1,049 例,830 例,開腹胆嚢摘

出術 363 例, 365 例, 結腸手術 1,657 例, 1,552 例, 胃手術 1,915 例, 2,013 例, 直腸手術 819 例, 912 例, 小腸手術 305 例, 206 例であった。手術手技コード 別にみた SSI の発生は虫垂切除術 10.8% (95/883), 16.7 % (85/509), (P < 0.01), 胃手術 10.0 % (191/1,915), 9.9% (199/2,013), (P = 0.93), 開腹 胆嚢摘出術 8.5% (31/363), 7.7% (28/365), (P =

で不利な条件でありながら吸収糸群で SSI が低値で あったことは十分に吸収糸の SSI に対する有用性を 示していると考えられた。

手術手技コード別でみると虫垂切除術と肝胆膵手術の2手術でのみSSIに有意な差が認められたが、他の術式では有意差を認めなかった。虫垂切除術は腹腔内で使用する糸は2~3本であり、腹壁の縫合においても多数の糸を使用するとは考えられないがSSI発生で差を認めた。施設により吸収糸の使用頻度が異なることから、施設別で検討したが差を認めなかった。すでに感染が成立してからの手術であることから吸収糸の関与が大きいものと推測された。

肝胆膵手術では他の手術に比べて比較的多くの縫合糸を使用する。臓器体腔感染が吸収糸群で有意に低率であった事からも吸収糸使用が感染予防に関与したと推察できる。また動物実験では肝切除術において吸収糸を使った方が絹糸を使うよりも SSI が少ないことが証明されている ⁶¹ 事からも合理的な結果と考えられた。

われわれのデータは比較試験でない事から背景因 子にも差があり、解釈に当たる際には注意が必要で あるが、SSI 予防の点からみて吸収糸に有用性があると考えられた。

汝 献

- 1) 清水潤三, 宮本敦史, 梅下浩司, ほか: 関西地区に おける多施設共同手術部位感染サーベイランス. 日 消外会誌 2006; 39: 435-439
- Krizek TJ, Robson MC: Evolution of quantitative bacteriology in wound management. Am J Surg 1975; 130: 579-584
- Noble WC: The production of subcutaneous staphylococcal skin lesions in mice. Br J Exp Pathol 1965: 46: 254-262
- Adams IW, Bell MS, Driver RM, et al: A comparative trial of polyglycolic acid and silk as suture materials for accidental wounds. Lancet 1977; 10: 1216-1217
- 5) Kronborg O: Polyglycolic acid (Dexon) versus silk for fascial closure of abdominal incisions. Acta Chir Scand 1976; 142: 9-12
- Togo S, Kubota T, Takahashi T, et al: Usefulness of absorbable sutures in preventing surgical site infection in hepatectomy. J Gastrointest Surg 2008; 12: 1041-1046

Suture material and surgical site infection in abdominal surgery — Result of multicenter SSI surveillance —

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[Purpose] We examined the efficacy of silk and synthetic absorbable suture in surgical site infection (SSI) of digestive tract surgery from the data of multi center SSI surveillance. [Method] The objective was digestive tract surgery performed in 19 hospitals in the Kansai area of western Japan. The method of surveillance conformed to JHAIS. SSI rate of silk suture (Silk group) was compared with that of synthetic absorbable suture (Absorbable group). [Result] SSI rate of Silk group was significantly higher than that of Absorbable group (17.3% vs 15.3%, P < 0.01). In gastric surgery, cholecystectomy, small bowel surgery, and colorectal surgery, there were no differences between both group. In appendectomy and biliary surgery SSI rate of Silk group was significantly higher than that of Absorbable group (16.7% vs 10.8%, p = 0.01, and 30.0% vs 18.3%, P < 0.01). [Conclusion] The synthetic absorbable suture must be used in digestive tract surgery especially appendectomy and biliary surgery for prevention of SSI.

原 著

当院における Stenotrophomonas maltophilia の検出状況の特徴について

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要旨:2004年から2008年に提出された細菌培養検体(130,021 検体)から分離された S.maltophilia2,788 検体(839 症例)を解析対象とした。検出症例の入院期間は51日(中央値),入院後 S.maltophilia が検出されるまでの期間は15日(中央値)であった。ほぼ全例に抗菌薬投与が施行されており、中心静脈カテーテル留置71.2%、人工呼吸器が48.8%に装着されていた。診療科別の検出率は救急集中治療部で3.6%と高く、検体別には喀痰や気管分泌物から7.0%と高率に検出された。IPM/CSや MEPMには感受性を示さなかったが、MINOには良い感受性を示した。839例中死亡は205例(24.4%)でそのうち96例(46.8%)は担癌患者であった。さらにMRSAと緑膿菌が同時検出された112症例中75例(67.0%)が死亡していた。

【索引用語】 Stenotrophomonas maltophilia, 複数菌感染症, メタロβ-ラクタマーゼ, 多剤耐性菌

はじめに

今回は当院での過去5年間のS.maltophiliaの検出 状況を調査し、その臨床的特徴について検討した。

I. 対象および方法

対象期間は2004年1月から2008年12月で,この期間に和歌山県立医科大学で実施された細菌培養 検体(130,021 検体)から分離されたS.maltophilia 2,788 検体(患者数839例)を対象としてretrospective に検討した。検討項目は、検出患者の年齢, 性別,入院期間,死亡患者数,分離までの期間,検 出された診療科,同時に検出された菌種および抗菌 薬の感受性である。抗菌薬感受性は CLSI 準拠によ り,Sensitive (S),Intermediate (I),Resistant (R) とし,それぞれを割合で示した。また,結果的に死 亡退院となった 205 例において同時に検出された菌 種の詳細な検討を行った。

なお、統計学的検討は χ^2 検定により、p-value<0.05 を統計学的有意とした。

Ⅱ. 結果

対象期間内の S.maltophilia の総検体数における検出率は 2.1%,検出症例数は 839 例で男性 565 例,女性 274 例と男性に多かった。平均年齢は 63 ± 22 歳(平均 \pm 標準偏差)で,入院期間の中央値は 51 日 $(1\sim739$ 日) と長期入院が特徴的であった(表 1)。また入院後 S.maltophilia が検出されるまでの中央値は 15 日(入院当日 $\sim1,009$ 日)であったが,転院例では前病院での入院期間は含まれておらず,継続入院期間はさらに長くなる可能性がある。

S.maltophilia 分離前 1 週間以内に抗菌薬が投与されていた症例は 765 例 (91.2%) であったが、転院 例では前医での投与歴が含まれていないので、ほぼ全例で抗菌薬投与を受けていたと考えられる。また

表1 S.maltophilia 検出患者一覧

	$(2004 \sim 2008)$
S.maltophilia 検出検体数 / 総検体数 (検出率)	2,788/130,021 (2.1%)
S.maltophilia 検出症例数(男 / 女)	839 (565/274)
年齢 (平均 ± 標準偏差)	63 ± 22 歳
入院期間 (日)	51 (1 ~ 739) *
S.maltophilia 分離までの期間(日)	15 (0 ~ 1,009) *
死亡症例数(%)	205 (24.4%)

*中央值(最低~最高)

表 2 S.maltophilia 検出患者背景

		(n = 839)
抗菌薬使用(1週間以内)	765	(91.2%)
尿道カテーテル留置	615	(73.3%)
中心静脈カテーテル留置	597	(71.2%)
人工呼吸器装着	406	(48.4%)
呼吸器疾患	428	(51.0%)
重症外傷・熱傷	276	(32.9%)
担癌患者	301	(35.9%)
血液疾患患者	42	(5.0%)
定期的透析施行患者	32	(3.8%)

^{*}重複症例を含む

同様に分離1週間以内に尿道カテーテルが挿入されていた症例は615例(73.3%),中心静脈カテーテル留置が597例(71.2%),人工呼吸器装着406例(48.8%)と重症例の多いことが示唆された(表2)。また患者背景として,肺癌などの悪性疾患を含め,急性,慢性肺炎(2次的なものを含める),気管支炎,慢性気管支拡張症,肺気腫などの呼吸気疾患を基礎疾患に認めるものが最も多くて428例(51.0%),担癌者で病状末期を含めて抗癌剤投与や手術などを受けた症例が301例(35.9%),主としてICU管理された重症外傷や熱傷症例が276例(32.9%)であった。さらに,抗癌剤やステロイドが投与されていた血液疾患患者42例(5.0%),定期的に透析が施行されていた症例が32例(3.8%)に認められた。

診療科別の S.maltophilia 検出率を検討すると, 救急集中治療部で 3.6%と他の診療科と比較して有意に高かった (p<0.001)。内科系では糖尿病・内分泌代謝内科, 呼吸器内科, 循環器内科でおのおの2.0%, 外科系では脳神経外科3.5%, 消化器外科2.1%, 心臓血管・呼吸器外科で1.8%と重症疾患を扱う科で高い検出率を認めた(表3)。

検体別に検出率を検討すると、喀痰や気管分泌物から S.maltophilia が 7.0%に検出されており、他部位からの検体検出率に対して有意に多く検出された (p<0.001)。胃液からも 4.6%と高率に検出されたが、同時に喀痰からも検出されている症例に多く、恐ら

く喀痰を嚥下したものと考えられた。逆に血液や尿からはそれぞれ 0.3%, 0.2%と検出率は高くなかった (表 4)。

S.maltophilia の抗菌薬感受性を示す (表 5)。元来 非常に強いメタロ β ラクタタマーゼ産生菌であるため,カルバペネム系薬の Imipenem/Cilastatin (IPM/CS) や Meropenem (MEPM) にはほとんど感受性を示さず、緑膿菌治療薬である Aztreonam (AZT) にも耐性を示した。一方、テトラサイクリン系薬の Minocyclin (MINO) には良好な感受性を示し、耐性症例はなかった。キノロン系薬では Levofloxacin (以下、LVFX) および Pazufloxacin (以下、PZFX) の感受性は保たれていたが、Ciprofloxacin (以下、CPFX) の感受性は 50%以下であった。

S.maltophilia の検出された 839 例中の死亡例数は 205 例, 死亡率 24.4%であった。その中で死亡患者 の基礎疾患としては担癌患者が96例(46.8%)と 最も多かった。診療科別には重症疾患に携わる救急 集中治療部で、356例中31.2%の死亡患者を認め、 他の診療科に比較して有意に (p<0.001) 死亡率が 高かった (表 6)。S.maltophilia が単独で分離された のはわずかに 7.6%に過ぎず、他の 92.4%は複数菌 感染であった。S.maltophilia と同時に検出された菌 種のうち Methicillin-resistant Staphylococcus aureus (以下, MRSA) が350例に検出され、そのうち 105 例は死亡(死亡例の51.7%)していた。つまり MRSA が同時に検出されると死亡する可能性が高 くなることが判明した (p<0.001)。Pseudomonas aeruginosa (以下, P.aeruginosa) についても同様で, 死亡例の 43.4%にあたる 89 例に検出され、同様の 可能性が示唆された (p<0.001)。MRSA または P.aeruginosa が検出された症例にまで広げると 68.3%にあたる 140 例が死亡しており、これら2 菌 種との同時検出例は非常に予後が悪いことが示唆さ れた。