

## Post-polypectomy surveillance: the present and the future

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An appropriate post-polypectomy surveillance program requires the effectiveness of reducing colorectal cancer and safety. In addition, the post-polypectomy surveillance program should consider the burden of limited medical resource capacity, cost-effectiveness, and patient adherence. In this sense, a risk-stratified surveillance program based on baseline colonoscopy results is ideal. Major international guidelines for post-polypectomy surveillance, such as those from the European Union and the United States, have recommended risk-stratified surveillance programs. Both guidelines have recently been updated to better differentiate between high- and low-risk individuals. In both updated guidelines, more individuals have been downgraded to lower-risk groups that require less frequent or no surveillance. Furthermore, increased attention has been paid to the surveillance of patients who undergo serrated polyp removal. Previous guidelines in Japan did not clearly outline the risk stratification in post-polypectomy surveillance. However, the new colonoscopy screening and surveillance guidelines presented by the Japan Gastroenterological Endoscopy Society include a risk-stratified post-polypectomy surveillance program. Further discussion and analysis of unresolved issues in this field, such as the optimal follow-up after the first surveillance, the upper age limit for surveillance, and the ideal method for improving adherence to surveillance guidelines, are warranted.

**Keywords:** Colonoscopy; Colorectal cancer; Colorectal polyp; Polypectomy; Surveillance

### INTRODUCTION

Colorectal cancer (CRC) screening and polypectomy can effectively reduce the mortality and incidence of CRC.<sup>1</sup> To maximize the effectiveness, appropriate follow-up is necessary. Significant efforts have been made in many regions to establish optimal post-polypectomy surveillance programs, and several relevant guidelines have been published and updated. In this paper,

we review major international guidelines (guidelines from the United States [US] and the European Union [EU]) as well as Japanese guidelines for post-polypectomy surveillance and discuss what has changed thus far and what needs to be resolved in the future.

### RISK STRATIFICATION IN POST-POLYPECTOMY SURVEILLANCE

Effectiveness and harm are the most important factors to be considered when establishing optimal post-polypectomy surveillance programs. Appropriate utilization of limited medical resources and budgets should be considered because the target population of post-polypectomy surveillance programs is too large.

Regarding the effectiveness of post-polypectomy colonoscopy surveillance, several studies have been conducted to examine

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the incidence and mortality of post-polypectomy CRC in individuals who underwent colonoscopy surveillance and those who did not. A retrospective multicenter cohort study was conducted in the United Kingdom to assess the incidence of post-polypectomy CRC in over 10,000 intermediate-risk individuals with three or four small adenomas <10 mm in size or one or two adenomas, at least one of which was ≥10 mm in size, for a median follow-up period of 7.9 years.<sup>2</sup> The study clarified the effectiveness of colonoscopy surveillance by showing that one or two surveillance visits were associated with a significant reduction in the incidence of post-polypectomy CRC. However, assessment with further risk stratification demonstrated that a significant reduction in the incidence of post-polypectomy CRC was only observed in a high-risk group of individuals who had undergone suboptimal baseline colonoscopy or those with adenomas ≥20 mm in size, showing high-grade dysplasia, and/or located in the proximal colon at baseline colonoscopy. The incidence of post-polypectomy CRC did not decrease significantly with colonoscopy surveillance in the low-risk group without the aforementioned factors. These findings indicate the necessity for risk stratification in post-polypectomy surveillance to maximize its effectiveness.

The consideration of harm related to colonoscopy further emphasizes the importance of risk stratification. In a retrospective cohort study conducted in the US assessing the adverse effects of surveillance colonoscopy in 27,628 individuals aged ≥50 years, hospitalization within 30 days was found in 711 patients (2.6%), including 19 with colonoscopy-related perforation, following surveillance colonoscopy.<sup>3</sup> The risk of hospitalization was shown to be higher in elderly patients aged ≥75 years and in those with comorbidities than in younger patients and those without comorbidities. Repeating surveillance colonoscopy without considering the balance between its benefits and harms should be avoided, particularly for populations with a low risk of post-polypectomy CRC.

Risk stratification in post-polypectomy surveillance is also essential from the perspective of cost-effectiveness and burden on medical resources, as it facilitates efficient utilization of limited medical resources and budgets according to the risk of post-polypectomy CRC. Recently, our group performed a cost-effectiveness analysis of post-polypectomy surveillance using a simulation model.<sup>4</sup> We compared the cost-effectiveness of non-risk stratified surveillance programs with fixed surveillance colonoscopy intervals and risk-stratified post-polypectomy surveillance programs wherein the surveil-

lance colonoscopy intervals are determined according to the results of baseline colonoscopy. We found that risk-stratified surveillance programs could be more favorable in terms of cost-effectiveness.

## UNITED STATES AND EUROPEAN UNION GUIDELINES FOR POST-POLYPECTOMY SURVEILLANCE

The major international guidelines for post-polypectomy surveillance, such as the US guidelines (the US Multi-Society Task Force on CRC [USMSTF] guidelines) and the EU guidelines (the European Society of Gastrointestinal Endoscopy [ESGE] guidelines), have recommended risk-stratified surveillance programs according to the risk of post-polypectomy CRC.<sup>5-9</sup> Recently, both the USMSTF and ESGE guidelines have been updated for better differentiation of high- and low-risk (Tables 1, 2). Guidelines have been updated in response to the increased detection of non-advanced colorectal polyps during colonoscopy and the increasing awareness of serrated lesions, particularly sessile serrated lesions (SSLs).<sup>10-12</sup>

In the updated USMSTF and ESGE guidelines, more individuals have been downgraded to lower-risk groups that require less frequent or no surveillance. Increasing evidence suggests that individuals with one or two non-advanced adenomas <10 mm in size have a very low risk of post-polypectomy CRC. This risk is reportedly as low as that in a population of people without adenomas.<sup>7,9,13-16</sup> In light of this evidence, the updated USMSTF guidelines recommend surveillance colonoscopy 7 to 10 years after polypectomy for these very low-risk individuals, and return to screening is recommended for them in the updated ESGE guidelines. Furthermore, several studies have indicated that individuals with three or four non-advanced adenomas <10 mm in size have a low risk of post-polypectomy CRC, and less intensive surveillance is recommended for this population in the updated USMSTF and ESGE guidelines compared to previous versions of the guidelines.<sup>7,9</sup>

Regarding post-polypectomy surveillance for individuals with serrated lesions, no or few recommendations have been described in the previous USMSTF and ESGE guidelines.<sup>5,8</sup> In contrast, detailed and informative recommendations are proposed in the updated guidelines.<sup>6,9</sup> However, the evidence supporting these recommendations is currently insufficient. Although various findings regarding serrated lesions and SSLs have been reported, several basic issues remain unclear.<sup>11,17</sup> For

**Table 1.** Updates in post-polypectomy surveillance guidelines from the United States Multi-Society Task Force on colorectal cancer

Baseline colonoscopy findings	2006	2012	2020
1–2 adenomas <10 mm	CS 5–10 years later	CS 5–10 years later	CS 7–10 years later
3–4 adenomas <10 mm	CS 3 years later	CS 3 years later	CS 3–5 years later
5–10 adenomas <10 mm	CS 3 years later	CS 3 years later	CS 3 years later
Adenoma ≥10 mm	CS 3 years later	CS 3 years later	CS 3 years later
Adenoma with tubulovillous or villous histology	CS 3 years later	CS 3 years later	CS 3 years later
Adenoma with HGD	CS 3 years later	CS 3 years later	CS 3 years later
>10 adenomas	CS <3 years later	CS <3 years later	CS 1 year later
≤20 HPs in rectum/sigmoid colon <10 mm	CS 10 years later	CS 10 years later	CS 10 years later
≤20 HPs proximal to sigmoid colon <10 mm	-	-	CS 10 years later
1–2 SSPs <10 mm	-	CS 5 years later	CS 5–10 years later
3–4 SSPs <10 mm	-	CS 5 years later	CS 3–5 years later
5–10 SSPs <10 mm	-	CS 5 years later	CS 3 years later
SSP ≥10 mm	-	CS 3 years later	CS 3 years later
SSP with dysplasia	-	CS 3 years later	CS 3 years later
HP ≥10 mm	-	-	CS 3–5 years later
TSA	-	CS 3 years later	CS 3 years later

CS, colonoscopy; HGD, high-grade dysplasia; HP, hyperplastic polyp; SSP, sessile serrated polyp; TSA, traditional serrated adenoma.

**Table 2.** Updates in post-polypectomy surveillance guidelines from the European Society of Gastrointestinal Endoscopy

Baseline colonoscopy findings	2013	2020
1–2 adenomas <10 mm	Return to screening (or CS 10 years later)	Return to screening (or CS 10 years later)
3–4 adenomas <10 mm	CS 3 years later	Return to screening (or CS 10 years later)
5–10 adenomas <10 mm	CS 3 years later	CS 3 years later
Adenoma ≥10 mm	CS 3 years later	CS 3 years later
Adenoma with villous histology	CS 3 years later	Not necessary to consider villous components
Adenoma with HGD	CS 3 years later	CS 3 years later
>10 adenomas	Genetic counseling	Genetic counseling
Serrated polyp <10 mm without dysplasia	-	Return to screening (or CS 10 years after)
Serrated polyp ≥10 mm	-	CS 3 years later
Serrated polyp with dysplasia	-	CS 3 years later

CS, colonoscopy; HGD, high-grade dysplasia.

instance, the true prevalence of these lesions is not fully understood because of the difficulties in detecting and diagnosing lesions using endoscopy. In fact, there are considerable discrepancies in the detection rates reported in previous studies.<sup>11,17</sup> Considering that the studies that showed high detection rates included those conducted using chromoendoscopy (indigo carmine spray), the lesions may have been easily overlooked in many cases. Further research is required to elucidate the true prevalence and clinical significance of serrated lesions and establish optimal surveillance programs for individuals with these lesions.

Comparing the updated USMSTF and ESGE guidelines

shows that recommendations regarding the management of adenomas with villous components differ between the guidelines.<sup>7,9</sup> Unlike the USMSTF guidelines, the presence of villous components is not considered in the updated ESGE guidelines when making decisions regarding post-polypectomy surveillance owing to the recent findings on the negligible influence of villous histology on the long-term risk for CRC.<sup>7,9</sup> The possibility of inter-observer variability among pathologists in the histological assessment of villous components is also a concern.<sup>18</sup> Further discussion should be needed to determine how to deal with lesions with villous components based on appropriate histological evaluations.

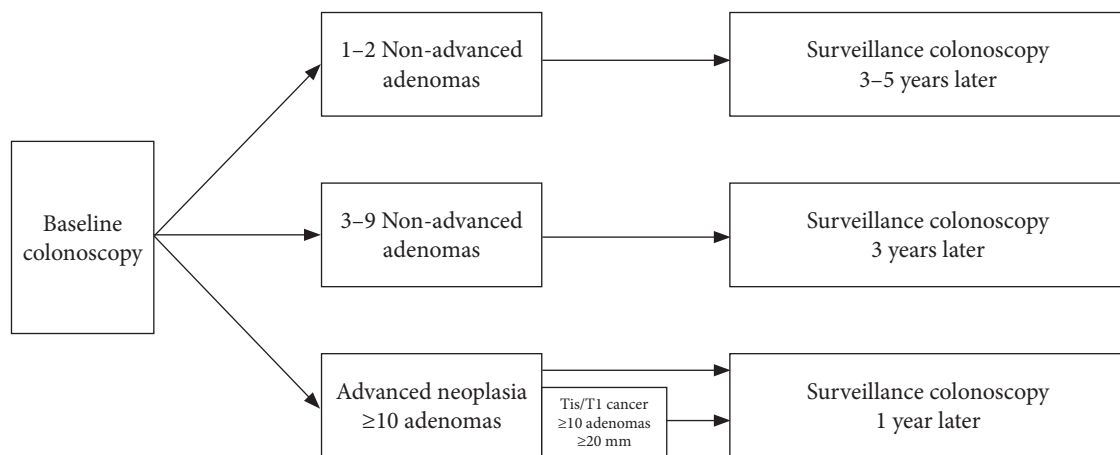
## JAPANESE GUIDELINES FOR POST-POLYPECTOMY SURVEILLANCE

The importance of post-polypectomy surveillance has been recognized in Japan as well as in the US, EU, and other countries. The Japan Polyp Study, which commenced in 2003, is an important clinical trial on post-polypectomy surveillance in Japan.<sup>19</sup> It is a large-scale prospective, multicenter, randomized, controlled trial that includes 11 Japanese institutions. The study assessed the incidence of advanced colorectal neoplasia following two baseline colonoscopies in two groups: a two-exam group wherein surveillance colonoscopy was performed at one and three years and a one-exam group in which surveillance colonoscopy was performed at three years. The incidence of advanced colorectal neoplasia in both groups was very low (1.7% vs. 2.1%), and the non-inferiority of the one-exam (at three years) group compared to the two-exam (at one and three years) group was clearly proven. Based on these findings, it can be concluded that after high-quality baseline colonoscopy, the surveillance interval can be set at a minimum of three years instead of one year. Furthermore, the low incidence of advanced colorectal neoplasia observed in both groups suggests that longer surveillance intervals are possible, particularly in low-risk populations. The Japan Polyp Study is currently ongoing with long-term follow-up, and more evidence is expected from this study in the future.

Until recently, there were no clear recommendations on risk stratification in post-polypectomy surveillance in Japan. Evidence-based clinical practice guidelines for the management of

colorectal polyps from the Japanese Society of Gastroenterology proposed that follow-up colonoscopy should be performed within 3 years after polypectomy.<sup>20</sup> However, the importance of risk stratification in post-polypectomy surveillance has gained more recognition in Japan. In 2020, the new guidelines from the Japan Gastroenterological Endoscopy Society (JGES), “Colonoscopy screening and surveillance guidelines,” have proposed risk-stratified surveillance programs.<sup>21</sup> The guidelines comprise eight background knowledge statements and 20 clinical question statements that include six clinical questions related to follow-up and surveillance. Figure 1 shows the risk-stratified surveillance programs for populations with adenomatous polyps, which are proposed in the guidelines for preventing mortality from CRC, the development of invasive cancer, and the preservation of the intestinal tract.<sup>21</sup> Surveillance colonoscopy performed 3 to 5 years and 3 years after polypectomy was proposed for individuals with 1 to 2 non-advanced adenomas <10 mm in size and those with 3 to 9 non-advanced adenomas <10 mm in size, respectively. The guidelines propose that patients with advanced neoplasia or ≥10 adenomas removed during baseline colonoscopy should undergo surveillance colonoscopy 1 to 3 years after polypectomy. Particularly, patients with Tis and T1 cancers, ≥10 adenomas, or adenomas ≥20 mm in size are considered to have a high risk for post-polypectomy CRC, and a one-year surveillance colonoscopy interval is proposed for them.

The surveillance intervals proposed for low-risk populations in the new JGES guidelines are shorter than those in other international guidelines such as the USMSTF and ESGE



**Fig. 1.** Proposal of risk-stratified post-polypectomy surveillance for individuals with adenomatous polyps in the new guidelines from the Japan Gastroenterological Endoscopy Society. Modified from Saito et al. *Dig Endosc* 2021;33:486–519.<sup>21</sup>

guidelines.<sup>7,9,21</sup> There are several factors and reasons behind this difference. First, the new JGES guidelines aim to prevent the development of invasive cancer and the need for colorectal surgery, as well as mortality from CRC. Second, neoplastic lesions that may be easily overlooked but can advance to invasive cancer within a short period, such as laterally spreading tumor non-granular type (LST-NG) and *de novo* cancer, are considered in the JGES guidelines. The Japan Polyp Study has shown that the risk of post-polypectomy advanced colorectal neoplasia is higher among individuals with LST-NG at baseline colonoscopy than in those without LST-NG.<sup>19</sup> Third, the current practice in Japan regarding post-polypectomy surveillance should be understood. According to a nationwide questionnaire survey of JGES board-certified institutions, a short surveillance colonoscopy interval is generally preferred in Japan. The survey showed that even after polypectomy of 1 to 2 non-advanced adenomas, over 50% and over 95% of the institutions selected one-year and within three-year intervals for surveillance colonoscopy, respectively.<sup>22</sup> Thus, it is difficult to propose long surveillance intervals in Japan at present. It is believed that the five-year colonoscopy interval for a low-risk population proposed in the new JGES guidelines is groundbreaking.

## ASPECTS OF POST-POLYPECTOMY SURVEILLANCE THAT REQUIRE FURTHER DISCUSSION

Several issues regarding post-polypectomy surveillance remain unresolved and require further assessment and discussion. As previously mentioned, optimal surveillance for individuals with serrated lesions needs to be clarified further. Follow-up after the first surveillance, the upper age limit for post-polypectomy surveillance, and surveillance for unresected diminutive benign adenomas also require further investigation.<sup>23</sup> The low adherence to post-polypectomy surveillance guidelines remains a serious problem. A recent systematic review and meta-analysis showed that global adherence to guidelines was low and that over 50% of individuals underwent repeat colonoscopies either too early or late.<sup>24</sup> Even if the guidelines are excellent, they cannot be completely useful if adherence to them is low. Therefore, improving the low global rate of adherence to guidelines is a top priority in this field.

Colonoscopy quality is a vital factor in post-polypectomy

surveillance. High-quality baseline colonoscopy is an essential prerequisite for optimal post-polypectomy surveillance. Several factors, including the adenoma detection rate (ADR), are regarded as colonoscopy quality measurements, and performance targets are set for them.<sup>25,26</sup> Despite a large amount of accumulated evidence, high-quality colonoscopy has not yet been clearly defined. Therefore, further assessments and elucidation of the features of high-quality colonoscopy are necessary. Even with regard to the target ADR, reconsideration may be necessary as adenomas are being increasingly detected during screening colonoscopy.<sup>10,27</sup> With further development of endoscopy technology, including image-enhanced endoscopy and artificial intelligence, we may aim at a higher ADR.<sup>21,28</sup> Monitoring and feedback are believed to be useful to ensure that the quality of colonoscopy is high.<sup>29</sup> Thus, a reliable monitoring and database system is necessary. The JGES has initiated the Japan Endoscopy Database Project in Japan, aiming to build a large-scale nationwide endoscopy database.<sup>21,30</sup>

## CONCLUSIONS

In this paper, we reviewed the USMSTF, ESGE, and JGES guidelines for post-polypectomy surveillance. The importance of risk stratification in post-polypectomy surveillance has been recognized in many regions, and efforts have been made to establish optimal risk-stratified post-polypectomy surveillance programs for better differentiation between high- and low-risk individuals. Nevertheless, several issues, including low adherence to guidelines, remain unresolved; thus, further improvement in this regard is warranted.

## Conflicts of Interest

The authors have no potential conflicts of interest.

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## Author Contributions

Conceptualization: MS, TM, KH, YS; Writing-original draft: MS; Writing-review & editing: MS, TM, KH, YS. All authors have contributed to the critical revision of the article for important intellectual content and approved the final submitted draft.

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