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REVIEW

Clinical practice guideline for post-ERCP pancreatitis

Tetsuya Mine[1] · Toshio Morizane[2] · Yoshiaki Kawaguchi[1] · Ryukichi Akashi[3] · Keiji Hanada[4] · Tetsuhide Ito[5] · Atsushi Kanno[6] · Mitsuhiro Kida[7] · Hiroyuki Miyagawa[8] · Taketo Yamaguchi[9] · Toshihiko Mayumi[10] · Yoshifumi Takeyama[11] · Tooru Shimosegawa[6]

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Abstract
Background Endoscopic retrograde cholangiopancreatography (ERPC) is used for the diagnosis and treatment of pancreatic and biliary diseases. Post-ERCP pancreatitis (PEP) is a complication which needs special care and clinical practice guideline for this morbidity is also needed.
Methods The key clinical issues of diagnosis and treatment of PEP were listed and checked, and then the clinical questions were formulated. PubMed (MEDLINE) and Ichushi-web (Japanese medical literature) were used as databases. For the study of diagnostic test accuracy, items similar to QUADAS-2, i.e., random selection from a population to which the diagnostic test is applied, blinding of index tests and reference tests, completeness of reference standard, completeness of test implementations, the same timing of tests, and missing data were assessed as well as the indirectness of the study subjects, index tests, reference standard, and outcomes. Grading of recommendations was determined as strong or weak. In clinical practice, the judgment of attending doctors should be more important than recommendations described in clinical practice guidelines. Gastroenterologists are the target users of this clinical practice guideline. General practitioners or general citizens are not supposed to use this guideline. The guideline committee has decided to include wide clinical issues such as etiological information, techniques of ERCP, the diagnosis, treatments, and monitoring of PEP in this guideline.
Results In this concise report, we described ten clinical questions, recommendations, and explanations pertaining to risk factors, diagnosis, prognostic factors, treatments, and preventive interventions in the medical practice for PEP.
Conclusions We reported here the essence of the clinical practice guideline for PEP.

Keywords Endoscopic retrograde cholangiopancreatography (ERPC) · Post-ERCP pancreatitis · Clinical guideline

✉ Tetsuya Mine
tetsu-m@is.icc.u-tokai.ac.jp

1 Tokai University, School of Medicine, Isehara, Japan
2 Japan Council for Quality Health Care, Tokyo, Japan
3 Kumamoto City Medical Association Health Care Center, Kumamoto, Japan
4 Onomichi General Hospital, Onomichi, Japan
5 Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
6 Department of Gastroenterology, Tohoku University, Sendai, Japan
7 Kitasato University School of Medicine, Sagamihara, Japan
8 Sapporo-Kosei General Hospital, Sapporo, Japan
9 Chiba Cancer Center, Chiba, Japan
10 University of Occupational and Environmental Health, Kitakyushu, Japan
11 Faculty of Medicine, Kinki University Hospital, Osakasayama, Japan

Introduction

Endoscopic retrograde cholangiopancreatography (ERPC) is used for diagnosis and treatment of pancreatic diseases and biliary tract diseases. ERCP needs sophisticated skills. Post-ERCP pancreatitis (PEP) is a complication which needs special care and a clinical practice guideline for this morbidity has been needed. The Japan Pancreas Society asked a committee to undertake the process of developing this clinical practice guideline. We report here the essence of the clinical practice guideline.

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The population to whom this guideline is meant to apply is adults who receive ERCP because of various diseases or morbidities. Gastroenterologists are the target users of this clinical practice guideline. General practitioners or general citizens are not supposed to use this guideline. We expect that gastroenterologists should be certified by the Japanese Society of Gastroenterology or the Japan Gastroenterological Endoscopy Society will use this guideline. The guideline committee decided to include wide clinical issues such as etiological information, techniques of ERCP, the diagnosis, treatments and monitoring of PEP in this guideline. In this concise report, we described all these clinical questions and recommendations, but mostly we omitted statements or explanations for them.

Materials and methods

Members

The chairman asked chief doctors of sections at which the yearly frequency of ERCP implementation was high in hospitals all over Japan to join as a member. The guideline development committee consisted of experts in this field and an expert of guideline development methodology.

Conflicts of interest were disclosed according to the guideline of the Japanese Society of Gastroenterology. Costs of literature gathering, meetings, and other logistic activities were covered by a research fund provided by the Ministry of Health, Labor, and Welfare Japan. During the period of developing this guideline, no committee members were asked or solicited about the development activities by other stakeholders.

Topic nomination and evidence search

Key clinical issues of diagnosis and treatment and other issues about PEP were listed and approved by the all members of the committee. Each member undertook a few key clinical issues and formulated clinical questions. These clinical questions were approved by all members of the committee. PubMed (MEDLINE) and Ichushi-web (a database of Japanese medical literature) were used as databases. Medical literature since 1985 was searched for each clinical question. The literature search was performed by members of the Japan Medical Library Association who suggested search queries and presented with search results in collaboration with the committee members.

Evidence assessment

Systematic reviews were done for each clinical question based on a literature set collected for each clinical question [1–4]. Qualitative systematic reviews were done evaluating the risk of biases and indirectness of each study. The domains of risk of bias were selection bias, performance bias, detection bias, attrition bias, and other biases. As for randomized controlled trials (RCTs), random allocation, concealment, blinding of healthcare provider and patients, blinding of outcome measurers, incomplete outcome data, intention-to-treat analysis, early stopping of trial, selective outcome reporting, and other items were assessed. As for observational studies, the same four domains were assessed but representativeness of study subjects, difference in background factors of groups compared, difference in care, appropriateness of outcome measurement, completeness of follow-up, inadequate confounder adjustments, dose–response relationship between risk factors or interventions and outcomes, assumed confounders which attenuate effectiveness, and magnitudes of effects were assessed as items. As for the study of diagnostic test accuracy, items similar to QUADAS-2 [5], i.e., random selection from a population to which the diagnostic test is applied, blinding of index tests and reference tests, completeness of reference standards, completeness of test implementations, the same timing of tests, and missing data were assessed. Indirectness of study subjects, index tests, reference standard, and outcomes were also assessed.

Formulating recommendations

The body of evidence was evaluated based on overall risk of biases, overall indirectness, inconsistencies across studies, reporting biases (publication biases), and when possible imprecision of effect measures was obtained from a quantitative systematic review (meta-analysis). Strength of the body of evidence was categorized into four levels [3]: A, strong; B, moderate; C, weak; and D, very weak. Strength reflects confidence in effectiveness and shows the strength to support a related recommendation. Grading of recommendations was determined as strong or weak (1 or 2) [3], based on evaluating benefits, harms, and burdens which a patient would receive. Recommendation grades were determined by unanimous agreement of the committee members.

Statements for legal matters

It is not anticipated that the recommendation is applied without considering conditions of individual patients, because conditions such as genetic background, comorbidities, severity of the disease, and disease stage vary among individuals. It is impossible for the guideline development committee to take into account individual conditions of each patient when they formulate recommendations. Thus, this clinical practice guideline should

not be used as legal basis to assess the appropriateness of individual medical practice.

Results

CQ1-01. Should ERCP be performed for the diagnosis of pancreatic tumors?

Recommendation The diagnostic ability of ERCP is not sufficient for evaluating solid pancreatic tumors. Therefore, the indication for ERCP should be carefully considered in cases involving these tumors. However, ERCP is necessary for the diagnosis of cases with intraductal papillary mucinous neoplasms or autoimmune pancreatitis (2-C).

Endoscopic biliary drainage should be selected for cases with obstructive jaundice due to pancreatic tumors (2-B; Table 1).

CQ1-02. Should ERCP be performed for the diagnosis?

Recommendation ERCP should be performed for the diagnosis of biliary tract cancer, such as detecting the spread of carcinoma during a histological diagnosis and for direct cholangiography, as well as for treatment, such as biliary drainage (1-B).

ERCP for gallbladder cancer should be performed for diagnosis of the histology and progression of the disease, as well as for treatment, such as biliary drainage (2-B; Table 2).

Table 1 Diagnostic performance of ERCP for pancreatic cancer

Author	Number of cases	Sensitivity (%)
Gilinsky et al.	117	80
Bakkevold et al.	2082	79
Niederau and Grendell	565	92
Burtin et al.	68	92
Rosch et al.	184	89

Table 2 Diagnostic abilities of ERCP-guided cytology and biopsy for biliary tract cancer

Author	Number of cases	Sensitivity (%)
Mansfield	16	75
Govil	22	68
Glasbrenner	27	66.7
Sugiyama	17	Cytology: 36 Biopsy: 71
Vandervoort	10	60
Macken	30	65
Farrell	4	50
Kitajima	51	Cytology: 71.6 Biopsy: 65.2

CQ1-03. Should ERCP be performed for the diagnosis and treatment of chronic pancreatitis?

Recommendation ERCP is useful for the diagnosis of chronic pancreatitis and the treatment of pancreatic stones (2-C).

CQ1-04. Should ERCP be performed for the treatment of cholelithiasis?

Recommendation For the treatment of bile duct stones, ERCP should be performed when the presence of bile duct stones is strongly suspected based on results from other diagnostic methods (2-B).

ERCP is not recommended for gallbladder drainage in cases of acute cholecystitis with gallbladder stones (2-C).

CQ2-1-1 If there is a pancreatic juice outflow obstruction, is PEP likely to develop?

Recommendation It is considered that PEP is likely to develop if there is a pancreatic juice outflow obstruction. Therefore, careful monitoring is necessary (2-B).

CQ2-01-2a Are the time for ERCP, volume and pressure of contrast medium injected, and number of sessions of cannulation related to PEP?

Recommendation The longer duration of obstruction of the pancreatic duct, contrast medium volume and pressure, and frequent cannulation are believed to cause pancreatic duct pressure hypertension; these are shown to be related to onset of PEP. Therefore, these risk factors should be as minimized as much as possible (2-B).

CQ2-01-2b Are pancreatic duct brushing and/or intraductal (IDUS) involved in onset of PEP?

Recommendation Pancreatic duct brushing and/or IDUS are thought to be involved in the onset of PEP. Care should be taken when ERCP is performed (2-C).

CQ2-01-2c Are dysfunction of the minor papilla and/or Santorini duct involved in the onset of PEP?

Recommendation Dysfunction of the minor papilla and/or Santorini duct is thought to be involved in the onset of PEP. Thus, cases such as the contrast agent stasis in the

main pancreatic duct at ERCP require attention for onset of PEP (2-C).

CQ3-01 Is it possible to get risk factors by hearing an anamnesis?

Recommendation There are risk factors of PEP, and it's recommended to hear a case history of previous diseases (1-B).

CQ3-02 Is there a possibility of PEP when strong abdominal pain appears after ERCP?

Recommendation Strong abdominal pain indicates a high probability of PEP and needs to confirm the diagnosis (1-A).

CQ3-03 Is abdominal palpation useful in diagnosing PEP after ERCP?

Recommendation Abdominal palpation is useful in diagnosing PEP after ERCP, and it's recommended (1-C).

CQ-4-01 What are the patient-related risk factors for PEP? Are young age, female sex, history of sphincter of Oddi dysfunction (SOD), history of PEP, and recurrent pancreatitis predisposing factors for PEP?

Recommendation Sufficient attention should be paid to suspected SOD, female sex, and history of pancreatitis as patient-related risk factors for PEP (2-B). Attention should be paid to young age, absence of extrahepatic bile duct dilatation, and normal serum bilirubin as patient-related risk factors for PEP (2-B).

CQ-4-02 What are the procedure-related risk factors for PEP? Are pancreatic sphincterotomy, endoscopic papillary balloon dilation (EPBD), difficulty in cannulation, and precutting predisposing factors for PEP?

Recommendation Attention should be paid to precutting and one or more contrast injections to the pancreatic duct as procedure-related risk factors for PEP (2-B). Attention should be paid to five or more cannulation attempts, pancreatic sphincterotomy, papillary balloon dilation, and residual bile duct stones as procedure-related risk factors for PEP (2-B). Attention should be paid to PEP when performing papillectomy (2-B).

CQ5-1. Is specific explanation about the incidence and mortality of severe acute pancreatitis essential in the informed consent for ERCP?

Recommendation The possibility of death caused by deteriorating pancreatitis after ERCP should be explained in advance (1-C; Table 3).

CQ5-2. Should it be explained that for diagnostic purposes ERCP can be substituted by magnetic resonance cholangiopancreatography (MRCP)?

Recommendation For diagnostic purposes, it is essential to explain that ERCP can be substituted by MRCP, except in some diseases, such as autoimmune pancreatitis (AIP; 1-B). Pathological examination of bile or pancreatic juice cytology through ERCP cannot be substituted by MRCP (1-C).

CQ6-01. How many hours after examination is the optimal time for early diagnosis of pancreatitis following ERCP?

Recommendation Measurement of serum pancreatic enzymes (P) and measurement of serum pancreatic enzymes (pP), primarily a serum amylase, 2–6 h after ERCP is recommended (1-B).

CQ6-02. Which enzyme is the best and easiest to use for diagnosis of acute pancreatitis after ERCP in clinical practice?

Recommendation In the diagnosis of pancreatitis after ERCP, measurement of serum amylase is recommended when measurement of serum lipase is difficult (1-A). For the diagnosis of acute pancreatitis, measurement of serum lipase is useful and preferable if possible (1-A). Urinary trypsinogen 2 (dipdisk test) is promising because of its excellent ability to rapidly diagnose acute pancreatitis, but it is not commercially available in Japan, limiting its use for research purposes at this time (1-B).

CQ6-03. Is measurement of procalcitonin (PCT) useful to determine the severity of PEP?

Recommendation Procalcitonin (PCT) is considered to be highly useful in determining the severity of PEP; however, at present, it is expensive and requires time to measure. Therefore, the level of recommendation for PCT as a general examination is low (1-B).

Table 3 Epidemiological survey of pancreatitis following ERCP

Year	2007	2008	2009	2010	2011
Total	11403	13869	14427	16848	18723
Pancreatitis incidences (%)	100 (0.877)	116 (0.836)	170 (1.178)	165 (0.979)	168 (0.897)
Severe pancreatitis incidences (%)	12 (0.105)	13 (0.094)	17 (0.118)	20 (0.119)	27 (0.144)

CQ7-1 Is chest and abdominal X-ray recommended for the diagnosis of PEP?

Recommendation When PEP is suspected, chest and abdominal X-ray may not be useful for the diagnosis of PEP (2-C).

CQ7-2 Are ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) useful for the diagnosis of PEP?

Recommendation When PEP is suspected, US is recommended (1-B). When US demonstrates poor images, CT is recommended (1-B). MRI may be useful in diagnosing bile duct stones causing pancreatitis and hemorrhagic necrotizing pancreatitis (2-C).

CQ8-01: Are the severity assessment criteria by the Ministry of Health, Labor, and Welfare (MHLW) appropriate for severity assessment of PEP?

Recommendation The severity assessment criteria by the MHLW are recommended (1-B).

Statement Of onset, it is not necessarily suitable in actual clinical practice. Currently in Japan, therefore, to assess the severity of PEP, we consider it reasonable to use the MHLW severity assessment criteria for acute pancreatitis.

As for patients whose conditions are complicated with infections such as cholangitis or renal impairment, the MHLW severity assessment criteria may lead to overestimation of severity. Therefore, severity assessment criteria suitable for the pathology of PEP should be established (Table 4).

CQ08-02 Does the early assessment of the severity of PEP contribute to the improvement of mortality rate and reduction in the incidence of complications?

Recommendation Once the condition is diagnosed as PEP, we recommend that its severity be immediately assessed and that the assessment be repeated thereafter (1-C).

Recommendations as below about treatment of PEP are in accordance with guidelines for pancreatitis

CQ9-01. Does the treatment of PEP with antibacterial agents shorten the treatment period as compared with the nonuse of these drugs?

Recommendation In patients with severe disease, the use of antibacterial agents might reduce the risk of infectious pancreatic complications such as pancreatic abscess, shorten the treatment period, and decrease mortality (2-B). Prophylactic treatment with antibacterial agents is basically not necessary in patients with mild disease, but is required in patients with biliary tract infection (1-A).

Statement As far as we searched, no study has reported on the use of antibacterial agents specifically for the treatment of PEP. In general, the treatment of pancreatitis with antibacterial agents remains highly controversial, and consensus has yet to be obtained. In particular, the need for treating mild cases remains unclear, although antibacterial agents have been reported to be effective in patients with severe pancreatitis [6–13]. Therefore, patients in whom PEP is expected to progress and become serious should receive antibacterial agents intravenously or via the celiac artery or superior mesenteric artery to prevent the progression of infection of the pancreas and surrounding tissue to sepsis and multiple organ failure [6–8]. The

Table 4 Severity classification of PEP

Mild	Moderate	Severe
Clinical symptoms of acute pancreatitis	Needs 4–10 days of hospitalization	Needs at least 10 days of hospitalization
Elevated serum amylase level		Cases of hemorrhagic pancreatitis
3 or more times higher than the normal level		Necrosis or pseudocyst formation
(24 h after the procedure of ERCP)		Needs percutaneous drainage or surgery
Needs emergency hospitalization		
Extension of hospitalization by 2–3 days		

recommended antibacterial agents are carbapenems such as imipenem [14–16] and meropenem [17–19] and new quinolones such as ciprofloxacin [20], which have a broad antibacterial spectrum and good penetration of pancreatic tissue.

CQ9-02 Does the treatment of post-pancreatitis ERCP with protease inhibitors shorten the treatment period as compared with the nonuse of these drugs?

Recommendation In patients with serious pancreatitis, pancreatic regional arterial infusion of protease inhibitors and antibacterial agents can decrease the incidence of infectious complications and mortality rates (2-B). In particular, this trend is significant in patients in whom treatment is begun within 48 h.

Statement At present, a general consensus has yet to be reached concerning the use of protease inhibitors for treatment of PEP alone. In principle, however, patients in whom acute pancreatitis is diagnosed are generally given protease inhibitors, approved for this indication by National Health Insurance. As for the administration method, drug penetration is poorer in pancreatic tissue than in the liver and kidney. In particular, because acute necrotic pancreatitis is associated with pancreatic circulatory disturbances, drug penetration is considered poor after intravenous administration. To solve this problem, a technique for arterial infusion therapy has been developed to directly infuse drugs into arteries that supply the pancreas. This method for arterial infusion therapy has been reported to increase concentrations of protease inhibitors and antibacterial agents in pancreatic tissue, inhibit the progression of pancreatitis, and decrease the risk of infectious complications [21–23].

In a study comparing pancreatic regional arterial infusion of nafamostat (a protease inhibitor) plus imipenem (an antibacterial agent), arterial infusion of nafamostat alone (an antibacterial agent was given intravenously), and intravenous infusion of nafamostat plus imipenem in patients with acute necrotizing pancreatitis, the mortality rates were 6.7, 13.6, and 43.8% and the incidences of infectious necrosis as a complication were 0, 22.8, and 50%, respectively. These results demonstrated that pancreatic regional arterial infusion of nafamostat plus imipenem was superior to the other treatments [24]. In another study, continuous regional arterial infusion of nafamostat plus imipenem was started within 48 h after disease onset, 48–72 h after onset, or more than 72 h after onset in patients with acute necrotizing pancreatitis. The incidence of respiratory failure and the mortality rate were significantly lower in patients in whom treatment was started within 48 h than in the other groups [25] (than in patients in whom treatment was started more than 72 h after onset).

In a national survey of pancreatic regional arterial infusion in patients with acute necrotizing pancreatitis, the mortality rates were significantly lower in patients in whom treatment was begun within 48 h after disease onset (11.9%) than in those in whom treatment was started more than 48 h after onset (23.6%).

CQ9-03 As compared with conventional infusion therapy, can high-volume infusion therapy improve treatment outcomes in patients with PEP? Does the infusion volume influence treatment outcomes in patients with PEP?

Recommendation In acute pancreatitis, increased vascular permeability can lead to the extravasation of plasma components into interstitial spaces, resulting in dehydration and shock. Appropriate infusion therapy should, therefore, be given soon after disease onset to maintain a urine volume of at least 0.5 mL/kg/h (1-A). Subsequently, the infusion volume should be managed while closely monitoring variables such as hemodynamics and urine volume to decrease the rates of complications and mortality (1-A).

Statement In patients with pancreatitis, extravasation of plasma components into interstitial spaces due to increased vascular permeability can cause dehydration and shock. Therefore, adequate infusion therapy should be begun soon after disease onset to maintain a urine volume of at least 0.5 mL/kg/h [26]. The results of a national survey conducted in 2009 by the Research Committee on Pancreatic Diseases, supported by the MHLW of Japan, showed that the infusion volume given within the first 24 h after starting infusion therapy was inadequate (less than 50 mL/kg) in all patients younger than 60 years who died of severe pancreatitis [27]. As compared with healthy adults who require a water intake of 1500–2000 mL per day (25–30 mL/kg body weight), patients with early-stage acute pancreatitis require a 2–5 times higher infusion volume (50–150 mL/kg body weight). At this time, extracellular fluid (acetated Ringer's solution or lactated Ringer's solution) is used. In particular, half to one third of the daily infusion volume should be given within the first 6 h. Even elderly patients and those with cardiovascular, pulmonary, or renal dysfunction should receive an adequate infusion volume while continuously monitoring the central venous pressure and other cardiovascular variables. If necessary, patients should be transferred to a full-service hospital with an intensive care unit that can carefully manage cardiovascular condition.

CQ10-01 Do protease inhibitors prevent PEP? Are there differences according to drug, dosing regimen, or dose?

Recommendation The results of individual RCTs have demonstrated that protease inhibitors may reduce the incidence of PEP; thus, they are generally used in clinical practice at present (1-C). The results of a recent meta-analysis have shown that protease inhibitors such as gabexate and ulinastatin did not reduce the incidence of PEP, and thus, evidence of the prevention of PEP was lacking (2-C). Five RCTs have exhibited that nafamostat mesilate has a prophylactic effect on PEP; however, further studies are needed (2-B).

Statement A meta-analysis of 18 RCTs in 2011 has reported that protease inhibitors cannot prevent PEP [28]. Several studies have been conducted to examine whether there are differences according to the type of protease inhibitors (gabexate mesilate, ulinastatin, and nafamostat mesilate).

With regard to gabexate mesilate, six high-quality RCTs [29–34] reported no difference in the incidence of PEP between the control group (6.3%) and the gabexate mesilate group (4.5%). In addition, a meta-analysis of four RCTs [35] and a meta-analysis of five RCTs [36] have demonstrated that gabexate mesilate has no prophylactic effect on PEP (OR 0.67, 95% CI 0.31–1.47), hyperamylasemia, or abdominal pain.

In a meta-analysis of studies of dosing regimens of gabexate mesilate, [37] neither short-term administration over 6 h or less nor long-term administration over 12 h or more was correlated with a prophylactic effect on PEP. Another meta-analysis of two RCTs [38] has concluded that long-term administration of gabexate mesilate had no prophylactic effect on PEP.

A subsequent meta-analysis [39] of seven RCTs in 2013 has also reported that gabexate mesilate is not effective.

There were four RCTs of ulinastatin; [40–43] in studies of ulinastatin versus control, pre-ERCP administration of ulinastatin 150,000 U showed a prophylactic effect [41], whereas post-ERCP administration of ulinastatin 100,000 U had no prophylactic effect [43]. In comparative studies of gabexate mesilate in Japan, [40, 42] no statistically significant difference was noted between among ulinastatin 450,000 U (high dose), ulinastatin 150,000 U (low dose), and gabexate mesilate 900 mg [40] or between ulinastatin 150,000 U and gabexate mesilate 600 mg [42]. Consequently, it was concluded that ulinastatin has no prophylactic effect on PEP.

Similarly, a study of six RCTs [39] has concluded that ulinastatin had no efficacy.

A study of five RCTs [39] has concluded that nafamostat mesilate has a prophylactic effect on PEP.

CQ10-02 Do nonsteroidal anti-inflammatory drugs (NSAIDs) prevent PEP? Are there differences according to dose?

Recommendation NSAIDs (transanal administration of indomethacin or diclofenac 50 or 100 mg) have a prophylactic effect on PEP (2-B).

Transanal administration of indomethacin or diclofenac 50 or 100 mg immediately before or after ERCP is recommended; however, the dose of NSAIDs in the Japanese population needs to be examined in the future (2-B).

Statement A meta-analysis of four RCTs in 2008 and 2009 [44–47] has examined the transanal administration of indomethacin or diclofenac 100 mg (indomethacin administration immediately before ERCP in two RCTs and diclofenac administration immediately after ERCP in two RCTs). It has reported that the prevention of PEP was significant in the NSAIDs group (relative risk [RR] 0.36, 95% CI 0.22–0.60, number needed to treat [NNT] 15), and there were no adverse events associated with NSAIDs.

A meta-analysis of nine RCTs in Japan in 2013 [47] has demonstrated the efficacy of NSAIDs (summary RR = 0.58, 95% CI = 0.44–0.76). Furthermore, subgroup analysis has also exhibited a prophylactic effect for both indomethacin and diclofenac.

A recent overseas meta-analysis [48] has concluded that transanal administration of NSAIDs has the most superior prophylactic effect (summary RR = 0.37, 95% CI = 0.21–0.59).

The prophylactic effect of NSAIDs (transanal administration of indomethacin or diclofenac 50 or 100 mg) has been reported in many studies with a high evidence level [49]; however, NSAID administration is not covered by health insurance in Japan. Since NSAIDs cause adverse reactions, their use as prophylactic treatment, including their doses, in all ERCP patients, needs to be examined further.

CQ10-03 Does somatostatin prevent PEP?

Recommendation Evidence of the efficacy of somatostatin on post-ERCP prevention is poor. Somatostatin may prevent PEP depending on dosing regimens (12-h administration of high-dose somatostatin and bolus administration). However, it is recommended to use somatostatin only in research setting (2-B).

CQ10-04 Do steroids prevent PEP?

Recommendation Evidence of a prophylactic effect of steroids on PEP is poor, and it is recommended that steroids not be administered (2-A).

CQ10-05 Does pancreatic duct stent placement prevent PEP? Does the prophylactic effect differ according to the diameter, length, and form of pancreatic duct stents?

Recommendation Prophylactic pancreatic duct stent placement is recommended in patients at high risk for PEP (2-A). The use of a straight-type, 5-Fr pancreatic spontaneous dislodgement stent is recommended. Sufficient attention should be paid to stent dislodgement; when the stent is not dislodged spontaneously, it needs to be endoscopically removed (2-A).

Statement Two meta-analyses [50, 51] have shown that pancreatic duct stents have a prophylactic effect in patients at high risk for PEP.

A meta-analysis of eight RCTs and non-RCTs in 2011 [52] has revealed that pancreatic duct stents have a prophylactic effect on both PEP and hyperamylasemia in patients at high risk for PEP.

A meta-analysis of RCTs published in Japan in 2007 [53] has shown that pancreatic spontaneous dislodgement stents significantly prevented PEP, regardless of the presence of risk factors for PEP (the PEP incidence in the stent and no-stent groups was 3.2 and 13.6%, respectively; $P = 0.019$).

An RCT comparing 5-Fr and 3-Fr pancreatic duct stents [54, 55] has revealed that the prophylactic effect on PEP was comparable, with a lower frequency of stent placement failure with 5-Fr stents.

If the pancreatic duct stent is not dislodged within 5–10 days after ERCP, it may induce pancreatitis; therefore, endoscopic stent removal is recommended [54, 56].

CQ10-06 Does wire-guided cannulation (WGC) prevent PEP?

Recommendation In deep cannulation of the bile duct, WGC is expected to reduce the incidence of PEP and increase the cannulation success rate as compared with conventional contrast-enhanced imaging. WGC is considered in deep cannulation of the bile duct (2-B).

Recent studies in Japan have reported that WGC does not reduce the incidence of PEP or increase the cannulation success rate as compared with the conventional method; the two are used differently, depending on the judgments of operators at each institution, at present.

Statement Some reports state that there is no difference in the incidence of PEP between the conventional contrast-enhanced imaging method and WGC, whereas a meta-analysis of four RCTs [67–69] has concluded that the incidence of PEP was lower with WGC than with conventional contrast-enhanced imaging. Analyses of five RCTs [67] and seven RCTs [69] yielded ORs of 0.23 (95% CI 0.13–0.41) and 0.38 (95% CI 0.19–0.76), respectively. The success rate of deep cannulation of the bile duct was improved according to both reports. A meta-analysis of 12 RCTs in the 2012 Cochrane review [70] has shown that WGC, which significantly increases the cannulation rate and reduces the risk of PEP, is the most appropriate first-line cannulation technique.

Although these results have been obtained in overseas meta-analyses, the results of multicenter studies in Japan [57, 58] have demonstrated that WGC does not decrease the incidence of PEP or increase the cannulation success rate as compared with the conventional method. The two techniques are used differently, depending on judgments of operators at each institution, at present.

Discussion

Clinical studies about PEP are sparse because the number of study participants is limited and effectiveness of potential treatments is not so high that small-size studies can prove. Further difficulty to conduct valid studies is that patients who needs ERCP are heterogeneous in etiology of individual disease, location of pathologic involvement, clinical stage, etc. Therefore, in many cases, we had to make recommendations on weak evidence with moderate to high uncertainty.

We extracted key information from our full version of clinical practice guidelines about PEP. We described clinical questions and recommendations but we could not provide a statement part for the all recommendations due to limited space. However, we think that the clinical questions and recommendations are useful for care of patients who need ERCP.

Conclusion

We presented with recommendations pertaining to risk factors, diagnosis, prognostic factors, treatments, and preventive interventions in the medical practice for PEP.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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