JJCO Japanese Journal of Clinical Oncology

Japanese Journal of Clinical Oncology, 2016, 46(11) 1053–1061
doi: 10.1093/jjco/hyw106
Advance Access Publication Date: 2 September 2016
Public Health Report

OXFORD

Public Health Report

Quality assurance manual of endoscopic screening for gastric cancer in Japanese communities

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Received 8 March 2016; Accepted 5 July 2016

Abstract

The Japanese government introduced endoscopic screening for gastric cancer in 2015 as a public policy based on the Japanese guidelines on gastric cancer screening. To provide appropriate endoscopic screening for gastric cancer in Japanese communities, we developed a quality assurance manual of endoscopic screening and recommend 10 strategies with their brief descriptions as follows: (i) *Formulation of a committee* responsible for implementing and managing endoscopic screening, and for deciding the suitable implementation methods in consideration of the local context; (ii) *Development of an interpretation system* that leads to a final judgement to standardize endoscopic examination and improve its accuracy; (iii) *Preparation of management and reporting systems* for adverse effects by the committee for safety management; (iv) *Obtaining informed consent* before operation following adequate explanations regarding the benefits and harms of endoscopic screening; (v) *Avoidance of frequent screenings* to reduce false-positive results and overdiagnosis. As a reference, the target age group is ≥50 years, and the screening interval is 2 years; (vi) *Keeping the biopsy rate within* 10% as post-biopsy bleeding may occur. Before endoscopic screening, any history of antithrombotic drug usage should be checked; (vii) *Nonadministration of sedation* in endoscopic screening for safety management; (viii) *Adherence to proper endoscopic cleaning and disinfection* to reduce infection; (ix) *Use of a checklist* to achieve optimal program preparation when municipal governments introduce endoscopic screening; (x) *Identification of the aims and roles* by referring to a checklist if primary care physicians decide to participate in endoscopic screening.

Key words: gastric cancer screening, upper gastrointestinal endoscopy, quality assurance, manual, population-based screening

Introduction

In 2014, there have been >360 000 cancer deaths reported in Japan, with gastric cancer accounting for 13% of the total number of these deaths (1). The reported age-standardized mortality rates of gastric cancer were 16.2 per 100 000 men and 6.2 per 100 000 women. Over the last 2 decades, the cancers causing mortality have changed. In particular, mortality from gastric cancer in men has decreased. In 2005, the gastric cancer mortality rate was half that in 1975. Despite these decreases, the burden of gastric cancer has remained; thus, gastric cancer screening plays a central role in making public health policies.

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Gastric cancer screening using the upper gastrointestinal series (i.e. radiographic screening), which was developed in Japan, has been conducted since the 1960s (2). Since 1983, nationwide cancer screening programs for gastric cancer have been implemented as a public policy under the Health Law for the Aged. In 2005, the Japanese guidelines for gastric cancer screening have also recommended the uses of radiographic screening based on a systematic review (3). In these guidelines, upper gastrointestinal endoscopy and serological testing (i.e. *Helicobacter pylori* antibody and serum pepsinogen testings) were also evaluated. However, these procedures were not recommended because of insufficient evidence regarding their effectiveness. Nevertheless, upper gastrointestinal endoscopy has been increasingly used in clinical practice and as a standardized examination procedure for gastrointestinal diseases. Since 2005, some studies to evaluate mortality reduction from gastric cancer have been published in Japan (4–8). In 2015, the Japanese guidelines were revised and endoscopic screening for gastric cancer was recommended on the basis of the results of case-control studies in Korea and Japan (8). Consequently, the Japanese government decided to introduce endoscopic screening for gastric cancer in communities as a public policy.

To effectively introduce population-based screening nationwide, quality assurance of endoscopic screening for gastric cancer must be carefully considered. Even if evidence has been established, mortality reduction from gastric cancer cannot be achieved without appropriate management. Implementation of population-based screening, prioritization of quality assurance activities such as standardization of records and interpretation of endoscopic images, management of adverse effects and monitoring are regarded as essential issues. In European countries, quality assurance guidelines for cervical, breast and colorectal cancers have been published, and these guidelines have become basic concepts and standards for the management of these programs (9–11). Since 2000, Korea has introduced endoscopic screening for gastric cancer as a national program (12). In Japan, several municipalities have already introduced endoscopic screening as an alternative to gastric cancer screening (13,14). However, a manual for quality assurance in the performance of endoscopic screening for gastric cancer at the national level remains to be produced.

We developed a quality assurance manual to effectively introduce endoscopic screening for gastric cancer in communities in Japan.

Methods

Although there is presently no standard manual for quality assurance of endoscopic screening for gastric cancer, technical manuals for endoscopic screening have been published by academic societies, and some local medical associations have already introduced endoscopic screening in communities. These manuals often lack information for the management of harms including false-positive cases, overdiagnosis and infection caused by endoscopy. We collected these manuals and referred to the European guidelines for quality assurance of breast, cervical and colorectal cancers (12–14). The necessary items were selected for quality assurance of endoscopic screening for gastric cancer. The guidelines for radiographic screening of gastric cancer (15) were also used as a reference. When there was insufficient evidence regarding the effective implementation of endoscopic screening for gastric cancer, we discussed various quality assurance aspects in our working committee. The following items were selected as contents of the manual for quality assurance of endoscopic screening for gastric cancer in Japanese communities:

1. Effectiveness of endoscopic screening for gastric cancer
2. Harms of endoscopic screening for gastric cancer
3. Target age groups and screening interval
4. Implementation requirements
5. Implementation procedures
6. Endoscopic screening checklists for local municipal governments and primary care physicians
7. Recommendations

Effectiveness of endoscopic screening for gastric cancer

To reduce mortality from gastric cancer, the appropriate screening method should be selected on the basis of evidence confirmed from reliable studies. The Japanese guidelines for gastric cancer screening recommend endoscopic screening as population-based screening in communities based on case-control studies in Korea and Japan (8). The effectiveness of endoscopic screening for gastric cancer was previously evaluated in a Japanese community-based case-control study. The findings of that study suggested a 30% reduction in gastric cancer mortality by endoscopic screening performed at least once within 36 months before the date of gastric cancer diagnosis (6). On the other hand, a nested case-control study from Korea reported a 57% mortality reduction by endoscopic screening based on a national database (16). Recently, the results of a new cohort study conducted in Tottori and Yonago, Japan have suggested a 67% mortality reduction from gastric cancer in the endoscopic screening group compared with the radiographic screening group (17). Although these results are consistent in terms mortality reduction, evidence is weak because these results were not obtained from a randomized controlled trial.

Harms of endoscopic screening for gastric cancer

The major harms of endoscopic screening for gastric cancer include false-negative result, false-positive result, overdiagnosis, infection and adverse effects.

'False-negative result' is defined as individuals who have gastric cancer that will develop into a significant disease in the future if it is not treated (18). The false-negative rate of endoscopic screening was higher than that of radiographic screening. The rate of endoscopic screening were reportedly 4.5% for prevalence screening and 3.2% for incidence screening (20).

'False-positive result' is a common harm in cancer screening which requires further examination to definitively diagnose gastric cancer. In breast cancer screening, it has been suggested that false-positive results induce psychological anxiety (19). Although the rates of endoscopic screeningfor gastric cancer were reportedly 14.9% for prevalence screening and 11.2% for subsequent screening (20), there are still no reports related to the psychological burden of endoscopic screening for gastric cancer.

'Overdiagnosis' is the most serious harm in cancer screening. To our knowledge, there is as yet no study estimating the rate of overdiagnosis in endoscopic screening for gastric cancer. Based on the results of a previous study of endoscopic screening for gastric cancer, the observed number was twice the expected number in the target group of endoscopic screening for gastric cancer (21). However, the excess cancers included not only cases of overdiagnosis but also cases of early cancers that can possibly progress to advanced cancers.

'Hepatitis B infection' caused by endoscopy was reported in the 1980s in Japan (22,23). Moreover, *H. pylori* infection was reportedly caused by endoscopy and induced the formation of acute gastric mucosal lesions (24,25). The Japan Gastrointestinal Endoscopy

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Society has published guidelines and manuals, and promoted appropriate cleaning and disinfection methods (26).

Over the last 3 years, the Japanese Association of Gastroenterological Cancer Screening has determined the number of adverse effects of endoscopic screening for gastric cancer (27–29). The total number of endoscopic examinations was 740 245 and the rate of adverse effects in endoscopic screening for gastric cancer was 78 per 100 000 participants. The most common adverse effects were nasal bleeding and gastric mucosal laceration. The number of cases of post-biopsy bleeding was 21 cases, and four cases required admission. However, the association between bleeding and antithrombotic drug usage was unclear. As endoscopic examinations are often performed after the temporary stoppage of antithrombotic drugs, the risks of thrombosis during antithrombotic drug holidays are real (30–32), as well as bleeding after retaking the drugs (33,34). However, regardless of taking antithrombotic drugs, there is a possibility of bleeding to occur (35,36). In these previous reports, although there were serious adverse effects including anaphylactic shock and respiratory depression, there were no cases of death. On the hand, a survey from the Japanese Gastrointestinal Endoscopy Society found cases of death caused by sedation for endoscopic examination (37).

Target age groups and screening interval

The Japanese guidelines for gastric cancer screening recommend endoscopic screening for individuals aged 50 years and older based on the trend of incidence and mortality of gastric cancer in the last 3 decades (8). The balance of benefits and harms was analyzed on the basis of the number needed to screen, which indicated the necessary number to save one death by cancer screening. The results suggested a gap of net benefits between individuals in their 40s and 50s (8). In Japan, the national government has not yet defined the upper age limit for all cancer screening programs. However, in elderly people, there is a high possibility for the occurrence of adverse effects and overdiagnosis.

Although the recommended screening interval was not clearly specified in these guidelines, this can be defined as 2–3 years based on the results of case-control studies in Korea and Japan. In a previous study in Korea, mortality reduction was evident even if the screening interval was extended to 3 years (16). The Korean guidelines defined screening interval as 2 years for national programs (38). Based on these results, the Japanese government has decided to introduce biennial endoscopic screenings for individuals aged 50 years and older. The present manual also recommends the same target age group and screening interval for the endoscopic screening for gastric cancer.

The rates of false-positive cases and overdiagnosis could increase in frequent unnecessary screenings (39). To avoid false-positive cases, the recommended starting age should be strictly adhered to (40). It should also be plausible to reduce frequent screening so as not to exceed the appropriate screening interval to minimize of false-positive cases and overdiagnosis.

Implementation requirements

Although the responsibility of implementing cancer screening rests on each municipal government, the national government has recommended the appropriate screening methods and their quality assurance based on available evidence. Local medical associations often play a central role in conducting endoscopic screening for gastric cancer because members of these associations perform endoscopic examinations in their clinical practices. On the other hand, endoscopic screening is not suitable for mass surveys because it requires specific equipment including an automatic endoscope reprocessor. These aspects cannot be provided in automobile screening. However, medical institutions and screening centers are limited, particularly in rural areas. Usually, endoscopic screening is performed in private clinics that collaborate with local medical associations in terms of the management of endoscopic screening. Therefore, in the implementation of endoscopic screening for gastric cancer, local municipal governments have to develop a committee for the management of endoscopic screening for gastric cancer in cooperation with local experts and local medical associations. This committee will define the implementation and management policy for endoscopic screening in consideration of the national policy and local context. Since the committee plays a central role in the management and implementation of endoscopic screening for gastric cancer, the committee has to define the following issues: target group, implementation method, accreditation of primary physicians who can participate in the endoscopic screening, interpretation system that leads to a final judgment, database management, safety management of adverse effects and preparation of training workshops. The most important role of the committee is to develop an interpretation system that leads to a final judgment (Fig. 1). The committee has to prepare a flow chart for reporting adverse effects and for monitoring the performance of endoscopic screening to minimize such adverse effects. Some local committees have collected information related to adverse effects. As severe adverse effects are rare but require immediate treatment, such information (e.g. admission cases and death) can be collected directly. However, minor adverse effects (e.g. nasal bleeding) have been often ignored. For safety management, the committee should collect information regarding all adverse effects regardless of disease severity. A database of adverse effects should be established for the purpose of safety management for the endoscopic screening of gastric cancer at the national level.

All primary care physicians who have participated in endoscopic screening have not been generally well trained in performing the endoscopic technique. The committees should accredit suitable primary care physicians who can participate in performing endoscopic screening as a basic requirement in local areas. The basic requirement is met when either one of the following conditions is met: (i) having a certification as a specialist of gastrointestinal cancer screening, gastrointestinalendoscopy or digestive diseases as awarded by Japanese academic societies; (ii) relevant experience of >100 upper gastrointestinal endoscopy examinations per year. However, the committee can accredit participation in endoscopic screening by primary care physicians who cannot match these basic requirements considering their own technical skills and the local context of medical resources.

The committee also has to manage the interpretation system that leads to a final judgment. Physicians, who perform endoscopy in the screening programs, have to submit all images of the endoscopic screenings for gastric cancer. The experts, who are mainly endoscopists, check the graphic contents of the endoscopic screenings and make a final judgement during a meeting for the interpretation system. The experts also check the appropriateness of the endoscopic images and indicate points for improvement. These are the basic requirements for the standardization and improvement of accuracy of endoscopic screening for gastric cancer.

The committee should also collect the results of endoscopic screenings and conduct further examinations based on the surveys of local hospitals and in reference to the cancer registry to confirm the diagnosis of gastric cancer. Based on the available database, performance indicators including the participation rate in endoscopic screening, biopsy rate, gastric cancer detection rate and positive predictive value can be calculated. These indicators are used for the performance management of endoscopic screening for gastric cancer.

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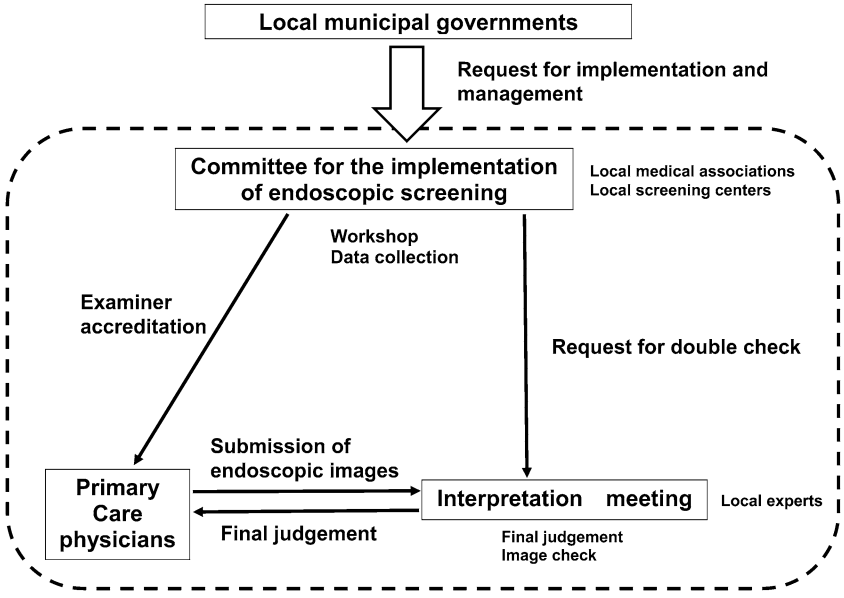

Figure 1. Role of management committee of endoscopic screening for gastric cancer. For proper implementation of endoscopic screening for gastric cancer, municipal governments have to develop a management committee of endoscopic screening for gastric cancer in cooperation with local experts and local medical associations. The committee will define the implementation and management policies for endoscopic screening in consideration of the national policy and local context. As the committee plays a central role in the implementation and management of the endoscopic screening program, the committee has to define the following issues; target group, implementation method, accreditation of endoscopists, interpretation system that leads to a final judgment, database management, safety management of adverse effects and preparation of training workshops. The most important role of the committee is the development of an interpretation system that leads to a final judgment. The committee has to prepare a flow chart for reporting adverse effects and monitor performance of endoscopic screening to minimize such effects.

Moreover, the committee must hold workshops for primary care physicians and their staff nurses who participate in endoscopic screening for gastric cancer. The curricula that should be included are shown in Table 1. Nurses, who participate in endoscopic screening in the clinics, should learn the appropriate methods for cleaning and disinfection of endoscopes.

Implementation procedures

Regarding endoscopic screening for gastric cancer, the endoscopic procedure involves the following steps: (i) general preparation including a medical interview, (ii) obtaining informed consent, (iii) preparation procedure including anesthesia, (iv) performing the endoscopic screening procedure, (v) cleaning and disinfection and (vi) accomplishing the reporting system.

Before the endoscopic screening, a physician should confirm if an individual meets the inclusion criteria for endoscopic screening for gastric cancer. When any symptoms related to gastric diseases are found, the individual is excluded from the target of endoscopic screening and should be recommended for consultation. Any history of the use of antithrombotic drugs is important in endoscopic screening because such usage can put the individual at a high risk of bleeding. When an individual takes these drugs, endoscopic examination is not recommended under conditions wherein the endoscopist cannot arrest the hemorrhage.

As for informed consent, this is needed so that appropriate information regarding the benefits and harms of endoscopic screening for gastric cancer is explained before participation.

In endoscopic examination, pharyngeal anesthesia is needed for oral endoscopy and nasal cavity anesthesia is necessary for nasal endoscopy. As the time of endoscopic examination is limited to ~10–15 minutes and the examination can be performed without sedation, the use of sedation is therefore not recommendduring endoscopic examination in the screening program. According to the Japanese Gastrointestinal Endoscopy Association, cases of death from sedation have been reported (36). Sedations pose a risk of respiratory depression, which can lead to death.

When endoscopic screenings are performed, the endoscopist observes and records pertinent findings from all locations in the stomach, including the esophagus and duodenal bulb. About 30–40 images are needed to observe for changes and record findings from all locations in the stomach (41). When biopsy is performed, the endoscope should be withdrawn after ascertainment of bleeding stoppage from the biopsy areas. Unnecessary biopsies should be avoided, such as those for a typical gastric fundic polyp.When the experts in the interpretation system have some suggestions regarding the endoscopic images, the endoscopist should carefully consider their suggestions and make the necessary improvements.

After the examination, the endoscope should be thoroughly cleaned because every participant could be a potential source of infection. Most guidelines have defined the following six procedural steps to follow: (i) cleaning, (ii) rinsing, (iii) disinfection, (iv) rinsing, (v) drying and (vi) storage (26,42). The external surfaces and components of an endoscope are usually cleaned and then the endoscope is placed in an automatic processor containing a liquid chemical germicide. Both processes should not be skipped to achieve a strict infection control in endoscopic screening. As the Japanese Association of Gastrointestinal Endoscopy has already defined the appropriate and detailed methods for cleaning and disinfection involved in endoscopic examinations (26), these steps should be rigorously followed. All physicians and nurses who participate in endoscopic screening should be properly trained, and they should

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Table 1. Workshop curricula on endoscopic screening for gastric cancer

1. **Trends of incidence and mortality of gastric cancer**
   - Cancer registry
   - Demographic statistics
2. **Risk factors of gastric cancer**
   - *Helicobacter pylori* infection
   - Lifestyle: smoking, high salt intake, etc.
3. **Basic concepts of cancer screening**
   - Target population: inclusion and exclusion criteria
   - Difference of screening and clinical practice
   - Organized screening and opportunistic screening
4. **Evaluation of efficacy/effectiveness of cancer screening**
   - Study design
   - Outcomes
   - Guidelines
5. **Benefits of cancer screening**
   - Mortality reduction
   - Others: assurance, improvement of QOL, etc.
6. **Harms of cancer screening**
   - False-negative: definition, management
   - False-positive: definition, management
   - Overdiagnosis: definition, management
   - Infection
   - Adverse effects
7. **Quality assurance**
   - Management methods
   - Performance indicators: participation rate, cancer detection rate, biopsy rate, participation rate of diagnostic examination, positive predictive value
   - Calculation of sensitivity and specificity
   - Follow-up survey
8. **Procedure of endoscopic screening for gastric cancer**
   - Target age group
   - Screening interval
   - Endoscopic procedure
   - Judgement standards
   - Case report
9. **Infection control**
   - Adverse effects: *H. pylori*, *Hepatitis B*, etc.
   - Cleaning and disinfection of endoscopes
10. **Management of adverse effects**
    - Adverse effects
    - Safety management
    - Reporting system of adverse effects

adhere to the standard infection control procedure for the protection of both the individuals being examined and the screening personnel.

All endoscopic images should be submitted to the committee which makes a final judgment in a meeting using the interpretation system. The results should be sent within 2 weeks after the endoscopic screening. However, if the final judgement is different from the initial judgement, a face-to-face explanation is needed for better understanding. When no abnormality is detected in the endoscopic examination, participation in endoscopic screening in the next 2 years should be recommended.

Endoscopic screening checklistsfor local municipal governments and primary care physicians

As local municipal governments have been given the responsibility, they can decide the introduction of endoscopic screening for gastric cancer at their level. However, before they can introduce the appropriate endoscopic screening program, they have to discuss the suitability of endoscopic screening in their local areas. When endoscopic screening for gastric cancer is introduced, the municipal governments have to prepare a management system of endoscopic screening for gastric cancer by referring to the checklist shown in Table 2. The checklist for municipal governments constitutes 22 items under the following six categories: (i) aim, (ii) target population, (iii) screening method, (iv) follow-up survey, (v) safety management and (vi) workshops.

On the other hand, if primary care physicians want to participate in endoscopic screening for gastric cancer in their communities, they should recognize the basic requirements referred to in the checklist shown in Table 3. The checklist for primary care physicians includes 23 items under the following six categories: (i) aim, (ii) preparation, (iii) explanation, (iv) procedure, (v) judgement and (vi) workshops.

Both checklists include the minimum requirements for implementing and managing the quality assurance of endoscopic screening for gastric cancer. If these basic requirements are difficult to fulfill, endoscopic screening should not be introduced until all preparations have been completed.

Discussion

Endoscopic screening has been anticipated to be introduced in national programs for gastric cancer screening over the last decades. In the previously published guidelines for gastric cancer screening, endoscopic screening has not been recommended because of insufficient evidence regarding its effectiveness (3). However, upper intestinal endoscopy has been the standard method for detecting gastric diseases in clinical practice, and access to endoscopic procedures by local area inhabitants would be easy because endoscopy has been rapidly introduced and used in private clinics. Although the Japanese government has decided to introduce endoscopic screening for gastric cancer in communities, several areas, need to be addressed particularly quality assurance. At present, there are no guidelines for quality assurance of cancer screening in Japan. In European countries, the European committee has defined and adopted quality assurance guidelines to promote the appropriate screening for breast, cervical and colorectal cancers (9–11). Indeed, gastric cancer screening using radiography has a long history, but the screening system used is different because radiographic screening has been conducted mainly by mass survey. Therefore, an original endoscopic screening system for gastric cancer must be developed in Japan.

As the target of endoscopic screening is asymptomatic people and the number of endoscopic examinations will inevitably increase, safety management is a big issue. The harms of endoscopic screening are more serious than those of radiographic screening because of the higher rate of adverse effects including cases of death. Bleeding is a common adverse effect of endoscopic screening, particularly nasal endoscopy (27–29). Although bleeding is considered to be a minor adverse effect, treatment by admission is occasionally needed. Even in the absence of a risk among the individuals to be examined, there is always a possibility of causing bleeding including the Mallory–Weiss syndrome. Therefore, endoscopists should check for any history of taking antithrombotic drug usage. The use of sedation is not adopted in endoscopic screening. In Japan, sedation has not been used in upper gastrointestinal endoscopic examinations for obtaining a diagnosis, and sedation is not covered by health insurance even in clinical practice. Although some studies have reported that sedation can help improve the accuracy of endoscopic examinations (43,44), such examinations can be performed without sedation. The Japanese Anesthesia Society has defined the anesthesia guidelines for day surgery, and this requires continual monitoring during anesthesia

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Table 2. Checklist for local governments who intend to introduce endoscopic screening for gastric cancer

1. **Aim**
   - Do you understand the aim of endoscopic screening for gastric cancer?
2. **Target population**
   - Have you defined the inclusion and exclusion criteria of endoscopic screening for gastric cancer?
   - Have you prepared the target population list of endoscopic screening for gastric cancer?
3. **Screening method**
   - Have you defined the interval of endoscopic screening for gastric cancer?
   - Have you defined the medical institutions that will implement endoscopic screening for gastric cancer in your municipality?
   - Have you defined the basic requirements for primary care physicians who can participate in endoscopic screening for gastric cancer?
   - Do you understand the preparation method of endoscopic examination?
   - Have you defined the examination procedure in endoscopic screening for gastric cancer?
   - Do you hold regular meetings that lead to a final judgement?
   - Do experts double check all the images of endoscopic screening for gastric cancer?
   - Do experts check the appropriateness of the images of endoscopic screening for gastric cancer?
4. **Follow-up survey**
   - Will you build a database of endoscopic screening for gastric cancer?
   - Do you collect results of endoscopic screening for gastric cancer on a regular basis?
   - Do you record that total number of biopsy cases?
   - Do you call individuals who need further examination but have not visited the medical office?
   - Do you record the final diagnosis of participants of endoscopic screening for gastric cancer?
   - Do you calculate the performance indicators of endoscopic screening for gastric cancer (i.e. participation rate, cancer detection rate, biopsy rate, participation rate of diagnostic examination and positive predictive value)?
   - Do you inform all the participants about the results of the endoscopic screening for gastric cancer?
5. **Safety management**
   - Do you prepare a flow chart for reporting adverse effects?
   - To check safety management, do you check reports of adverse effects? Do you audit to clinics that participate in endoscopic screening?
6. **Workshops**
   - Do you hold workshops for endoscopic screening at least once a year?
   - Do you provide nurses who participate in endoscopic screening for gastric cancer opportunities to learn more about cancer screening?

(45). Therefore, when such type of management is difficult to adopt during endoscopic examinations, sedation should not be used in endoscopic screening for gastric cancer. When the number of endoscopic examinations increases, the possibility of developing adverse effects also increases. Therefore, constant focus on safety management is a must.

In Japan, there is no upper age limit set for all cancer screening programs. However, the participation rates of individuals aged 70 years and over have increased and represent 36.7% of all participations in gastric cancer screening (46).Older people who have a shorter life expectancy have participated in screening for breast, cervical, prostate and colorectal cancer (47–49). Although older people often have comorbidities, these are not barriers to participating in colorectal cancer screening (49).Some cancer screening guidelines define 65–75 years as the age limits of cancer screening. In older people aged >75 years who are not in good health, cancer screening can detect a cancer that otherwise would not cause any problems but may lead to harms from treatment (48). However, there is no standardized method for defining the age limits, but the balance of benefits and harms should be considered for older people and the original background in each country. Although the harms of gastric cancer screening in elderly people have been suggested, evidence defining the upper age limits in Japan remains insufficient. Further study is required to define the appropriate target age group considering the Japanese context.

In radiographic screening for gastric cancer, judgment of the results has been conducted using the double check system (15). This system has contributed to the standardization of interpretation and improvement of the accuracy of radiographic screening. As reported, the sensitivity and specificity of radiographic screening are 60–90% and 90%, respectively (50,51). A high accuracy has been supported by a high-quality radiographic technique and a standard interpretation using the double check system. A similar system is also required in endoscopic screening because not all primary care physicians have good endoscopic techniques. Standard recording of all relevant findings in the stomach and a final judgment by the experts are helpful in promoting standardization and improving/maintaining accuracy. Several municipalities have already introduced endoscopic screening and have established such an interpretation system that leads to a final judgement. In these municipalities, the biopsy rate was ~15%, and this has decreased to 10% according to continuous endoscopic screening (19,52). Minimization of unnecessary biopsy avoids adverse effects in endoscopic screening. These improvements are the main results of the interpretation system that leads to a final judgement.

Notably, the number of endoscopic screenings has increased nationwide, and this has been primarily dependent on private clinics and not on hospitals. However, there has been a disparity of resources for endoscopic screening because of insufficient clinics and hospitals in various local areas. In actuality, the current number of endoscopic examinations was based on clinical practice, but a further increase in the number of endoscopic examinations is needed to spread the use of endoscopic screening nationwide. In reality, however, it is difficult to quickly replace radiographic screening with endoscopic screening as the main method of gastric cancer screening. For the efficient use of limited resources, resource allocation should be considered in large areas, namely, medical districts and prefecture levels. When endoscopic screening has reached and been implemented in all local areas, radiographic screening can then be gradually replaced, particularly in these local areas. In addition, the appropriate target age group and screening interval should be carefully investigated for the efficient use of limited resources.

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Table 3. Checklist for primary care physicians who intend to participate in endoscopic screening for gastric cancer

1. **Aim**
   - Do you understand the aim of endoscopic screening for gastric cancer?
2. **Preparation**
   - Do you regularly check if the endoscope and automated endoscopy processor work property?
   - Do you explain the whole process of endoscopic examination to the nurses?
   - Do you prepare and check an emergency cart in your clinic? Do you have regular trainings for emergency cases?
   - Do you understand how to report cases of adverse effects?
3. **Explanation**
   - Before endoscopic examination, do you explain the endoscopic examination procedure?
   - Before endoscopic examination, do you explain the benefits and harms of endoscopic screening for gastric cancer?
   - Before endoscopic examination, do you check the past and present medical histories?
   - Before endoscopic examination, do you check the drugs that were previously taken?
   - Before endoscopic examination, do you confirm receipt of informed consent on endoscopic screening for gastric cancer?
   - After endoscopic examination, do you explain the results of the endoscopic examination?
   - If there are no problems, do you provide information regarding the next screening schedule?
   - Do you introduce the appropriate medical institution for diagnostic examination?
   - When the initial results have to be changed on the basis of the final judgment by experts, do you explain the reasons for the diagnostic change?
4. **Procedure**
   - Do you prepare for endoscopic examination appropriately?
   - Do you understand how to observe changes and record them from all locations in the stomach?
   - Do you limit your biopsy for gastric cancer and suspected lesions of gastric cancer?
   - Can you clean and disinfect an endoscope appropriately?
5. **Judgment**
   - Do you diligently submit all graphics of endoscopic screening for the final judgment by experts?
   - Do you attend interpretation meetings that lead to a final judgment by experts?
   - Do you make every effort to improve the images of endoscopic screening based on the suggestions from experts?
6. **Workshop**
   - Do you attend workshops on endoscopic screening for gastric cancer?
   - Do you provide nurses who participate in endoscopic screening for gastric cancer opportunities to learn more about cancer screening?

Helicobacter pylori is one of the main causes of gastric cancer, and 78% of all gastric cancer cases are estimated to be attributed to chronic *H. pylori* infection (53). International agency for research on cancer has recommended *H. pylori* screening and treatment strategies in consideration of disease burden and the local context (53). Although risk stratification can be performed by *H. pylori* antibody and serum pepsinogen tests (54), it is difficult to predict individuals who have never had gastric cancer in the future because of their low predictive specificity. On the other hand, it is possible to diagnose *H. pylori* infection by endoscopy based on a specific feature in the gastric mucosa (55). Although the discrimination ability for predicting the development of gastric cancer using biomarkers and endoscopy remains insufficient, it might be useful to adapt an expansion of the screening interval. Further study is needed as to how endoscopic screening corroborates with these biomarkers.

Recommendations

To provide the appropriate endoscopic screening for gastric cancer, we recommend the following strategies:

1. A committee for the implementation and management of endoscopic screening for gastric cancer must be developed. The committee should decide the implementation methods in consideration of the local context.
2. An interpretation system that leads to a final judgement must be established for the standardization of the endoscopic examination and improvement of its accuracy.
3. For safety management, the implementation and management committee has to prepare both a management system and a reporting system of adverse effects.
4. Before the endoscopic examinations, informed consent must be obtained after the appropriate explanations regarding the benefits and harms of endoscopic screening for gastric cancer.
5. The target age group of endoscopic screening for gastric cancer is 50 years and above, and the screening interval is 2 years. Based on these references, frequent screening should be avoided to minimize false-positive cases and overdiagnosis.
6. Since there is a possibility of post-biopsy bleeding, the biopsy rate should be kept within 10%. Before endoscopic screening, any history of antithrombotic drug usage should be ascertained. When an individual takes these antithrombotic drugs, endoscopic examination is not recommended under conditions wherein the endoscopist cannot arrest the hemorrhage.
7. For safety management, it is preferable not to use sedation in endoscopic screening for gastric cancer.
8. To reduce infection caused by endoscopy, appropriate cleaning and disinfection is required. Automatic reprocessing with a liquid chemical germicide is needed for endoscopic disinfection.
9. When municipal governments decide to introduce endoscopic screening for gastric cancer, a checklist should be used for the appropriate preparation of all the programs.
10. When a primary care physician decides to participate in endoscopic screening, the aim and role should be recognized by referring to the appropriate checklist.

Acknowledgements

We are indebted to Dr Edward F. Barroga, Associate Professor and Senior Medical Editor of Tokyo Medical University for reviewing and editing the manuscript.

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We also thank Ms Kanoko Matsushima and Ms Ikuko Tominaga for research assistance.

Funding

This study was supported solely by a Grant-in-Aid for Research for Promotion of Cancer Control Programs from the Japanese Ministry of Health, Labour and Welfare (H27-Toku-Shitei-005). The funder had no role in the conceptualization of the study design, data collection and analysis, decision to publish or preparation of the manuscript.

Conflicts of interest statement

None declared.

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Appendix

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