

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: This manuscript showed that endoscopic screening detected more gastric cancer than direct radiographic screening did, but both screening methods had similar effects on reducing the mortality rate from gastric cancer. Gastric cancer screening, especially early screening, has always been a concern. This article compared the effectiveness of the two screening methods, which is scientific and has certain guiding significance for clinical diagnosis and treatment, but there are still several points to be addressed.

1. There is a significant difference in staging between radiologic and endoscopic groups, which may lead to different treatment options, thus affecting the mortality of the two groups, and there is a potential deviation; Would it be better to assess in detail the value of the two in different stages (E. G. early stages) ?

Although there is a clear difference in the stage of gastric cancer detected by screening endoscopy and direct radiography, there is no significant difference between the two examinations in the accuracy of detecting advanced gastric cancer, which is associated with gastric cancer death.

2. The study enrolled participants aged 40 to 79 years who were screened by direct radiography (n = 11 155) or endoscopy (n = 10 747). There were no other inclusion and exclusion criteria except age. In addition, during the follow-up period, what kind of screening did these participants continue to take, and did they have new gastric cancer?

Gastric cancer screening recipients can undergo either endoscopic or direct radiographic screening once a year. They are free to choose the screening method each year; however, many screening recipients continue to undergo the same screening method.

3. Please delete the tables in the figure 1~4 and describe it in the article. And code (a)(b)(c) for three graphs in Figure 4.

The explanation of Figure 1~4 is provided in the text. Each graph in Figure 4 has been labeled from A to C.

4. In the discussion, it was mentioned that endoscopic operation experience and false negative were important bias factors, which were difficult to avoid, and would seriously reduce the credibility of the article, and could not get the exact conclusion.

In screening endoscopy, a small number of false negatives have been reported even by endoscopic specialists. The text also mentioned that false negatives are even more common in endoscopic examinations in which non-endoscopic specialists are free to participate. Therefore, we concluded that it is necessary to limit the number of participating endoscopists to those with a certain level of endoscopic skill to reduce false negatives in endoscopic examinations.

Reviewer #2:

Scientific Quality: Grade D (Fair)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors: This article aims to evaluate the impact on gastric cancer mortality rate of two types of gastric cancer screening in Maebashi City, Japan. At present, gastroscopy is the gold standard of gastric cancer screening, which plays an irreplaceable role. For the cavity organ, the roles of radiation detection has been classified. This paper only expands the number of queue population, so the article is generally innovative. Besides, no significant difference in the reduction of gastric cancer mortality rate between the two screening methods was found. On the whole, it is difficult to find out the advantages of the article. Therefore, it is suggested that the authors find a better entry point for analysis.

It goes without saying that endoscopic examination is an excellent method of gastric cancer screening as it has a higher detection rate for gastric cancer and a higher rate of early cancer detection than radiographic examination. However, it has also been reported that false-negative cancers are more common than expected in screening endoscopy, even in endoscopy specialist facilities. In Japan, endoscopic examination was approved in 2016 as a population-based gastric cancer screening as part of a personal health check, and it is expected to expand nationwide in the future. However, maintaining the quality of endoscopic examination is an important issue in a population-based gastric cancer screening program in which many unspecialized endoscopists also participate. This paper is important because it shows that if the quality of endoscopists is not sufficiently maintained in population-based gastric cancer screening for personal health checks, it may not lead to a reduction in gastric cancer mortality.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors: I am glad to review this paper. This study compared the gastric cancer incidence and mortality between endoscopic screening and radiographic screening. This research has important clinical implications. I have a few comments:

1. Are the screening for mass screening or opportunistic screening? Please explain it.

The screening program is a population-based screening program for personal health checks. In Japan, mass screening by indirect radiography, screening for personal health checks by direct radiography, or endoscopy, are conducted at medical institutions commissioned by the government through medical associations.

2. The end of follow-up time is almost nine years ago. Is there any updated follow-up data available?

It took about one year to approve the research plan of this study, and a lot of time was needed to match the data with cancer registries. To obtain the latest follow-up data, we need to submit an additional research plan for approval.

3. Information on the change of screening method during the follow-up time is lacking, which should be a significant limitation for this research. Also, the statement of annual screening is a bit vague. Can the authors provide more detailed information on screening frequency and screening interval during the follow-up?

There is no data on the extent of change in the screening method during the follow-up period. However, most examinees did not change their screening method during the follow-up period. It is mentioned in the text that each year screening recipients can choose one of either of the two screening methods.

4. One strength of endoscopic screening is that it can detect precancerous lesions (atrophic gastritis, metaplasia, polyps) and treat them before progression to cancer. Could authors provide biopsy results and treatment of precancerous lesions in the endoscopic group?

Gastric cancer screening in Maebashi city does not biopsy precancerous lesions because the rule is not to biopsy lesions other than those that are cancerous or strongly suspected to be cancerous. In addition, H. pylori eradication therapy for Hp-infected gastritis was not covered by insurance at the time of this study and was not performed.

5. Are lymphoma, GISTs also regarded as gastric cancer in this research? Please provide the pathological type of gastric cancer if it is available.

In this study, lymphoma and GIST were not included as gastric cancer. In addition, no new lymphomas or GISTs occurred during the follow-up period. Unfortunately, the histological types of gastric cancer that newly occurred during the screening period could not be ascertained due to the accuracy of cancer registration.

Incidentally, the histological types of gastric cancer detected by gastric cancer screening in 2006 (age 40–79 years) were as follows: well diff. adenocarcinoma 39.2%, moderate diff. adenocarcinoma 17.6%, poor diff. adenocarcinoma 29.4%, and unknown 13.7% for endoscopic screening, and was 9.1%, 36.4%, 36.4%, and 18.2%, for direct X-ray screening, respectively.

6. The baseline characteristics are quite simple. The adjusted covariates were only age and sex, which seems to be not enough. If possible, can more covariates be adjusted in this study? For example, screening frequency, screening institutions, history of screening, precancerous diseases, H. pylori infection, diabetes, smoking, medications (aspirin, statins, proton pump inhibitors), and family history. These known risk factors may be associated with gastric cancer mortality.

As commented by the reviewer, reported risk factors for gastric cancer include, among others, a history of Hp infection, smoking, alcohol consumption, and salt intake. However, as mentioned in the text, these risk factors were not examined in the screening, consequently we could not adjust for them as covariates.

7. There are a few statistical questions. The calculated results from Cox proportional hazards model should be hazard ratio (HR), not relative risk (RR). Their definitions are slightly different. Meanwhile, proportional hazard assumption should also be tested before the use of the Cox proportional hazards model. In Tables 4 and 5, The column name "Adjusted reduction rate" is unclear. Could authors revise it to the adjusted hazard ratio for xxx deaths? To facilitate readers to understand statistical methods, please write the main R packages used in this study.

The results of the Cox proportional hazards model have been changed to (Hazard Ratio) HR. We revised "Adjusted reduction rate" to the adjusted hazard ratio for xxx deaths.

8. More early-stage gastric cancer was detected by endoscopic screening than radiographic screening. This finding is advised to be written in the abstract. Good luck! In the results section of the abstract we state that endoscopic screening often detects early gastric cancer.

"However, most gastric cancers detected by endoscopic screening were early cancers that may not have resulted in death."

Reviewer #4:

Scientific Quality: Grade C (Good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors:

1. The data is nine years before. How to guarantee the timeliness?

It is true that the data is a little old; however, there is no data on the improvement in the accuracy of gastric cancer detection in recent years for either endoscopic or direct radiographic screening.

As replied to another reviewer, it took about one year to approve the research plan of this study, and a lot of time was needed to match the data with cancer registries. To obtain the latest follow-up data, we need to submit an additional research plan for approval.

2. Endoscopy is now commonly used to diagnose gastric lesions, especially the diagnosis of early gastric cancer. How can the clinical significance of radiography be highlighted when compared with endoscopy?

The purpose of population-based gastric cancer screening is to reduce gastric cancer death. Direct radiographic screening is not inferior to endoscopic screening for not missing advanced cancer. The advantage of radiographic screening is that it is less expensive than endoscopic screening and requires less human resources. In future population-based gastric cancer screening, it is necessary to construct an efficient gastric cancer screening system that considers gastric cancer risk by combining endoscopic and radiographic screening.