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Thank you very much for your kind introduction. It's a great honor for me to speak in this wonderful symposium, especially just after professor Tanaka.

Outcome after endoscopic resection of EGC is usually presented by the indication groups, such as conventional indication, expanded indication and beyond expanded indication. However, it is controversial whether EGCs with undifferentiated type histology should be part of expanded indication.

In our institution, at Samsung Medical Center, we usually recommend surgery for EGCs with undifferentiated type histology, so most cases have differentiated type histology. After endoscopic resection, the results can be either curative resection or non-curative resection based on the pathological findings.

Outcome after curative resection of EGC has been established by two types of evidences; the long-term follow-up data and the comparison with surgery such as propensity score matched studies.

I'll start with our long-term follow-up outcome after curative resection.

For about 9 years, there were almost nineteen differentiated-type EGCs.

After exclusion of patients with surgery, residual or synchronous lesions, and short follow-up, about thirteen hundred of patients (1,306 patients with 1,341 EGCs) were finally included in the analysis of long-term outcomes after curative ESD.

Among them, 79.0% (1,032/1,306) were absolute indication cases, and 21% (274/1,306) were expanded indication cases.

The median follow-up period was 61 months. Excluding metachronous recurrences, we experienced only one case (0.08%) of local recurrence, and 2 cases (0.15%) with extragastric recurrences. The 5-year survival rate was 97.3% for the absolute indication group and 96.4% for the expanded indication group.

There were two cases of extragastric recurrences. The top case belonged to the absolute indication group, and the lower case belonged to the expanded indication group.

The red dot is the absolute indication group and the green solid line is the expanded indication group. There was no statistical difference between them.

Next topic is another kind of evidence – comparison with surgery.

To reduce the effect of selection bias, we performed a propensity score-matching

analysis between the two groups.

In the propensity score matched cases, about 60 percent were absolute indication cases.

The rate of R0 resection was 82% in the endoscopic resection group

This is the overall survival of the two groups in the all sample analysis and the propensity matched analysis. In the all sample analysis, the survival of surgery patients looks like a little bit better. However, in the propensity matched samples, the two survival curves are almost the same.

Because of the metachronous recurrences, disease free survival and recurrence free survival is better in the surgery group. However, there was no difference in the disease specific survival.

Based on these two types of evidences, I can say that the long-term outcome after curative endoscopic resection of early gastric cancer has been established. The remaining question is the long-term outcome after non-curative endoscopic resection.

So the next topic is non-curative resection.

Standard treatment for non-curative resection is surgery, but it's not clear whether the surgery is always required. First, the risk of lymph node metastasis is less than 10%. Second, the risk of surgery is quite high due to old age and other medical conditions.

We performed a retrospective study for more than two thousand cases, which were endoscopically resected at our institution.

There are two subgroups in non-curative resection. One is lateral margin positive only group, and the other is cases with risk of lymph node metastasis. Lateral margin positive cases were excluded in this study, because most of them are treated by additional endoscopy. In cases with risk of lymph node metastasis, 70% were operated, and 30% were observed without surgery. The main reason of observation is patient's refusal to surgery.

When we compared the two groups, patients in the observation group were older and have more cardiovascular diseases, and have higher Charlson comorbidity score...

And have bigger tumor. The rate of lymphovascular invasion was higher in the surgery group.

In the surgery group, 11 have lymph node metastasis, which means 5.7%. Patients with lymph node metastasis were older. To our surprise, the rate of lymph node

metastasis was not different by the tumor size, depth of invasion, histological differentiation, and lymphovascular invasion in the endoscopically resected specimen. So, basically we found no predictor of lymph node metastasis in this analysis.

I'll show you some representative pictures of 11 cases with lymph node metastasis in additional surgery after ESD for EGC. As you can see, some cases were actually not indicated for ESD in terms of absolute indication or expanded indication. So, if we strictly adhere to the indications, the rate of lymph node metastasis must be less than our results.

Rate of progression into the advanced cancers were different between 2 groups. Five advanced cancers were found in the observation group, and only one metastatic disease was found in the surgery group. This difference - 6.3% versus 0.5% - was statistically significant.

This is the summary of six cases with documented progression of gastric cancer. As you can see, all cases have submucosal invasion of more than 200 micrometer and all have evidence of endolymphatic invasion.

This is the initial endoscopy of the six cases. Some are elevated, some are depressed, and some are flat. There is no uniform characteristics.

The next two slides are the main findings of this study. We compared the overall

survival by some factors. As you can see in the figures, age less than 65, low Charlson score...

... and additional surgery were related with longer survival.

In the Cox proportional hazard model, additional surgery was the only significant independent factor related to the longer survival. So surgery was beneficial for patients with non-curative resection after ESD.

In brief summary, progression to advanced stage in non-curative resection without surgery is at least 6.3% within 40 months. In this setting, additional surgery confers a survival benefit and should be positively considered.

However, the 5 year survival rate is about 80% without surgery in non-curative resection patients with risk of lymph node metastasis. So the next question is whether surgery is always required after non-curative resection with risk of lymph node metastasis?

I will briefly discuss selection of patients for surgery

Researchers in Japan tried to answer this question in a multicenter retrospective case collection study. Among more 15 thousands of patients who underwent ESD at 19 institutions in Japan between 2000 and 2011, about 2 thousands patients

not meeting the curative criteria were analyzed. Patients were divided into radical surgery group and no additional treatment group. Surgery group was 54%.

This is the comparison of the two groups. First of all, the invasion was deeper in the surgery group. SM2 invasion was 63%. Similarly, the rate of lymphatic invasion, vascular invasion, vertical margin involvement was higher in the surgery group.

This is the overall survival. The 3-year overall survival rate was 96% in the surgery group, and 84% in the follow-up group. The difference was statistically significant.

However, the disease-specific survival was not different between the two groups.

This is the risk factors for gastric cancer recurrence in the follow-up group. In multivariate analysis lymphatic invasion was the most important factor for gastric cancer recurrence.

They concluded that although radical surgical resection is currently indicated for these patients, we suggest that follow-up with no additional treatment after ESD may be an acceptable option for patients at low risk. Consequently, further risk stratification is needed for appropriate individualized treatment strategies.

In the previous KINGCA conference, the Korean international gastric cancer society conference, professor Gotoda showed their scoring system for predicting

gastric cancer recurrence after non-curative endoscopic resection of early gastric cancer. They calculated the odds ratio of recurrence and suggested 1 to 3 points for each risk factors. As you can see in the slide, lymphatic invasion was considered three times riskier than other factors.

Using the eCura system, the rate of lymph node metastasis is 2% in the low risk group, and 22% in the high risk group. This kind of data can give valuable information for selecting patients for surgery in cases with non-curative resection.

Ladies and gentlemen, I'd like to conclude my presentation by saying that until now, the standard treatment after non-curative resection is surgery. Because the 5 year survival without surgery is about 80%, careful observation may be an option in patients with operational risk factors. Prediction model like eCura system seems to be promising.

Thank you for your attention.