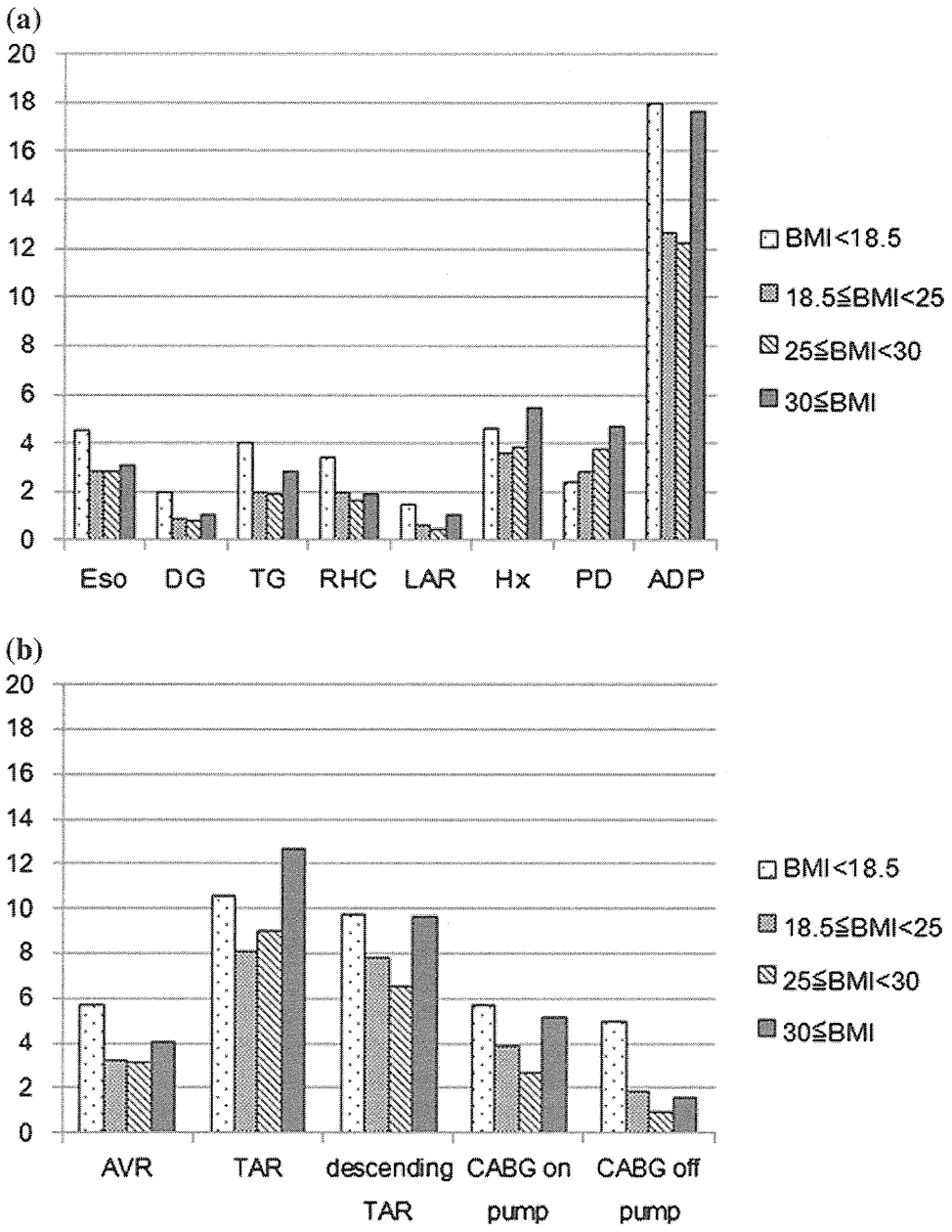

Fig. 3 **a** Operative mortality for the gastroenterological surgery procedures (%). *Eso* esophagectomy, *DG* distal gastrectomy, *TG* total gastrectomy, *RHC* right hemicolectomy, *LAR* low anterior resection, *Hx* hepatectomy performed for >1 segment except for the lateral segment, *PD* pancreaticoduodenectomy, *ADP* surgery for acute diffuse peritonitis. **b** Operative mortality for the cardiovascular surgery procedures (%). *AVR* aortic valve replacement, *TAR* total arch replacement, *CABG* coronary artery bypass graft

obese and underweight patients had high mortality rates. This Japanese nationwide study provides further evidence that obesity and very low bodyweight are both factors with significant adverse effects on operative outcomes.

Compliance with ethical standards

Conflict of interest None of the authors has any conflicts of interest to disclose.

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REVIEW ARTICLE

National Clinical Database feedback implementation for quality improvement of cancer treatment in Japan: from good to great through transparency

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Abstract The National Clinical Database (NCD) of Japan was established in April, 2010 with ten surgical subspecialty societies on the platform of the Japan Surgical Society. Registrations began in 2011 and over 4,000,000 cases from more than 4100 facilities were registered over a 3-year period. The gastroenterological section of the NCD collaborates with the American College of Surgeons' National Surgical Quality Improvement Program, which shares a similar goal of developing a standardized surgical database for surgical quality improvement, with similar variables for risk adjustment. Risk models of mortality for eight procedures; namely, esophagectomy, partial/total gastrectomy, right hemicolectomy, low anterior resection, hepatectomy, pancreaticoduodenectomy, and surgery for acute diffuse peritonitis, have been established, and feedback reports to participants will be implemented. The outcome measures of this study were 30-day mortality and operative mortality. In this review, we examine the eight risk models, compare the procedural outcomes, outline the feedback reporting, and discuss the future evolution of the NCD.

Keywords Gastrointestinal surgery · National Clinical Database · Nationwide web-based database · Mortality · Risk model

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Abbreviations

NCD	National Clinical Database
ACS NSQIP	The American College of Surgeons National Surgical Quality Improvement Program
ASA	American Society of Anesthesiologists
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
DIC	Disseminated intravascular coagulation
JSS	The Japan Surgical Society
JSGS	The Japanese Society of Gastroenterological Surgery
ROC	Receiver operating characteristic
SIRS	Systemic inflammatory response syndrome
SSI	Surgical site infection

Introduction

Until recently, no nationwide data on cancer were available in the field of gastroenterological surgery in Japan. In 2006, the Japanese Society of Gastroenterological Surgery (JSGS) formed a committee to devise a database to track surgical patients treated in Japan over the 3 years from 2006 to 2008, and reported relatively low mortality rates for the major surgical procedures [1, 2]. The JSGS acknowledged the importance of risk-adjusted surgical outcomes for accurate comparisons and quality improvement; thus, in April, 2010, it created the database as a subset of the National Clinical Database (NCD) of Japan with major support from the Japan Surgical Society (JSS). Eight other surgical professional societies, including the Japanese Society for Cardiovascular Surgery, the Japanese Society for Vascular Surgery, the Japanese Association for Thoracic Surgery, the Japanese Association for Chest Surgery, the Japanese Society of Pediatric Surgeons, the Japanese Breast Cancer

Society, the Japan Association of Endocrine Surgeons, and the Japanese Society of Thyroid Surgery, joined the NCD. Registrations began in 2011, since when more than 4100 facilities have enrolled and over 4,000,000 cases have been registered over a 3-year period.

The gastroenterological section of the NCD collaborates with the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) [3], which shares a similar goal of developing a standardized surgical database for quality improvement. The NSQIP was originally developed in the 1990s by the United States Veterans' Health Administration and led to marked improvement in surgical quality [4]. The American College of Surgeons (ACS) initiated the ACS-NSQIP in 2006 and demonstrated improved surgical outcomes across all participating hospitals in the private sector [5]. The core members of the NCD joined the meetings and seminars of the ACS-NSQIP and debated various aspects of clinical databases, such as data collection methods and public relations [3]. In addition, the NCD implemented the same items as those of the ACS-NSQIP to conduct international cooperative studies. Reliable 30-day outcomes, including mortality and morbidity, serve as a quality improvement catalyst for ACS-NSQIP-participating institutions. Risk adjustment is a key component of the ACS-NSQIP and most variables included in risk adjustment models focus on patient factors and comorbidities. In this article, we focused on the gastrointestinal surgery subset of the NCD. All cases are input with items representing the surgical performance in each specialty for the following eight procedures: esophagectomy (Eso), total/distal gastrectomy (TG/DG), right hemicolectomy (RHC), low anterior resection (LAR), hepatectomy performed for more than one segment apart from the lateral segment (Hx), pancreaticoduodenectomy (PD), and surgery for acute diffuse peritonitis (ADP). Risk models of mortality for each procedure were created using approximately 120,000 cases registered in 2011, and each model has been accepted and published in peer-reviewed journals [6–13]. We review the results and discuss the future evolution of the NCD using these risk models in terms of the surgical quality improvement program in Japan.

NCD data entry system

Submitting cases to the NCD is a prerequisite for all member institutions of the JSS and JSGS, and only registered cases can be used for board certification [3]. To assure the traceability of data, the NCD continuously tracks persons who approve data, persons in departments who are in charge of annual cases, and persons responsible for data entry, through its web-based data management system. The NCD also continuously validates data consistency through random site visits.

The NCD variables are almost identical to those applied in the ACS-NSQIP (http://www.site.acsnsqip.org/wp-content/uploads/2013/10/ACSNSQIP.PUF_.UserGuide.2012.pdf#search='user+guide+for+the+2012+ACS+NSQIP). The potential independent variables include patient demographics, pre-existing comorbidities, preoperative laboratory values, and perioperative data. The demographic variables include age, sex, smoking status, and drinking status. Patients were categorized according to whether they were brought to hospital directly, by ambulance. General factors such as the patient's body mass index (BMI) and preoperative functional status, defined as independent, partially dependent, or totally dependent, according to their ability to perform activities of daily living (ADL) in the 30 days prior to surgery and immediately before surgery, were also considered. We evaluated the physical status classification by the American Society of Anesthesiologists (ASA) and considered pre-existing comorbidities, including the cardiovascular status, respiratory status, renal status, hematological status, oncological status, preoperative blood transfusion, chronic steroid use, ascites, sepsis, diabetes, open wound, and pregnancy. The laboratory parameters included in the analysis were the white blood cell count, hemoglobin level, hematocrit, platelet count, prothrombin time, and activated partial thromboplastin time, as well as the serum levels of albumin, total bilirubin, aspartate amino transferase, alanine aminotransferase, alkaline phosphatase, urea nitrogen, creatinine, sodium, hemoglobin A1c, and C-reactive protein. The length of surgery, intraoperative blood loss, amount of transfusion, and any accident during the operation were also considered.

Postoperative outcomes evaluated 30 days after surgery were categorized according to the Clavien and Dindo classification [14]. The outcomes included relaparotomy within 30 days after surgery, wound events, anastomotic leak, respiratory events, urinary tract events, central nervous system events, cardiac events, other events, systemic sepsis, sepsis, systemic inflammatory response syndrome, and 24 other complications added by the NCD. For Hx procedures, the indications for surgery and resected subsegments (S1–S8) were included as preoperative variables to create risk models [9].

Outcome measures and statistical analysis

The outcome measures of this study were 30-day mortality and operative mortality. The former was defined as death within 30 days of surgery, regardless of the patient's geographical location, even if the patient had been discharged from hospital. The latter was defined as death within the index hospitalization period, regardless of the length of hospital stay (up to 90 days), as well as any death after discharge, up to 30 days after surgery. Data were randomly

Table 1 Registered cases used to create risk models for 8 surgical procedures [6–13]

	Eso	TG	DG	RHC	LAR	Hx	PD	ADP
Registered cases	5354	20,011	33,917	19,070	16,695	7732	8575	8482
Participating hospitals	713	1623	1737	1689	1620	987	1167	1285
(%)	34.9	79.4	84.9	82.6	79.2	48.3	57.1	62.8
30-day mortality (%)	1.2	0.9	0.5	1.1	0.4	2.0	1.2	9.0
Operative mortality (%)	3.4	2.3	1.2	2.3	0.9	4.0	2.8	14.1
Cancer surgery (%)	98.4	98.5	99.9	92.6	98.5	94.5	91.4	10.8
Emergent case (%)	0.8	2.0	0.9	8.4	1.1	0.8	0.9	92.9

Esophagectomy (Eso), total/distal gastrectomy (TG/DG), right hemicolectomy (RHC), low anterior resection (LAR), hepatectomy performed for >1 segment except for the lateral segment (Hx), pancreaticoduodenectomy (PD), and operation for acute diffuse peritonitis (ADP)

assigned into two subsets that were split 80/20: the first, for model development, and the second, for validation. The two sets of logistic models (30-day mortality and operative mortality) were constructed for dataset development using step-wise selection of the predictors with a probability (p) value for inclusion of 0.05. A "goodness-of-fit" test was performed to assess how well the model could discriminate between patient survival and death. The receiver operating characteristic (ROC) curves for the 30-day and operative mortalities were created for the validation dataset. An ROC curve is a plot of a test's true-positive rate (sensitivity) versus its false-positive rate (1—specificity). Model calibration, being the degree to which the observed outcomes matched the predicted outcomes from the model across a group of patients, was examined by comparing the observed and predicted averages with each of 10 equally sized subgroups, arranged in the order of increasing patient risk.

Case number and participating hospitals for each procedure and mortality rates

The NCD is a nationwide project in cooperation with Japan's board certification system in surgery, for which more than 1,200,000 surgical cases from over 3500 hospitals were collected in 2011. The number of participating hospitals in the gastroenterological section was 2045 at the time of the analysis (July, 2012). Among these cases, approximately 120,000 were used to create the risk models. Table 1 lists the number of cases for each procedure and the number of hospitals performing the respective procedure with its ratio to the total number of hospitals (%). Most procedures, except for ADP, were performed for cancer. Emergency surgery was most common for ADP (93 %). The 30-day mortality and operative mortality rates for the eight procedures were as follows: Eso, 1.2/3.4; TG, 0.9/2.3; DG, 0.5/1.2; RHC, 1.1/2.3; LAR, 0.4/0.9; HX, 2.0/4.0; PD, 1.2/2.8; and ADP, 9.0/14.1 %, respectively (Table 1). The operative mortality for each procedure, apart from ADP, was more than twice that of the 30-day mortality.

Risk models in the eight procedures

The 30-day mortality and operative mortality risk models for the eight procedures were created, and the C-index for those in the validation data sets was as follows: Eso, 0.767/0.742; TG, 0.811/0.824; DG, 0.785/0.798; RHC, 0.836/0.854; LAR, 0.75/0.766; HX, 0.714/0.761; PD, 0.675/0.725; and ADP, 0.851/0.852, respectively (Tables 2, 3). The final logistic models for the 30-day mortality with odds ratios for the eight procedures are listed in Table 2. Age; sex; emergency surgery; ADL; ASA class; BMI; cardiovascular, pulmonary, and renal comorbidities; and other patient conditions such as disseminated cancer, ascites, preoperative transfusion, bleeding disorder, diabetes, weight loss, sepsis, and chronic steroid use, including 121 variables, were found to be risk factors for certain procedures. Age, ADL ASA, BMI, disseminated cancer, bleeding disorder, and weight loss appeared to be common risk factors in most of the procedures. Table 3 lists the final logistic models for the operative mortality with odds ratios for the eight procedures, including 159 variables. New and additional 38 variables were captured for these models.

Feedback implementation (risk calculator)

A risk-adjusted analysis based on nationwide data allows personnel to establish and provide feedback on the risks that patients face before undergoing a procedure. On the basis of these objective data, healthcare professionals can then determine the treatment indicators and obtain informed consent. The risk calculator for all eight procedures will be available soon, on the websites of the hospitals that are a part of NCD, although the calculators for TG, PD, Hx, Eso, RHC, and LAR are currently available (February, 2015). The real-time feedback system gives the predicted mortality of patients simultaneously with data input. Standardized information on patient risk and predicted mortality can be reformulated as case reports and shared at conferences.

Table 2 Risk models for 30-day mortality after 8 gastrointestinal procedures (refs 6–13)

Variables	Eso	TG	DG	RHC	LAR	Hx	PD	ADP
Age category	1.5	1.2	1.2		1.3	1.4	1.3	1.2
Male sex						1.6	2.0	
Ambulance transport								1.4
Emergent surgery				1.9		3.8	4.3	
ADL within 30 days before surgery								
Any assistance	4.2					2.1		
Total			3.0					
ADL immediately before surgery								
Any assistance		2.1		2.8				
Total								1.4
ASA								
Class 3				2.3				2.7
Class 4								4.3
Class 5								8.7
Class 3, 4, 5			2.0			2.0	2.2	
Class 4, 5		9.4		4.0				
BMI								
>25 kg/m^2							2.4	
>30 kg/m^2					7.0			
Congestive heart failure				2.3				
Previous cardiac surgery		2.3						
Myocardial infarction			3.1					
Previous PCI								2.0
Previous PVD surgery					6.2			2.5
Cerebrovascular disease			2.1					
COPD							2.4	
Preoperative pneumonia			2.8					
Respiratory distress								1.6
Acute renal failure				3.2				
Preoperative dialysis		3.9						
Cancer with multiple metastases				2.2				
Disseminated cancer		2.6			4.9			2.2
Preoperative transfusion		1.9			5.4			1.6
Bleeding disorder without treatment			3.2		5.2			1.6
Bleeding disorder							4.4	
Diabetes		2.2						
Smoking within 1 year	2.6							
Ascites		2.0				2.1		
Without control			3.0					
Chronic steroid use								1.7
Weight loss	2.4		2.3					
Sepsis				2.0				
Habitual alcohol consumption			1.6					
WBC								
>12,000/μl	3.7		3.7					
>9000/μl				1.5				
<4000/μl	2.8							1.4

Table 2 continued

Variables	Eso	TG	DG	RHC	LAR	Hx	PD	ADP
Hemoglobin								
M < 13.5 g/dl, F < 12.5 g/dl		1.7	1.8					
<10.0 g/dl								1.3
Platelet								
>400,000/μl	2.5							
<150,000/μl								1.5
<120,000/μl				1.9	5.0	1.7		
<80,000/μl		3.1						1.5
<50,000/μl				5.6				
Albumin								
<4.0 g/dl				2.0	3.4			
<3.5 g/dl		1.7	1.5			2.0		
<2.0 g/dl								1.7
Total bilirubin								
>3.0 mg/dl				3.1				1.7
>2.0 mg/dl		2.9						
AST								
>35 U/l		2.3		3.1		2.3		1.4
ALP								
>600 U/l		2.5						1.7
>340 U/l		1.7	2.2					
BUN								
>25 mg/dl		1.9			2.5			1.4
>20 mg/dl								1.8
<8.0 mg/dl							2.3	
Creatinine								
>2.0 mg/dl						3.9		
>1.2 mg/dl			1.8					
Serum Na								
>145 mEq/l								1.7
<138 mEq/l				2.1	3.6			
<135 mEq/l	3.6		2.5					
<130 mEq/l								1.7
CRP								
<10.0 mg/dl								1.5
APTT								
>40 s							3.2	
PT-INR								
>1.25		2.2	2.0					
>1.1	2.0			1.5		1.7		
Non-tumor bearing								0.6
Surgical procedures						#1		
Indication for surgery						#2		

#1 Hepatectomy with S8 (2.2), hepatectomy with revascularization (3.8)

#2 Hilar bile duct carcinoma (2.5), gallbladder cancer (4.1)

ADL, Activities of daily living, PT-INR Prothrombin time-international normalized ratio, *WBC* white blood cells, *ASA* American society of anesthesiologists, *ADL* activities of daily living, *PCI* percutaneous coronary intervention, *COPD* chronic obstructive pulmonary disease, *AST* aspartate amino transferase, *ALP* alkaline phosphatase, *APTT* activated partial thromboplastin time

Table 3 Risk models for operative mortality after 8 gastrointestinal procedures [6–13]

Variables	Eso	TG	DG	RHC	LAR	Hx	PD	ADP
Age category	1.4	1.3	1.3	1.1	1.4	1.4	1.3	1.3
Male sex	2.3				1.9	1.5		
Emergent surgery		1.7	1.9	1.9		2.8		
ADL within 30 days before surgery								
Any assistance	4.7					2.8	2.5	
Total								1.6
ADL immediately before surgery								
Any assistance		2.0		2.5	2.5			1.4
Total			3.0		2.9			
ASA								
Class 3		1.8		1.6				2.3
Class 4								4.7
Class 5								6.5
Class 3, 4, 5			1.9			2.0	2.1	
Class 4, 5		5.2		2.9				
BMI								
>25 kg/m^2							1.9	
>30 kg/m^2					4.6			
Congestive heart failure				2.2				
Angina							2.6	
Previous PVD surgery				3.1	5.8			
Cerebrovascular disease			1.8					
Cerebrovascular accident		1.9						
Respiratory distress								
Any		1.7	2.4		2.9		2.4	
COPD	2.1					2.0		
Preoperative pneumonia						3.8		1.4
Preoperative dialysis		2.6		2.1				
Cancer metastasis/relapse	4.5			1.6				
Disseminated cancer		3.5	2.9	3.1	2.8			2.1
Preoperative transfusion					2.6			1.8
Bleeding disorder without therapy								1.6
Brinkman index							1.6	
Ascites								
Any		1.8		1.6	4.0	1.9		
Without control			2.8					
Chronic steroid use			2.8	2.0				1.9
Weight loss	2.0	1.6	2.2	1.6			2.1	1.4
Sepsis				1.7				
WBC								
>11,000/μl		2.0	2.5				3.1	
>9000/μl				1.6				
<4500/μl	1.8							1.5
<3500/μl		1.6						
Hemoglobin								
M < 13.5 g/dl, F < 12.5 g/dl					2.6			1.3
<10 g/dl						1.8		
Hematocrit								
M > 48 %, F > 42 %					3.6			

Table 3 continued

Variables	Eso	TG	DG	RHC	LAR	Hx	PD	ADP
M < 37 %, F < 32 %			1.4	1.4				
<30 %		1.3						1.2
Platelet								
<120,000/μl	2.0		2.0	1.7	3.4	1.6	2.1	1.4
<80,000/μl				2.6		2.1		
Albumin								
<3.8 g/dl			1.7					
<3.5 g/dl	2.2	1.4				1.6		
<3.0 g/dl		1.4		1.5		1.7		1.4
<2.5 g/dl					2.7			
<2.0 g/dl								1.5
Total bilirubin								
>3.0 mg/dl								2.0
>2.0 mg/dl		2.8	2.6					
>1.0 mg/dl				1.6				
AST								
>40 U/l			1.5	2.7	1.9	1.7		
>35 U/l		1.7						1.4
ALP								
>600 U/l		3.1						1.6
>340 U/l			1.6					
BUN								
>60 mg/dl				2.4				
>25 mg/dl								1.3
>20 mg/dl								1.8
<8 mg/dl	2.6			1.6				
Creatinine								
>2.0 mg/dl								1.5
>1.2 mg/dl			1.8					
Serum Na								
>145 mEq/l				1.9				
<138 mEq/l	2.1	1.4		1.9	2.5			
<135 mEq/l			2.3					
<130 mEq/l								1.8
CRP								
<10.0 mg/dl								1.5
APTT								
>40 s			1.6				2.0	
PT-INR								
>1.25	3.0	1.9						
>1.1			1.5	1.4		1.4	1.5	
Non-tumor bearing								0.5
Surgical procedure		#1				#2		
indication for surgery						#3		

#1 Pancreatico splenectomy (2.2)

#2 Hepatectomy with S1 (1.6), S7 (1.6), S8 (2.0), left tri-segmentectomy with S1 resection (3.9), hepatectomy with revascularization (3.0)

#3 Intrahepatic cholangiocarcinoma (1.8), hilar bile duct carcinoma (2.0), gallbladder cancer (3.2)

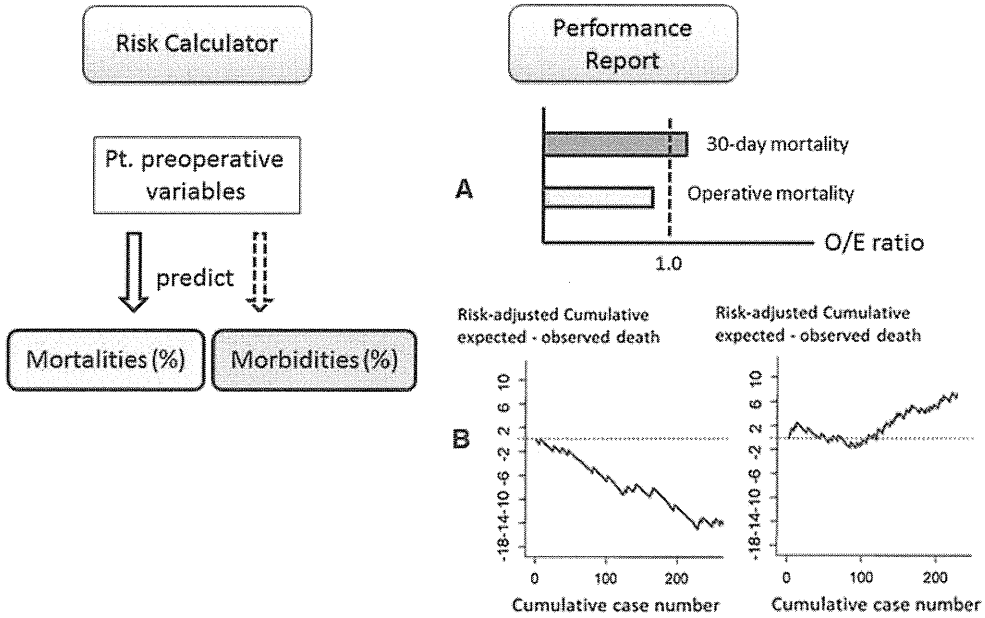

Fig. 1 The National Cancer Database feedback system includes a risk calculator for the mortality and morbidity of preoperative patients (*left schema*) and performance reports of each participating hospital (*right schema*). The latter includes each facility's severity-adjusted clinical performance (*benchmark*) in comparison with the national data (**a**) and the risk-adjusted cumulative expected–observed death (**b**). Better (*right*) or worse (*left*) outcomes can be detected by the monitoring report

The NCD will soon be able to provide data on each facility's severity-adjusted clinical performance (benchmark), which can be compared with national data (Fig. 1a). Cumulative observed–expected mortality can be traced periodically after each operation and used to detect special cause variations showing better (right) and worse (left) outcomes (Fig. 1b).

Future evolution of NCD

A complete data acquisition system link to board certification

More than 4,000,000 cases were retrieved from the NCD during the 3 years before April 2013. The number of esophagectomy and pneumonectomy cases registered in the NCD accounted for approximately 95 % of all cases registered in the Regional Bureau of Health and Welfare. Thus, most cases in Japan appear to be captured by the NCD system. This NCD project started with support from Health and Labor Sciences Research Grants by the Ministry of Health Labour and Welfare (Principal Investigators; MG, T.I.) and considerable funding from the JSGS and JSS. Participating institutions can now use the database system at no cost; however, it is mandatory for the institutions to participate in the benchmarking project when applying for the board certification system. Currently, the board certification system is operating adequately on the web for surgical society members and allows members to obtain information on their cases being used to assess a member's qualifications for certification during a certain period. Any applicant who has a sufficient number of cases for application no longer needs to write case reports. All participating healthcare professionals use information acquired from the NCD. Moreover, the board certification system itself can be revalidated using the surgical improvement program of the NCD.

Share benefits and costs of the NCD with relevant stakeholders

A previous study by Hall et al. [5] showed that participation in the benchmark reporting system of the ACS-NSQIP improved surgical outcomes across all participating hospitals in the private sector. Improvement is reflected for both poor- and well-performing facilities. They speculated in the model using 183 participating hospitals that each institution may have avoided 200–500 complications and 12–36 deaths. Participation in the ACS-NSQIP benefits patients, surgeons, and hospitals and costs 10,000–29,000 (US$) depending on the ACS-NSQIP options [15.]

In the gastroenterological section, risk models of mortality for the eight procedures were created to enable feedback. Simultaneously, risk models of morbidities for the eight procedures are being created to enable feedback for the next year. Currently, the database system is built up to enable efficient provision of benchmark reports to each institute. The benefits and costs can now be shared with the relevant stakeholders. A participation fee depending on the number of cases for retrieval is expected to be charged by the NCD to each hospital. Research grants from various sources are also expected to support clinical investigations using the NCD data.

Eliminating burden on physicians and maintaining data accuracy

To avoid burdening physicians, the NCD allows data entry by other medical staff members. The NCD data entry privileges allow people other than physicians to enter the data. An appropriate educational system for data managers would be mandatory to maintain the accuracy of data and reduce the burden on physicians. This could be achieved by holding an annual data manager educational meeting and eventually introducing an e-learning system. The JSGS is planning to create an audit committee separately from the NCD, with the goal of achieving accurate data inputs and of educating data managers.

Quality improvement of surgical care for cancer patients

The NCD generalizes site-specific cancer registries by taking advantage of their excellent organizing ability. Some site-specific cancer registries have already been combined with the NCD [16]. Cooperation between the NCD and site-specific cancer registries can establish a valuable platform upon which a cancer care plan can be developed in Japan. Furthermore, information on the prognosis of cancer patients gathered using population- and hospital-based cancer registries can enable efficient data accumulation into the NCD.

Currently, quality assessment of hospitals is being carried out using the Diagnosis Procedure Combination (DPC) data from the participating hospitals [17, 18]. The DPC data include variables for preoperative morbidities, cancer variables, and postoperative complications, but they are based mainly on administrative claim data. A low participation rate by very small hospitals in the DPC system covers 50% of institutions conducting surgical services [17] and hampers complete enumeration. The NCD is a quality assessment and improvement program in which clinical data are used with a high collection rate (95 %). Site-specific cancer registries in the NCD would not only be more accurate and suitable for perioperative assessment, but also for long-term outcomes of cancer patients.

Further improvements through transparency

Public reporting and transparency are being demanded by multiple stakeholders [19, 20]. Although it has been shown that performance data released to the public promote quality improvement activity at the hospital level [21, 22], opponents counter that public reporting induces gaming and other unintended consequences such as "cherry picking" (hospitals selecting lower-risk patients to avoid poorer outcomes) or losing patients to better-performing hospitals [23]. With the consent of participating surgical societies, the NCD stated that the performance of each institute would be fed back only to respective institutes but not to the general public. This practice is similar to that of the ACS-NSQIP, from which a report is prepared for administrators and surgical services staff to compare their risk-adjusted surgical outcomes with those of participating sites that are blinded to data other than their own.

In 2012, the ACS-NSQIP partnered with the Centers for Medicare and Medicaid Services (CMS) to promote public reporting and transparency of surgical outcomes [24]. Although there were few measurable differences between CMS-NSQIP-participating and CMS-NSQIP-nonparticipating hospitals, it was found that of all possible hospital structural characteristics, only the teaching hospital status predicted participation in the CMS-NSQIP public reporting initiative. It may be a challenge for participating hospitals to show their performance to the general public. There is an interesting study by Sherman et al. [25, who investigated surgeons' perceptions of public reporting of hospital and individual surgeon quality. They stated that surgeons recommended patient education, simplified data presentation, and continued risk-adjustment refinement, and conducted an internal review before public reporting to make public reporting more acceptable for them. Linkage between hospital information systems and the NCD registry system may improve data accuracy and save costs. Presentation of care quality is increasingly regarded as imperative to support patients' choice and efficiency of care provision. We want medical professionals to realize that good to great performance can be achieved only through transparency for providers and patients.

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Conflict of interest None of the authors have any commercial sponsorship to disclose regarding this research.

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特別寄稿

制吐薬適正使用ガイドラインに関するアンケート調査

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The Survey for Anti-Emetic Guideline by Using Questioner: Working Group for the Revision of JSCO Anti-Emetic Guideline, Working Group of the Evaluation Committee for JSCO Anti-Emetic Guidline, and Study Group for Clinical Utility and Evaluation for JSCO Anti-Emetic Guideline: Toshiaki Saeki[*1], Kazuo Tamura[*2], Keisuke Aiba[*3], Kenjiro Aogi[*4], Keiko Iino[*5], Chiyo Imamura[*6], Kenji Eguchi[*7], Kenji Okita[*8], Yoshikazu Kagami[*9], Ryuhei Tanaka[*10], Kazuhiko Nakagawa[*11], Hirofumi Fujii[*12], Narikazu Boku[*13], Kazuo Matsuura[*14], Makoto Wada[*15], Tatsuo Akechi[*16], Yuichi Kakudo[*17], Yong-Il KIM[*18], Hidenori Sasaki[*19], Yasuo Shima[*20], Masayuki Takeda[*11], Eijiro Nagasaki[*3], Toshihiko Nishidate[*8], Mitsue Saito[*21], Yukino Ashikaga[*22], Yusuke Tanigawara[*6], Koichi Hirata[*8], Chikashi Ishioka[*17] and Masahiko Nishiyama[*23] (*[1]*Dept. of Breast Oncology, International Medical Center, Saitama Medical University,* *[2]*Division of Oncology, Hematology, and Infectious Diseases, Dept. of Medicine, Fukuoka University School of Medicine,* *[3]*Division of Hematology and Oncology, Jikei University School of Medicine,* *[4]*Dept. of Breast Oncology, Shikoku Cancer Center,* *[5]*National College of Nursing,* *[6]*Dept. of Clinical Pharmacokinetics and Pharmacodynamics, Keio University School of Medicine,* *[7]*Dept. of Medical Oncology, Teikyo University School of Medicine,* *[8]*Dept. of Surgery, Surgical Oncology and Science, Sapporo Medical University,* *[9]*Radiation Oncology Division, Dept. of Radiology, Showa University School of Medicine,* *[10]*Dept. of Medical Oncology, International Medical Center, Saitama Medical University,* *[11]*Dept. of Medical Oncology, Kinki University Faculty of Medicine,* *[12]*Dept. of Clinical Oncology, Jichi Medical University,* *[13]*Gastrointestinal Medical Oncology, National Cancer Center Hospital,* *[14]*Breast Surgery, Hiroshima Prefectural Hospital,* *[15]*Dept. of Psycho-Oncology and Palliative Medicine, Osaka Medical Center for Cancer and Cardiovascular Diseases,* *[16]*Dept. of Psychiatry and Cognitive-Behavioral Medicine, Nagoya City University Graduate School of Medical Sciences,* *[17]*Kondo Hospital,* *[18]*Dept. of Medical Oncology, Seirei Hamamatsu General Hospital,* *[19]*Dept. of Medical Oncology, National Hospital Organization Kanmon Medical Center,* *[20]*Palliative Medicine, Tukuba Medical Center Hospital,* *[21]*Dept. of Breast Oncology, Juntendo University Faculty of Medicine,* *[22]*Kobe branch, Japanese Nursing Association,* *[23]*Dept. of Clinical Oncology, Institute of Development, Aging and Cancer, Tohoku University,* *[24]*Dept. of Molecular Pharmacology and Oncology, Gunma University Graduate School of Medicine*)

Summary

Background: Japan Society of Clinical Oncology published a guideline for anti-emetic therapy two years ago. This guideline was a first evidence based guideline of anti-emetic treatment for the patients who received chemotherapy in Japan. To investigate a current situation of anti-emetic treatment in Japan, we analyzed the data from nationwide questionnaire. Material: Questionnaire analysis; From June 2012 to August 2012, we gave 24 questionnaires on the Japan Society of Clinical

制吐薬適正使用ガイドライン改訂ワーキンググループ／制吐薬適正使用ガイドライン評価ワーキンググループ／厚生労働省科学研究・がん診療ガイドラインの普及促進とその効果に関する研究及び同ガイドライン事業の在り方に関する研究班（埼玉医科大学国際医療センター[*1]乳腺腫瘍科，[*10]小児腫瘍科，[*2]福岡大学腫瘍・感染・内分泌内科学，[*3]東京慈恵会医科大学腫瘍・血液内科，[*4]独立行政法人国立病院機構四国がんセンター乳腺・内分泌外科，[*5]国立看護大学校成人看護学，[*6]慶應義塾大学医学部臨床薬剤学，[*7]帝京大学腫瘍内科，[*8]札幌医科大学第1外科，[*9]昭和大学医学部放射線医学教室，[*11]近畿大学腫瘍内科，[*12]自治医科大学臨床腫瘍科，[*13]国立がん研究センター中央病院，[*14]広島県立病院，[*15]大阪府立成人病センター心療・緩和科，[*16]名古屋市立大学大学院医学研究科精神・認知・行動医学分野，[*17]医療法人敬和会近藤病院，[*18]聖隷浜松病院化学療科，[*19]独立行政法人国立病院機構関門医療センター，[*20]筑波メディカルセンター緩和医療科，[*21]順天堂大学医学部乳腺・内分泌外科学，[*22]社団法人日本看護協会神戸研修センター，[*23]東北大学加齢医学研究所臨床腫瘍学分野，[*24]群馬大学医学系研究科病態腫瘍薬理学）

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SPECIAL ARTICLE

Japanese Society of Clinical Oncology clinical practice guidelines 2010 for antiemesis in oncology: executive summary

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Abstract The purpose of this article is to disseminate the standard of antiemetic therapy for Japanese clinical oncologists. On the basis of the Appraisal of Guidelines for Research and Evaluation II instrument, which reflects evidence-based clinical practice guidelines, a working group of the Japanese Society of Clinical Oncology (JSCO) reviewed clinical practice guidelines for antiemesis and performed a systematic review of evidence-based domestic practice guidelines for antiemetic therapy in Japan. In addition, because health-insurance systems in Japan are different from those in other countries, a consensus was reached regarding standard treatments for chemotherapy that induce nausea and vomiting. Current evidence was collected by use of MEDLINE, from materials from meetings of the American Society of Clinical Oncology National Comprehensive Cancer Network, and from European Society of Medical Oncology/Multinational Association of Supportive Care in Cancer guidelines for antiemesis. Initially, 21 clinical questions (CQ)

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were selected on the basis of CQs from other guidelines. Patients treated with highly emetic agents should receive a serotonin (5-hydroxytryptamine; $5HT_3$) receptor antagonist, dexamethasone, and a neurokinin 1 receptor antagonist. For patients with moderate emetic risk, $5HT_3$ receptor antagonists and dexamethasone were recommended, whereas for those receiving chemotherapy with low emetic risk dexamethasone only is recommended. Patients receiving high-emetic-risk radiation therapy should also receive a $5HT_3$ receptor antagonist. In this paper the 2010 JSCO clinical practice guidelines for antiemesis are presented in English; they reveal high concordance of Japanese medical circumstances with other antiemetic guidelines that are similarly based on evidence.

Keywords Antiemetic treatment · Cancer chemotherapy · Clinical practice guideline

Introduction

Recent developments in cancer chemotherapy have improved the survival of patients with a variety of malignancies. However, antiemetic treatments for chemotherapy which induce nausea and vomiting (CINV) are critical for successful chemotherapy. Consensus and/or evidence-based guidelines for antiemetic treatment in oncology have been issued by the National Comprehensive Cancer Network (NCCN) [1], the Multinational Association of Supportive Care in Cancer (MASCC)/European Society of Medical Oncology (ESMO) [2], and the American Society of Clinical Oncology (ASCO) [3]. However, application of these guidelines in Japan is limited because of different clinical circumstances and different domestic insurance coverage. Hence the Japanese clinical practice guideline for antiemetics was established and published on May 1st, 2010 as the first publication of the Japanese Society of Clinical Oncology (JSCO).

Methods

Initially, JSCO selected members of a working group for these guidelines on the basis of the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument [4], which assesses the methods used to generate evidence-based clinical practice guidelines. The members of a working group were included medical oncologists, oncological surgeons, palliative care physicians, and psycho-oncologists. The AGREE II Instrument is available as a PDF or in electronic form from http://www.agreetrust.org/resource-centre/agree-ii/. A draft of the guidelines was developed systematically, and members of the medical staff were in unanimous agreement with regard to all recommendations for treatment and clinical questions (CQ). However, domestic factors including ethnicity and health policy formation at the system level required further consideration. Hence, a consensus of all medical practitioners was held at a consensus meeting, and recommendations for antiemetic treatments were discussed in the context of Japanese medical circumstances.

Literature search strategy

A systematic review and meta-analysis of the effectiveness of antiemetic therapy was performed by use of the major international guidelines NCCN, MASSC/ESMO, and ASCO as sources of information [1–3]. Subsequently, high-level evidence was selected from the literature, and structured abstracts were generated for each of the manuscripts included. MEDLINE searches were also performed to identify other randomized controlled trials, and the Cochrane library was reviewed during 2008–2010 [5]. Materials from ASCO and MASSC annual meetings were reviewed and some Japanese manuscripts containing sufficiently strong evidence were included. Materials that were available in abstract form only were not considered.

Inclusion criteria for published studies

Systematic reviews and reports of randomized controlled trials were included if the intervention was for treatment of nausea or vomiting after cancer therapy, and nausea and/or vomiting outcomes were reported. This guideline was reviewed and approved by the JSCO Clinical Practice Guidelines Committee and the Board of Directors, and was reviewed and approved for publication in the International Journal of Clinical Oncology.

Guidelines and conflicts of interest

The Update Committee was assembled in accordance with ASCO's Conflict of Interest (COI) Management Procedures for Clinical Practice Guidelines ("Procedures", summarized at http://www.asco.org/guidelinescoi). The members of the working group provided disclosure forms that required disclosure of financial and other interests to the board of directors of JSCO. Subsequently, the COI

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committee reviewed the COI of each member and allowed all members without COIs to contribute to the guideline.

Recommendation grade

Recommendation grades were stated as follows:

A	Strongly recommended clinical action
B	Recommended clinical action
C1	Clinical action may be useful although there is a lack of high-level scientific evidence
C2	Not recommended because of insufficient scientific evidence
D	Clinical action not recommended

Results

The working group of JSCO clinical practice guidelines for antiemesis adopted a clinical question (CQ) form as the main guideline format and selected the following 21 CQs:

CQ1. How is the emetic risk induced by cancer chemotherapy categorized?

Recommendation (Grade A): the emetic risk induced by cancer chemotherapy is classified as high, moderate, low, and minimum according to the frequency of patient nausea and vomiting experiences, and antiemetic prophylactic treatments are prescribed in accordance with these categories.

The emetic risks of cancer chemotherapy depend on the potential emetogenicity of combined chemotherapeutic regimens. The emetic risk is evaluated on the basis of the percentage of untreated patients who experience acute emesis within 24 h of initiation and/or administration of cancer chemotherapy and is categorized as follows:

High emetic risk: 90 % or more patients experience acute emesis

Moderate emetic risk: 30–90 % of patients experience acute emesis

Low emetic risk: 10–30 % of patients experience acute emesis

Minimum emetic risk: fewer than 10 % of patients experience acute emesis

CQ2. How are intravenous chemotherapeutic agents categorized for the emetic risk?

Recommendation (Grade A): proper and sufficient antiemetic prophylaxis should be recommended in accordance with the four risk categories (Table 1).

Recommendation (Grade C1): antiemetic treatments for domestic chemotherapeutic agents developed in Japan are uncertain because of limited evidence of drug efficacy and low frequency of usage.

Emetic risks of chemotherapeutic agents are classified in Table 1 on the basis of the recommendations of existing guidelines produced with a high level of consensus, for example NCCN, MASSC, and ASCO; they were modified in consideration of particular clinical circumstances in Japan [6, 7]. Most chemotherapeutic regimens with high or moderate emetic risk include intravenous chemotherapeutic agents, and proper and flexible management of their emetic risks is essential because they are usually administered over several days and include several drugs. Although the 2009 NCCN guidelines indicate that high and low-dose cisplatin regimens have high and moderate emetic risk, respectively, the 2008 MASCC and 2006 ASCO guidelines categorized cisplatin as a drug of high emetic risk irrespective of dosage [8, 9]. Accordingly, all cisplatin regimens, including those administered over several days were regarded as regimens of high emetic risk (CQ10). However, combined regimens that include anthracycline and cyclophosphamide, for example AC, CAF, EC, and FEC, are usually regarded as having high emetogenicity. The 2009 NCCN guidelines categorized these anthracycline-containing regimens as high emetic risk similar to other monotherapeutic agents with high emetogenicity. Hence, this categorization was used for all anthracycline-containing regimens.

CQ3. How are the emetic risk categories for oral chemotherapeutic agents defined and managed?

Recommendation (Grade C1): according to clinical study protocols designed to assess efficacy as supportive co-treatments, suspension and/or dose reduction of chemotherapeutic agents should be considered to limit nausea and vomiting to grade 3 or less.

The emetic risk of oral chemotherapeutic agents is listed in Table 2. In Japan, oral fluoropyrimidine-based regimens are frequently used as adjuvant treatments with tegafur-uracil and/or leucovorin and capecitabine for colorectal cancer, S-1 for gastric cancer, and tegafur-uracil for breast and lung cancers, and several clinical trials have demonstrated efficacy is reasonable. Moreover, the Japanese clinical practice guidelines have indicated that S-1 and tegafur-uracil and/or leucovorin are efficacious treatment strategies for advanced gastric and colorectal cancers. Although these oral chemotherapeutic agents have lower emetogenicity when administered alone, adverse digestive events occur after repeated daily administration. Hence, antiemetic treatments are important to achieving higher drug adherence and to optimizing treatment.

CQ4. How should acute nausea and vomiting induced by cancer chemotherapy be prevented?

Recommendation (Grade A): a triple regimen of neurokinin 1 (NK1) receptor antagonist (aprepitant), serotonin (5-hydroxytryptamine: $5HT_3$) receptor antagonist, and dexamethasone is recommended for acute emesis during highly emetic cancer chemotherapy.

Table 1 Emetic risk category for intravenous chemotherapeutic agents

JSCO emetic risk category	Agent (regimen)	
High emetic risk (emetic frequency >90 %)	Cisplatin	*Altretaine*
	Cyclophosphamide (>1500 mg/m^2)	*Carmustine (>250 mg/m^2)*
	Dacarbazine	*Mechlorethamine*
	Doxorubicin + cyclophosphamide	*Streptozocin*
	Epirubicin + cyclophosphamide	
Moderate emetic risk (emetic frequency 30–90 %)	Actinomycin D	Irinotecan
	Amrubicin	Melphalan (≥50 mg/m^2)
	Arsenic trioxide	Methotrexate (≥250 mg/m^2)
	Busulfan (>4 mg/day)	Nedaplatin
	Carboplatin	Oxaliplatin (≥75 mg/m^2)
	Cyclophosphamide (≤1500 mg/m^2)	Temozolomide
	Cytarabine (>200 mg/m^2)	Therarubicin
	Daunorubicin	*Amifostine (≥300 mg/m^2)*
	Doxorubicin	*Azacitidine*
	Enocitabine	*Bendamustine*
	Epirubicin	*Carmustine (≤250 mg/m^2)*
	Idarubicin	*Clofarabine*
	Ifosphamide	
	Interferon α (≥10 million IU/m^2)	
	Interleukin-2 (>12–15 million IU/m^2)	
Low emetic risk (emetic frequency 10–30 %)	Interleukin-2 (≤12 million IU/m^2)	Mitoxantrone
	Cytarabine (100–200 mg/m^2)	Nab-paclitaxel
	Docetaxel	Nimustine
	Etoposide	Paclitaxel
	5-Fluorouracil	Pemetrexed
	Gemcitabine	Pentostatin
	Interferon α (5–10 million IU/m^2)	Ranimusutine
	Liposomal doxorubicin	Topotecan
	Methotrexate (50–250 mg/m^2)	*Amifostine (<300 mg)*
	Mitomycin C	*Ixabepilone*
Minimum emetic risk (emetic frequency: <10 %)	L-Asparaginase	Vinblastine
	Bevacizumab	Vincristine
	Bleomycin	Vinorelbine
	Bortezomib	Trastuzumab
	Cetuximab	Vindesine
	Cladribine	*Alemtuzumab*
	Cytarabine (<100 mg/m^2)	*Decitabine*
	Fludarabine	*Denileukin diftitox*
	Gemtuzumab ozogamicin	*Dexrazoxane*
	Methotrexate (≤50 mg/m^2)	*Panitumumab*
	Nelarabine	*Pegaspargase*
	Peplomycin	*Temsirolimus*
	Rituximab	*Valrubicin*

Agents in italics are not approved for clinical use in Japan

Recommendation (Grade A): regimens containing $5HT_3$ receptor antagonists and dexamethasone are basically recommended for acute emesis during moderately emetic cancer chemotherapy. For particular chemotherapeutic regimens, addition of an NK1 receptor antagonist to regimens of $5HT_3$ receptor antagonist and dexamethasone are considered.

Table 2 Emetic risk category for oral chemotherapeutic agents

JSCO emetic risk category	Agent (regimen)	
High emetic risk (emetic frequency >90 %)	Procarbazine	
Moderate emetic risk (emetic frequency 30–90 %)	Cyclophosphamide	Temozolomide
	Etoposide	Vinorelbine
	Imatinib	
Low emetic risk (emetic frequency 10–30 %)	Capecitabine	S-1
	Doxifluridine	Sobuzoxane Tegafur-Uracil (UFT)
	Mercaptopurine	
	Nilotinib	
Minimum emetic risk (emetic frequency <10 %)	Dasatinib	Sorafenib
	Erlotinib	Sunitinib
	Fludarabine	Thalidomide
	Gefitinib	Tretinoin
	Hydroxyurea	Tamibarotene
	Lapatinib	*Chlorambucil*
	Melphalan	*6-Thioguanine*
	Methotrexate	

Agents in italics are not approved for clinical use in Japan

Acute onset of nausea and vomiting occurs within a few minutes to several hours, and intensity generally peaks from 5 to 6 h after administration of chemotherapy and usually recovers within 24 h. Management and control of CINV are essential for successful cancer chemotherapy, because unfavorable side effects of nausea and vomiting are associated with poor treatment adherence and effects. In addition, incomplete prevention of acute emesis may lead to uncontrollable delayed emesis [10]. Hence, according to the four emetic risk categories indicated in CQ2 and 3, appropriate and sufficient antiemetic treatments are needed from the start of chemotherapy. The standard model of antiemetic treatment regimens is detailed in the four diagrams in Fig. 1. In the high emetic risk diagram, evidence of antiemetic actions of AC regimens was taken from clinical trials of other highly emetic cancer agents, and suggests no additional effects of dexamethasone after day 2. Upon issue of the 1st guideline, oral aprepitant was the only NK1 receptor antagonist available for clinical use in Japan. Subsequently, in November 2011, the Japanese Ministry of Health, Labour, and Welfare approved the intravenous NK1 receptor antagonist, fosaprepitant. Accordingly, we immediately modified the diagram and included additional information about fosaprepitant as a minor revision of the guideline, with careful consideration of the limited evidence of its efficacy and safety.

CQ5. How should delayed nausea and vomiting after cancer chemotherapy be prevented?

Recommendation (Grade A): a combined regimen of NK1 receptor antagonist (aprepitant) and dexamethasone is recommended for treatment of delayed emesis during highly emetic cancer chemotherapy.

Recommendation (Grade A): single administration of dexamethasone is basically recommended for delayed emesis during moderately emetic cancer chemotherapy. However, regimens of NK1 antagonist and/or dexamethasone are considered.

Delayed onset of nausea and vomiting occurs later than 24 h after administration of chemotherapy. In these circumstances, control of delayed emesis is essential to maintaining patients' quality of life and for motivating further treatment with a healthy mentality. As described in CQ4, complete prevention of acute emesis is the most important and fundamental strategy for preventing delayed emesis (Fig. 1). In specific cases in which dexamethasone should be restricted, 2–4 days of 5HT3 antagonist is recommended instead of dexamethasone.

CQ6. What kinds of serotonin ($5HT_3$) receptor antagonist are available in Japan?

Recommendation (Grade A): $5HT_3$ receptor antagonists are effective treatments for prevention of nausea and vomiting during cancer chemotherapy; seven drugs are approved in Japan: granisetron, palonosetron, ramosetron, ondansetron, tropisetron, azasetron, and indisetron.

Several $5HT_3$ receptor antagonists are currently available in Japan, and efficacy for management of CINV has been demonstrated for all these agents, particularly under conditions of acute phase emesis. However, the efficacy of these agents for treatment of delayed emesis remains controversial because no further antiemetic effects of additional treatments have been observed after initial use

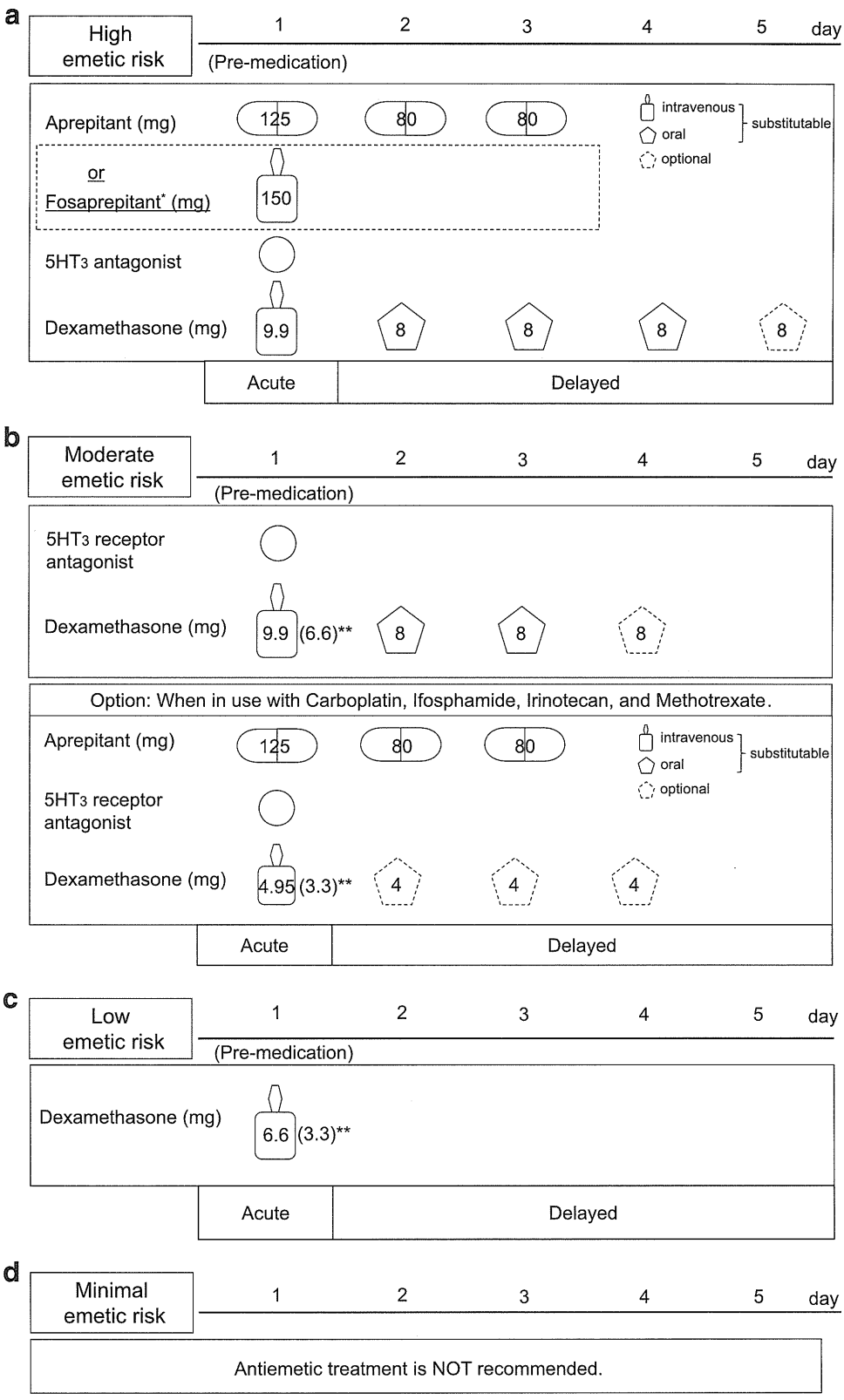

Fig. 1 Antiemetic treatments for intravenous cancer chemotherapy. **a** High emetic risk: in the absence of aprepitant, 13.2–16.4 mg dexamethasone should be given on day 1; **b** moderate emetic risk; **c** low emetic risk; **d** minimum emetic risk. *Asterisk*, optional fosaprepitant was added to the diagrams in a revised edition (version 1.2). *Double asterisk*, optional dose of dexamethasone. The diagrams indicate standard examples of antiemetic treatment regimens. Flexible modifications are necessary according to specific conditions of each patient. Intravenous dexamethasone contains 3.3 mg/mL dexamethasone out of a total 4 mg/mL dexamethasone sodium phosphate

of $5HT_3$ receptors with antagonistic agents. It has been proved that palonosetron is not inferior to granisetron in the acute phase and is superior to granisetron in the delayed phase [11].

CQ7. What is the recommended dose of corticosteroid for antiemetic treatment?

Recommendation (Grade A): corticosteroid is an effective antiemetic at recommended doses determined

according to the emetic risk categories of chemotherapeutic regimens.

Corticosteroid has been used as an antiemetic prophylactic during cancer chemotherapy for 25 years [12], although its mechanism of action remains unclear compared with those of $5HT_3$ and NK1 antagonists, which have recently been approved with clear evidence of mechanisms. Although several classes of corticosteroid are available, dexamethasone and methylprednisolone are most frequently used as antiemetics, with strong evidence of their effects [13, 14]. In particular, oral and intravenous dexamethasone (4–20 mg/day) has been approved as antiemetic treatment during cancer chemotherapy in Japan. However, the efficacy of high-dose dexamethasone has not been compared with that of 20-mg treatments among either Western [13, 14] or Japanese populations [15].

CQ8. How should breakthrough nausea and vomiting be managed?

Recommendation (Grade B): fixed around-the-clock administration of a variety of drugs should be considered according to patient symptoms. In addition, antiemetic $5HT_3$ receptor antagonists should be replaced with another type of $5HT_3$ receptor antagonist.

Breakthrough emesis refers to nausea and vomiting despite prophylactic antiemetic treatment, and requires additional treatment with antiemetic agents with mechanisms of action that differ from that of the primary antiemetic agent. Among these, the dopamine antagonists metoclopramide, butyrophenone, corticosteroid, and lorazepam may be considered for breakthrough emesis, despite poor evidence of their efficacy. A systematic review of antiemetic treatments for patients with advanced cancer showed that metoclopramide is superior to placebo and equivalent to ondansetron, although responses were only 23–36 % and 18–52 % for nausea and vomiting, respectively [16]. Moreover, a randomized clinical controlled study of 51 advanced cancer patients showed no significant effects of additional dexamethasone for nausea after failure of antiemetic response to metoclopramide [17].

Some reports recommend antiemetic prophylaxis using agents that are not $5HT_3$ receptor antagonists.

CQ9. How should acute nausea and vomiting induced by low and minimum emetic chemotherapy be managed?

Recommendation (Grade B): during low emetic chemotherapy, dexamethasone should be considered according to chemotherapeutic regimen and patient background.

Recommendation (Grade C1): routine usage of dexamethasone is not recommended for minimum emetic chemotherapy.

Prophylactic antiemetic treatment is not recommended for low or minimum emetic chemotherapy, because patients do not progress to definite nausea and vomiting. Nonetheless, some patients suffer from emesis during treatment with low or minimum emetic chemotherapy, necessitating flexible and appropriate treatment despite the absence of high-level evidence. The 2006 ASCO and 2008 MASCC guidelines recommended administration of 4–8 mg dexamethasone [13, 18], and include prochlorperazine [19] and metoclopramide as optional antiemetics.

CQ10. How is nausea and vomiting managed for such regimens as several cisplatin treatments daily?

Recommendation (Grade B): a triple antiemetic regimen of $5HT_3$ antagonist, dexamethasone, and aprepitant is recommended for acute nausea and vomiting during more typical chemotherapeutic regimens. A double regimen of dexamethasone and aprepitant is recommended for delayed nausea and vomiting, even during regimens of several cisplatin treatments daily.

It is widely accepted that cisplatin is a highly emetic chemotherapeutic agent, and it is commonly administered every 3 or 4 weeks at $\geq$50 mg/m^2 for treatment of a variety of malignancies. However, different cisplatin regimens have been established with reasonable evidence, including several cisplatin treatments daily at <50 mg/m^2 for oncologic tumors such as cholangiocarcinomas, bladder cancers, and germinomas [20, 21], and continuous cisplatin injections at 100 mg/m^2 over 4 days for non-Hodgkin malignant lymphomas.

CQ11. How should anticipatory nausea and vomiting be managed?

Recommendation (Grade B): initially, complete prevention of emesis is essential during acute and delayed phases, so patients never experience nausea and vomiting.

Recommendation (Grade B): benzodiazepine is effective for anticipatory nausea and vomiting.

Recommendation (Grade B): such psychological therapy as systematic desensitization and/or behavioral treatment, relaxation therapy, and hypnotherapy for pediatric patients effectively ameliorate anticipatory nausea and vomiting.

Anticipatory nausea and vomiting occurs immediately before treatment, and reflects previous negative experiences of cancer chemotherapy [22–24], although nausea is more common than vomiting among such cases. The ideal prophylaxis for this symptom is complete prevention of emesis from the initial treatment [23–26]. Hence, appropriate antiemetic treatments are essential, and require accurate assessment of emetic risks for planned chemotherapeutic regimens. The 2009 NCCN and 2008 MASCC guidelines recommended treatments with lorazepam [27] for anticipatory nausea and vomiting, and alprazolam [28] for anticipatory nausea.

CQ12. How are emetic risks categorized for radiation therapy?

Recommendation (Grade A): emetic risks of radiation therapy are classified (Table 3) according to tissue targets and volumes for irradiation.