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JPN Guidelines for the management of acute pancreatitis: cutting-edge information

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Abstract

The JPN Guidelines for the Management of Acute Pancreatitis are organized under the subject headings: epidemiology, diagnosis, management strategy, severity assessment and transfer criteria, management of gallstone pancreatitis, nonsurgical management, and surgical management. The Guidelines contain cutting-edge information on each of these subjects, as well as a section on the Japanese medical insurance system which provides information that should prove useful to physicians in other countries. The quality of the evidence was evaluated by the evidence-based classification method used at the Cochrane Library. The levels of recommendation of the individual management methods contained in the Guidelines were determined on the basis of the evaluation of evidence by the consensus of the members of the Working Group (see below). The Japanese Society for Abdominal Emergency Medicine, the Japan Pancreas Society, and the Research Group for Intractable Diseases and Refractory Pancreatic Diseases (which is sponsored by the Japanese Ministry of Health, Labour, and Welfare) were commissioned to produce the JPN Guidelines for the Management of Acute Pancreatitis. A Working Group of 20 physicians specializing in pancreatic diseases and emergency medicine investigated and analyzed 14821 cases retrieved by means of a Medline (1960–2004) search and discussed the available literature on acute pancreatitis (limited to human pancreatitis). The Working Group held many general discussions in order to reach a consensus on the content of the Guidelines. After producing a draft, the Publishing Committee of the JPN Guidelines for the Management of Acute Pancreatitis posted it on a website and asked for comments and criticisms. Subsequently, a final version of the Guidelines was published in Japanese in 2003. The Publishing Committee is now making the Guidelines available to a much wider readership by bringing out an English version.

Key words EBM · Acute pancreatitis · Gallstone pancreatitis · Pancreatitis epidemiology · Pancreatitis etiology

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Introduction

Acute pancreatitis is often managed clinically, not only by specialists in surgery, internal medicine, and emergency medicine but also by general physicians, gastroenterologists, and general surgeons. Consequently, the Guidelines have been prepared in order to help these physicians to diagnose acute pancreatitis accurately and to manage patients by means of an appropriate treatment policy, thus improving survival rates. According to the available literature, the mortality rate for patients with severe acute pancreatitis ranged between 30% and 21.4% from 1987 to 1999. Which cases are likely to be fatal? Which categories of morbidity are likely to become more severe? And under what circumstances should patients be transferred to a special hospital? There is a great need for Guidelines that clearly answer these and other questions.

Several sets of evidence-based guidelines for the management of acute pancreatitis have been published; those of the Atlanta Symposium of 1992,[1] the United Kingdom Guidelines of 1998,[2] and the Santorini Consensus Conference of 1999[3] are representative. However, they were based on the evidence available at the time, and the validity of any set of guidelines is short-lived and guidelines need to be revised every 2 years.[1] Indeed, new evidence is reported almost daily, and guidelines for management in clinical settings are changing nearly as fast, thanks to the remarkable advances in medical equipment and treatment techniques developed in recent years. The International Association of Pancreatology guidelines[4] were most recently published in 2002, but they are concerned solely with the surgical management of acute pancreatitis.

The Guidelines Publishing Committee very much hopes that this publication will help clinicians worldwide to become familiar with the Guidelines, and the Committee hopes that those professionals will offer their comments and criticisms once they have had the opportunity to compare them with the guidelines in use in their own countries.

Purpose of the Guidelines

The mortality rate among patients with severe acute pancreatitis remains high, although various current diagnostic criteria, methods of severity assessment, and new treatments have been used at a number of institutions. However, there are inter-institutional differences in the ways in which the disease is managed, due to the lack of evidence-based guidelines.

In view of this situation, the Guidelines have been formulated with the aim of providing practical management guidelines to clinicians engaged in the management of acute pancreatitis. The Working Group has striven to ensure that the Guidelines will help general clinicians not only to assess the severity of acute pancreatitis promptly but also to manage the disease appropriately and efficiently. The Guidelines should also help patients, their families, and the general public to acquire better knowledge of acute pancreatitis, and thereby lead to a better standard of medical management based on mutual understanding between those who provide medical treatment and those who receive it.

How the Guidelines were formulated

With evidence-based medicine (EBM) as the core concept, an initial draft of the Guidelines was prepared by members of the Guidelines Preparation Committee and the Working Group, both of which consisted of special-ists from the Japanese Society of Abdominal Emergency Medicine, who searched the available documents and evaluated the evidence they found there[5]. Following this process, a Guidelines Investigation Committee — consisting of members of the Working Group, the Japan Pancreas Society, and the Research Group for Intractable Diseases and Refractory Pancreatic Diseases — was formed to examine the draft Guidelines.

In addition to the Investigation Committee, an Evaluation Committee — whose members were drawn from the Japanese Society of Abdominal Emergency Medicine, the Japanese Ministry of Health, Labour, and Welfare, and several external institutions — was formed to critique the Guidelines whenever necessary.

Defining and extending the search of the literature

Works were selected as follows. Using "pancreatitis" as the key search word, a MeSH-based exploration of the Ovid Medline database (1960–2004) yielded approximately 28000 items under the headings "pancreatitis", "acute necrotizing pancreatitis," and "alcoholic pancreatitis." The items were then screened to confine the entries to those related to human pancreatitis. This yielded 14821 items in English, and after examination of all the titles and abstracts, 1348 were selected, and a careful examination of the full texts was conducted. Other sources quoted in these selected works, together with works suggested by the specialist members, as well as reports prepared by the Research Group, were included in the examination.

Categories of evidence and the grading of recommendations

The evidence obtained from each reference item was evaluated in accordance with the scientific classification method used at the Cochrane Library (Table 1),[6] and the quality of evidence for each parameter associated with the diagnosis and treatment of acute pancreatitis was determined. The relevant terms used are explained the footnote of Table 1.[6] Based on the results obtained from these procedures, recommendation grades of A to E, were determined according to the definitions shown in Table 2, and these recommendation grades are mentioned, as required, in the text of the Guidelines. The grading is based on the Kish[7] method of classification.

Recommendations graded as either A or B indicate high quality. However, those graded as D or E are considered to be unacceptable. It must be borne in mind that such recommendation grades merely represent standards and should not be used to compel adherence to a given method of medical management in an actual clinical setting. The medical management method that is applied should be selected after taking into account

Table 1. Categories of evidence (see footnote for explanation of terms).[6] The evidence-based classification used at the Cochrane Library: Oxford Centre for Evidence-based Medicine, Levels of Evidence (May 2001) (http://www.cebm.net/levels_of_evidence.asp#levels)[5] was used as a basis to evaluate evidence presented in each item of literature, and the quality of evidence for each parameter associated with the diagnosis and treatment of acute pancreatitis was determined

Level	Therapy/prevention, etiology/harm	Prognosis	Diagnosis	Differential diagnosis/symptom prevalence study	Economic and decision analyses
1a	SR (with homogeneity*) of RCTs	SR (with homogeneity*) of inception cohort studies; CDR† validated in different populations	SR (with homogeneity*) of Level 1 diagnostic studies; CDR† with 1b studies from different clinical centers	SR (with homogeneity*) of prospective cohort studies	SR (with homogeneity*) of Level 1 economic studies
1b	Individual RCT (with narrow confidence Interval‡)	Individual inception cohort study with >80% follow-up; CDR† validated in a single population	Validating** cohort study with good††† reference standards; or CDR† tested within one clinical center	Prospective cohort study with good follow-up****	Analysis based on clinically sensible costs or alternatives; systematic review(s) of the evidence; and including multiway sensitivity analyses
1c	All or none§	All or none case series	Absolute SpPins and SnNouts††	All or none case series	Absolute better-value or worse-value analyses††††
2a	SR (with homogeneity*) of cohort studies	SR (with homogeneity*) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity*) of Level >2 diagnostic studies	SR (with homogeneity*) of 2b and better studies	SR (with homogeneity*) of Level >2 economic studies
2b	Individual cohort study (including low-quality RCT; e.g., <80% follow-up)	Retrospective cohort study or follow-up of untreated control patients in an RCT; derivation of CDR† or validated on split-sample§§§ only	Exploratory** cohort study with good††† reference standards; CDR† after derivation, or validated only on split-sample§§§ or databases	Retrospective cohort study, or poor follow-up	Analysis based on clinically sensible costs or alternatives; limited review(s) of the evidence, or single studies; and including multiway sensitivity analyses
2c	"Outcomes" research; ecological studies	"Outcomes" research		Ecological studies	Audit or outcomes research
3a	SR (with homogeneity*) of case-control studies		SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies	SR (with homogeneity*) of 3b and better studies
3b	Individual case-control study		Nonconsecutive study; or without consistently applied reference standards	Nonconsecutive cohort study, or very limited population	Analysis based on limited alternatives or costs, poor quality estimates of data, but including sensitivity analyses incorporating clinically sensible variations

	Case series (and poor-quality cohort and case-control studies§§)	Case series (and poor-quality prognostic cohort studies***)	Case control study, poor or nonindependent reference standard	Case series or superseded reference standards	Analysis with no sensitivity analysis
4	Case series (and poor-quality cohort and case-control studies§§)	Case series (and poor-quality prognostic cohort studies***)	Case control study, poor or nonindependent reference standard	Case series or superseded reference standards	Analysis with no sensitivity analysis
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or "first principles"	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or "first principles"	Expert opinion without explicit critical appraisal, based on physiology, bench research, or "first principles"	Expert opinion without explicit critical appraisal, or based on economic theory or "first principles"

Users can add a minus sign to denote the level that fails to provide a conclusive answer because of:

NOTE 1 EITHER a single result with a wide confidence interval (such that, for example, an ARR in an RCT is not statistically significant but whose confidence intervals fail to exclude clinically important benefit or harm)

NOTE 2 OR a systematic review with troublesome (and statistically significant) heterogeneity

NOTE 3 Such evidence is inconclusive, and therefore can only generate Grade D recommendations

SR, Systematic review; RCT, randomized controlled trial; ARR, absolute risk ratio

* By "homogeneity," the Publishing Committee means a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a minus sign at the end of their designated level

† Clinical decision rule (these are algorithms or scoring systems that lead to a prognostic estimation or a diagnostic category)

‡ See NOTE 2 for advice on how to understand, rate, and use trials or other studies with wide confidence intervals

§ Met when all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it

§§ By "poor-quality cohort study," the Publishing Committee means one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded) objective way in both exposed and nonexposed individuals, and/or failed to identify or appropriately control known confounders, and/or failed to carry out a sufficiently long and complete follow-up of patients. By "poor-quality case-control study," the Publishing Committee means one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded) objective way in both cases and controls, and/or failed to identify or appropriately control known confounders

§§§ Split-sample validation is achieved by collecting all the information in a single tranche, then artificially dividing this into "derivation" and "validation" samples

†† An "absolute SpPin" is a diagnostic finding whose specificity is so high that a positive result rules in the diagnosis. An "absolute SnNout" is a diagnostic finding whose sensitivity is so high that a negative result rules out the diagnosis

††† "Good reference standards" are independent of the test, and are applied blindly or objectively to all patients. "Poor reference standards" are haphazardly applied, but are still independent of the test. Use of a nonindependent reference standard (where the "test" is included in the "reference," or where the "testing" affects the "reference") implies a Level 4 study

†††† "Better-value treatments" are clearly as good but cheaper, or better at the same or reduced cost. "Worse-value treatments" are as good and more expensive or worse and equally or more expensive

** "Validating studies" test the quality of a specific diagnostic test, based on prior evidence. An "exploratory study" collects information and trawls the data (e.g., using a regression analysis) to find which factors are "significant"

*** By "poor-quality prognostic cohort study," the Publishing Committee means a study in which sampling was biased in favor of patients who already had the target outcome, or the measurement of outcomes was accomplished in fewer than 80% of study patients, or outcomes were determined in an unblinded, nonobjective way, or there was no correction for confounding factors

**** Good follow-up in a differential diagnosis study is more than 80%, with adequate time for alternative diagnoses to emerge (e.g., 1–6 months, acute; 1–5 years, chronic)

"Good," "better," "bad," and "worse" refer to the comparisons between treatments in terms of their clinical risks and benefits

Table 2. Japan Abdominal Emergency Society Grading System for ranking the recommendations in the clinical Guidelines

Grade of recommendation	Definition
A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation or the effect may not exceed the adverse effects and/or inconveniences (toxicity, interaction between drugs and cost)
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use

the conditions prevailing in the relevant institution (staff, experience, equipment, etc.) and the characteristics of the individual patient.

Notes on the use of the Guidelines

The Guidelines are evidence-based and determined with a grade for each medical practice, taking actual conditions into account. The Guidelines specify the criteria for the diagnosis of acute pancreatitis and the assessment of its severity that have been prepared by the Research Group and are in widespread use in Japan. Because the Guidelines address so many different topics, an index of all works used is included at the end of the series of articles for the convenience of readers. The dosages described in the text of the Guidelines are for adult patients.

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