

## COMMENTARY

# Have we Comprehensively Evaluated the Effectiveness of Endoscopic Screening for Gastric Cancer?

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## Abstract

Endoscopy has been increasingly used in clinical practice and as a standardized examination procedure for gastrointestinal diseases. However, only a few studies on endoscopic screening for evaluating mortality reduction from gastric cancer have been carried out. Even if a high detection rate is obtained in clinical practice, such a rate cannot be directly accepted as evidence providing the effectiveness of cancer screening. Endoscopic screening for gastric cancer is not an exception of possibility to detect overdiagnosis. If detection rate is used for the evaluation of the effectiveness of cancer screening, the possibility of overestimating the effectiveness of cancer screening cannot be ruled out. To avoid the effect of overdiagnosis and confirm the effectiveness of endoscopic screening, mortality reduction from gastric cancer must be carefully evaluated by conducting reliable studies. The burden of gastric cancer remains real and this cannot be ignored in Eastern Asian countries. To determine the best available method for gastric cancer screening, evaluation of its effectiveness is a must. Endoscopic screening for gastric cancer has shown promising results, and thus deserves further comprehensive evaluation to reliably confirm its effectiveness and how its optimal use can be strategically promoted.

**Keywords:** Gastric cancer screening - upper gastrointestinal endoscopy - mortality reduction - overdiagnosis

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Endoscopy has been increasingly used in clinical practice and as a standardized examination procedure for gastrointestinal diseases. Notably, the uses of upper gastrointestinal series with barium meal for diagnostic examination have progressively decreased. This situation has ushered the gradual introduction of endoscopic screening in clinical settings. In fact, high detection rates of gastric cancer have been reported with endoscopic screening (Tashiro et al., 2006; Lu et al., 2014). Regarding effectiveness, there is great expectation that endoscopic screening has a high possibility of reducing mortality from gastric cancer. However, only a few studies on endoscopic screening for evaluating mortality reduction from gastric cancer have been carried out. To evaluate the effectiveness of cancer screening, the appropriate target population and study design with final outcomes should be identified. The European guidelines for quality assurance in cervical cancer screening previously defined the ranking of study designs and outcomes for the evaluation of cervical cancer screening (International Agency for Research on Cancer, 2006). The basic concept can be adopted for the assessment of endoscopic screening. To confirm the effectiveness of endoscopic screening, the following basic requirements should be included in the evaluation points: target population, outcome, and study design.

The target of cancer screening is an asymptomatic individual with an average risk, which is different from individuals presenting with symptoms. Even if a high

detection rate is obtained in clinical practice, such rate cannot be directly translated as evidence providing the effectiveness of cancer screening. The target subjects are usually different between cancer screening and clinical practice. In a previous Japanese study, although the subjects of endoscopic screening were the selected participants who were examined by multiphasic health check-up, the comparators were selected from patients in the hospital (Hosaokawa et al., 2008). To evaluate the effectiveness of endoscopic screening, comparators should also be chosen from the asymptomatic population. This is because patients might have risks of gastric cancer even if they did not have examination histories of upper gastrointestinal series with barium meal and endoscopy.

The effectiveness of cancer screening should be evaluated based on mortality reduction from cancer. Although the detection rate is often reported as the outcome measure in cancer screening, it is not a preferable indicator for showing evidence regarding the effectiveness of cancer screening. Cancers detected by screening include early stages of gastric cancer which has a possibility to progress to the death of the individual or overdiagnosis cases. Overdiagnosis is defined as the detection of cancers that might never progress to manifest symptoms during a person's life and it could not be the cause of death (International Agency for Research on Cancer, 2002). Since overdiagnosis leads to unnecessary examinations and overtreatment, patients who are diagnosed as having

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indolent cancers do not have any benefit from cancer screening. Endoscopic screening for gastric cancer is not an exception. Endoscopy can detect cases of early stage cancer which is often the target for endoscopic surgical resection. Although there is currently no report of overdiagnosis for gastric cancer screening, the numbers of detected cancer by endoscopic screening were twice the expected numbers (Hamashima et al., 2006). These cases might be included in the overdiagnosis cases. If detection rate is used for the evaluation of the effectiveness of cancer screening, the possibility of overestimating the effectiveness of cancer screening cannot be ruled out. To avoid the effect of overdiagnosis and confirm the effectiveness of endoscopic screening, mortality reduction from gastric cancer must be carefully evaluated by conducting reliable studies.

The most reliable method for evaluating mortality reduction is a randomized controlled trial (RCT) (International Agency for Research on Cancer, 2006). In fact, the efficacies of mammographic screening and colorectal cancer screening using fecal occult blood test have been evaluated by RCTs. However, the previous results related to such effectiveness of gastric cancer screening were solely based on a few observational studies (Hamashima et al., 2008). Recently, our group has published the results of a community-based case-control study to evaluate the effectiveness of endoscopic screening for gastric cancer. The findings of this study suggest a 30% reduction in gastric cancer mortality by endoscopic screening within 36 months before the date of gastric cancer diagnosis (Hamashima et al., 2013). Interestingly, a Korean study also reported a 57% mortality reduction by endoscopic screening of a nested case-control study based on the national database (Cho, 2014). These results suggest a high possibility of achieving mortality reduction from gastric cancer by endoscopic screening. However, the results have been obtained from observational studies only. Realistically, it is difficult to perform RCT for endoscopic screening in Korea and Japan, countries that have already established national programs for gastric cancer screening (Oshima, 1994; Kim et al., 2011). Although case-control and cohort studies are the second best methods, there is a serious need for the accumulation of more valid evidence from Asian countries if the introduction of endoscopic screening to communities is to be realized.

The burden of gastric cancer remains real and this cannot be ignored in Eastern Asian countries. To determine the best available method for gastric cancer screening, evaluation of its effectiveness is a must. Endoscopic screening for gastric cancer has shown promising results, and thus deserves further comprehensive evaluation to reliably confirm its effectiveness and how its optimal use can be strategically promoted.

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