Accepted Manuscript

Submission Date: 2023-10-15
Accepted Date: 2024-02-16
Accepted Manuscript online: 2024-02-20

Endoscopy

Prevalence and predictive factors of colorectal sessile serrated lesions in younger individuals

Jen-Hao Yeh, Chih-Wen Lin, Po-Jen Hsiao, Daw-Shyong Perng, Jen-Chieh Chen, Kuo-Tung Hung, Chia-Chang Hsu, Chia-Chi Chen, Yu-Peng Liu, Yi-Chia Lee, Jaw-Yuan Wang.

Affiliations below.

DOI: 10.1055/a-2272-1911

Please cite this article as: Yeh J-H, Lin C-W, Hsiao P-J et al. Prevalence and predictive factors of colorectal sessile serrated lesions in younger individuals. Endoscopy 2024. doi: 10.1055/a-2272-1911

Conflict of Interest: The authors declare that they have no conflict of interest.

This study was supported by National Science and Technology Council (http://dx.doi.org/10.13039/501100020950), MOST 111-2314-B-037-070-MY3,NSTC 112-2314-B-037-050-MY3,NSTC 112-2314-B-037-090, Ministry of Health and Welfare (http://dx.doi.org/10.13039/501100003625), 12D1-IVMOHW02, Kaohsiung Medical University (http://dx.doi.org/10.13039/501100004694), KMU-TC112A04,KMUH-SH11207,KMUH112-2M27,KMUH112-2M28,KMUH112-2M29,KMUH112-2R37,KMUH112-2R38,KMUH112-2R39, E-Da Hospital (http://dx.doi.org/10.13039/501100004738), EDAHS112014,EDAHS112029,EDDHP112001

Abstract:
Introduction
Sessile serrated lesions (SSLs) are obscured lesions predominantly at right sided colon and associated with interval colorectal cancer. However, the prevalence and risk factors among younger individuals remain unclear.

Methods
This retrospective study enrolled individuals who underwent index colonoscopy. The primary outcomes were SSL prevalence between younger (<50 years) and older (≥50 years) groups, whereas the secondary outcomes included clinically significant serrated polyps (CSSPs). Multivariable logistic regression was employed to identify predictors.

Results
Of the 9854 eligible individuals, 4712 (47.8%) were categorized into the younger age group. Individuals in the younger age group exhibited a lower prevalence of adenomas (22.6% vs. 46.2%, P < 0.001) and right-sided adenomas (11.2% vs. 27.2%, P < 0.001) compared with their older counterparts. However, both groups exhibited a similar prevalence of SSLs (7.2% vs. 6.5%, P = 0.157) and CSSP (10.3% vs. 10.3%, P = 0.956). Multivariable analysis results revealed that age = 40–49 years (odds ratio [OR] = 1.81, 95% confidence interval [CI] = 1.01–3.23), longer withdrawal time (OR = 1.18, 95% CI = 1.15 – 1.21 per minute increment), and endoscopist performance (OR = 3.35, 95% CI = 2.44 – 4.58) were independent predictors of SSL detection in the younger age group. No significant correlation was observed between adenoma and SSL detection rates among endoscopists.

Conclusion
SSLs are not uncommon among younger individuals. Moreover, diligent effort and expertise are of paramount importance in SSL detection. Future studies should explore the clinical significance of SSLs in younger age individuals.

Corresponding Author:
Prof. Jaw-Yuan Wang, Kaohsiung Medical University Hospital, Department of Surgery, Kaohsiung, Taiwan, jawyuanwang@gmail.com

Affiliations:
Jen-Hao Yeh, Kaohsiung Medical University, Graduate Institute of Clinical Medicine, Kaohsiung , Taiwan
Jen-Hao Yeh, E-Da DaChang Hospital, I-Shou University, Department of Internal Medicine, Kaohsiung, Taiwan
Chih-Wen Lin, E-Da Hospital/I-Shou University, Department of Internal Medicine, Kaohsiung, Taiwan
[...]
Jaw-Yuan Wang, Kaohsiung Medical University Hospital, Department of Surgery, Kaohsiung, Taiwan

Thieme

Prevalence and predictive factors of colorectal sessile serrated lesions in younger individuals

Jen-Hao Yeh, MD[1,2], Chih-Wen Lin, MD, PhD[3], Po-Jen Hsiao, MD[2], Daw-Shyong Perng, MD[3], Jen-Chieh Chen, MD[4], Kuo-Tung Hung, MD[2], Chia-Chang Hsu, MD[2,4], Chia-Chi Chen, MD[5], Yu-Peng Liu, PhD[1,6], Yi-Chia Lee, MD, PhD[7] and Jaw-Yuan Wang, MD, PhD[1, 8-11]

[1]Graduate Institute of Clinical Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan.

[2]Division of Gastroenterology and Hepatology, Department of Internal Medicine, E-Da DaChang Hospital, I-Shou University, Kaohsiung, Taiwan

[3]Division of Gastroenterology and Hepatology, Department of Internal Medicine, E-Da Hospital, I-Shou University, Kaohsiung, Taiwan

[4]Department of Health examination, E-Da Hospital, I-Shou University, Kaohsiung, Taiwan

[5]Department of Pathology, E-Da Hospital, I-Shou University, Kaohsiung, Taiwan

[6]Research Center for Environmental Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan.

[7]Division of Gastroenterology and Hepatology, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan

[8]Division of Colorectal Surgery, Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

[9]Department of Surgery, Faculty of Medicine, College of Medicine, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

[10]Center for Cancer Research, Kaohsiung Medical University, Kaohsiung, Taiwan

[11]Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

Corresponding author:

Prof. Jaw-Yuan Wang, M.D., Ph.D., Division of Colorectal Surgery, Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung Medical University, No. 100 Tzyou 1st Road, Kaohsiung 807, Taiwan

Tel: +886-7-3122805
Fax: +886-7-3114679
E-mail: cy614112@ms14.hinet.net; jawyuanwang@gmail.com

Financial support: This study was supported by the EDDHP112001, EDAHS112014, and EDAHS112029 project of E-Da Hospital granted to Dr. Jen-Hao Yeh, and partially supported through funding from the National Science and Technology Council (MOST 111-2314-B-037-070-MY3, NSTC 112-2314-B-037-090, NSTC 112-2314-B-037-050-MY3) and the Ministry of Health and Welfare (12D1-IVMOHW02) and funded by the health and welfare surcharge of on tobacco products, and the Kaohsiung Medical University Hospital (KMUH112-2R37, KMUH112-2R38, KMUH112-2R39, KMUH112-2M27, KMUH112-2M28, KMUH112-2M29, KMUH-SH11207) and Kaohsiung Medical University Research Center Grant (KMU-TC112A04). In addition, this study was supported by the Grant of Taiwan Precision Medicine Initiative and Taiwan Biobank, Academia Sinica, Taiwan, R.O.C.

Conflict of interest: The authors declare no conflict of interests.

Author contribution:

Conceptualization, Jen-Hao Yeh, Yi-Chia Lee, and Jaw-Yuan Wang; **Methodology**, Jen-Hao Yeh, Yi-Chia Lee and Yu-Peng Liu; **Patient inclusion**: Jen-Hao Yeh, Chih-Wen Lin, Po-Jen Hsiao, Daw-Shyong Perng, Kuo-Tung Hung, Chia-Chang Hsu and Jen-Chieh Chen; **Pathological consultation and analysis**: Chia-Chi Chen; **Formal analysis**, Jen-Hao Yeh and Chih-Wen Lin; **Data curation**, Po-Jen Hsiao and Kuo-Tung Hung; **Investigation and data review**, Daw-Shyong Perng, Chia-Chang Hsu, and Jen-Chieh Chen; **Project administration**, Jen-Hao Yeh; **Funding acquisition**, Yi-Chia Lee and Jaw-Yuan Wang; **Writing—Original draft preparation**, Jen-Hao Yeh and Chia-Chi Chen; **Writing—review and editing**, Jaw-Yuan Wang, Yu-Peng Liu and Yi-Chia Lee; **Supervision**, Jaw-Yuan Wang. All authors have read and agreed to the published version of the manuscript.

Abstract

Introduction

Sessile serrated lesions (SSLs) are obscured lesions predominantly at right sided colon and associated with interval colorectal cancer. However, the prevalence and risk factors among younger individuals remain unclear.

Methods

This retrospective study enrolled individuals who underwent index colonoscopy. The primary outcomes were SSL prevalence between younger (<50 years) and older (≥50 years) groups, whereas the secondary outcomes included clinically significant serrated polyps (CSSPs). Multivariable logistic regression was employed to identify predictors.

Results

Of the 9854 eligible individuals, 4712 (47.8%) were categorized into the younger age group. Individuals in the younger age group exhibited a lower prevalence of adenomas (22.6% vs. 46.2%, $P < 0.001$) and right-sided adenomas (11.2% vs. 27.2%, $P < 0.001$) compared with their older counterparts. However, both groups exhibited a similar prevalence of SSLs (7.2% vs. 6.5%, $P = 0.157$) and CSSP (10.3% vs. 10.3%, $P = 0.956$). Multivariable analysis results revealed that age = 40–49 years (odds ratio [OR] = 1.81, 95% confidence interval [CI] = 1.01–3.23), longer withdrawal time (OR = 1.18, 95% CI = 1.15 – 1.21 per minute increment), and endoscopist performance (OR = 3.35, 95% CI = 2.44 – 4.58) were independent predictors of SSL detection in the younger age group. No significant correlation was observed between adenoma and SSL detection rates among endoscopists.

Conclusion

SSLs are not uncommon among younger individuals. Moreover, diligent effort and expertise are of paramount importance in SSL detection. Future studies should explore the clinical significance of SSLs in younger age individuals.

Keywords: colorectal polyps, colorectal neoplasm, early onset colorectal cancer, sessile serrated lesion, sessile serrated polyp/adenoma

Introduction

Colorectal cancer (CRC) has consistently ranked as a prominent malignancy in developed countries [1-3]. The majority of CRC cases originates from adenomatous polyps. However, nearly 10%–15% of CRC cases have a different origin, stemming from a distinct premalignant lesion known as sessile serrated lesions (SSLs) [4, 5]. Unlike conventional adenoma, SSLs tend to be located in the right-sided colon, exhibit a flat and obscure appearance, and are often covered by mucus (**Figure 1.**) [6-8]. These characteristics can pose challenges in their detection through current screening tools, potentially leading to screening failure [9-11]. Moreover, the under-detection of SSLs may be associated with the development of subsequent interval CRCs [12, 13].

The natural progression of SSLs is characterized by an indolent course, often taking more than 10–15 years to advance to cytological dysplasia and ultimately malignant transformation [14-16]. Progressive promoter hypermethylation, a prerequisite for SSL carcinogenesis, becomes more pronounced with advanced age [17]. Interestingly, research has indicated that serrated CRCs are relatively rare in younger patients [18, 19]. Nevertheless, whether this rarity in younger age groups is attributable to the infrequency of SSLs in this population or is a consequence of the gradual and indolent nature of the carcinogenesis process remains an unresolved question.

A systematic review indicated that the combined overall prevalence of SSLs was 4.6%, with only a modest increase with advanced age compared with conventional adenoma [6]. However, this review did not include individuals under the age of 50 due to the lack of available data. Until recently, most CRC screening programs and databases have focused on the "average-risk population," typically aged ≥50 years. Therefore, it is imperative to determine the true prevalence of SSLs and the proportion of cases with cytological dysplasia among younger individuals to gain a more comprehensive understanding of SSLs in early onset CRC. At present, only a few studies have explored the prevalence of SSLs in this younger age group [20, 21]. However, the results were mixed with other types of lesions such as hyperplastic polyp, and none of both studies have identified clinical risk factors in this population. Therefore, our study aims to address this research gap by examining the prevalence of SSLs and identifying potential clinical risk factors associated with SSLs in younger individuals. During 2018–2022, our institute achieved a noteworthy SSL detection rate of 7.1% through index colonoscopies, which is higher than that in historically pooled data [6] and meets the conventionally stipulated detection benchmark [22]. The present study aimed to explore the prevalence of SSLs and determine the potential clinical risk factors for SSLs in younger individuals.

Materials and Methods

Study design

This retrospective, single-center study analyzed colonoscopy records obtained from outpatient services and health checkup services at E-Da Dachang Hospital. The data were collected between June 2018 and June 2022. E-Da Dachang Hospital, established in 2016 in downtown Kaohsiung, served as the primary source of these records. The study protocol was approved by the institutional review board of our institute (No. EMRP111149).

The study included individuals aged ≥20 years who underwent a complete index colonoscopy. Individuals who visited outpatient services were mostly symptomatic, were eligible for screening colonoscopy, or had abnormal fecal/tumor marker test results. Additionally, asymptomatic individuals who underwent health checkups at their own expense or who adhered to national labor law requirements were included. The exclusion criteria were as follows: (1) instances of duplicated cases due to prior colonoscopy examinations, (2) cases with inadequate bowel preparation, (3) history of hospitalization or colonoscopy as part of an emergency room visit, (4) cases of unsuccessful cecal intubation or flexible sigmoidoscopy, and (5) suspicious or confirmed inflammatory bowel disease. Notably, individuals who had previously undergone colonoscopy at other hospitals, as confirmed by their electronic medical records or chart review, were also excluded. Eligible individuals were subsequently classified into two groups: a younger age group (20–49 years) and an older age group (>50 years).

Colonoscopy procedures and histological evaluation

All colonoscopies in this study were performed by experienced endoscopists who had conducted >500 colonoscopy procedures annually, with ≥300 diagnostic or therapeutic procedures. They used the EvisLucera CV-290 colonoscope (Olympus Medical Systems, Tokyo, Japan). They received bowel preparation regimens that included split-dose sodium phosphate, sodium picosulfate/magnesium citrate, or same-day polyethylene glycol solution. During the examinations, the decision to perform a biopsy, snare polypectomy, or endoscopic mucosal resection for colorectal neoplasms was made at the discretion of the endoscopist. In cases involving difficult-to-treat polyps, subsequent endoscopic or surgical resection was performed within 6 months following the index colonoscopy. The final histologic diagnosis was based on results from both the index colonoscopy and the subsequent analysis. However, polyps and lesions that were not removed within 6 months of the index colonoscopy were excluded from the analysis, regardless of the initial endoscopic diagnosis. Ten pathologists involved in the histological evaluation in the study period. All the lesions included in this study were confirmed through histologic evaluation by the on-duty pathologist, in our hospital.

Outcome assessment

The primary outcome of this study was SSL prevalence. The secondary outcomes were the prevalence of SSLs with cytological dysplasia, clinically significant serrated polyps (CSSPs), and the detection rate of right-sided hyperplastic polyps. CSSP is defined as the combination of (1) SSLs, (2) traditional serrated adenomas, and (3) any hyperplastic polyp ≥1cm in the left-sided colon or ≥0.5 cm in the right-sided colon [22]. Additional auxiliary outcomes included the prevalence of adenomas, advanced adenomas, and CRC. Advanced adenoma is characterized by polyps meeting one of the following criteria: (1) high-grade dysplasia, carcinoma in situ, or intramucosal carcinoma, (2) a size of ≥1 cm, or (3) containing >25% villous component. Right-sided colon refers to the cecum, ascending colon, and transverse colon. Various baseline and endoscopic characteristics, including age, sex, use of intravenous anesthesia, withdrawal time, bowel preparation status, and any family history of CRC, were recorded for predictive factor analysis. Adequate bowel preparation was defined as excellent or good based on the Aronchick scale [23]. The definitions of metabolic disease included obesity, metabolic syndrome, hypertension, diabetes mellitus and fatty liver disease were described in **Supplementary Appendix** according to our previous article [24].

Statistical analysis

In this study, continuous variables were compared using Student's *t* test and are presented as mean ± standard deviation. Categorical variables were compared using the chi-square test and are presented as frequency (percentage). $P < 0.05$ indicated statistical significance. To compare the primary outcomes, odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were calculated. All statistical analyses were conducted using SPSS version 22.0 (IBM, Armonk, NY, USA).

To evaluate the predictors of SSLs in the younger age group, we considered several variables, including age, sex, any family history of CRC, presence of symptoms (abdominal pain, bowel habit changes or hematochezia), the proportion of positive fecal immunochemical tests, the use of intravenous anesthesia, colonoscopy withdrawal time and the presence of relevant neoplasms. Significant variables in the univariable analyses were included in the multivariable binary logistic regression model by using the enter method. Subsequently, the significant variables were subjected to validation and sensitivity analysis by using data from the older age group. To further examine the potential correlation between variables, we employed a two-sided partial correlation analysis by using SPSS software.

Results

Study participants and baseline characteristics

In all, 14,181 records were initially retrieved from the database. A flowchart of the participant selection process is presented in **Figure 2**. Following the exclusion criteria were applied, a final cohort of 9,854 individuals (female, 51.5%) was eligible for the analysis. With this cohort, 4,712 and 5,142 individuals belonged to the younger and older age groups, respectively.

The baseline characteristics of each group are summarized in **Table 1**. The younger and older age groups had mean ages of 39.7 and 61.6 years, respectively. A larger proportion of individuals in the younger age group underwent colonoscopy as part of a health checkup compared with the older age group (47.6% vs. 24.3%, $P < 0.001$). Compared with those in the younger age group, a significantly higher proportion of individuals in the older age group had adenomas (22.6% vs. 46.2%, $P < 0.001$), advanced adenomas (4.0% vs. 14.2%, $P < 0.001$), and CRC (0.4% vs. 1.4%, $P < 0.001$). Significantly longer withdrawal time (7.5 ± 3.5 mins vs. 9.4 ± 5.3 mins, $P < 0.001$) and numbers of adenoma (0.3 ± 0.6 vs. 0.7 ± 1.0, $P < 0.001$) was also found in the older age group. However, the detection rate of SSLs was similar in both the groups (7.2% vs. 6.5%, $P = 0.157$). Furthermore, the older age group exhibited a nearly twofold higher occurrence of cytological dysplasia, although this difference did not reach statistical significance (2.6% vs. 5.1%, $P = 0.100$). Similarly, the prevalence of CSSPs was comparable between the two groups (10.3% vs. 10.3%, $P = 0.956$).

Clinical features between outpatient and health checkup cases in the younger age group

Nearly half (47.6%) of the younger individuals underwent colonoscopy as part of a health checkup service, and their clinical characteristics are further detailed in **Table 2**. Compared with those who underwent health check-ups, younger individuals who visited outpatient service were less likely to had intravenous anesthesia use (69.0% vs. 96.8%, $P < 0.001$) and positive fecal occult blood test (0.5% vs. 7.2%, $P < 0.001$). No significant differences in age and sex were observed between the two subgroups. Moreover, younger individuals who visited the outpatient service had lower risks of overall adenomas (20.7% vs. 24.6%, $P = 0.001$) and right-sided adenoma (8.8% vs. 13.8%, $P < 0.001$), but greater risks of advanced adenomas (4.7% vs. 3.2%, $P = 0.009$) and CRC (0.6% vs. 0.1%, $P = 0.005$). Nevertheless, the younger outpatients had a lower rate of SSLs (5.4% vs. 9.3%, $P < 0.001$), right-sided hyperplastic polyps (2.8% vs. 5.0%, $P < 0.001$), and CSSPs (7.8% vs. 13.1%, $P < 0.001$) and a slightly longer withdrawal time (7.7 ± 3.8 mins vs. 7.4 ± 3.0 mins, $P < 0.001$) compared with those who underwent health checkups. The proportion of SSLs with cytological dysplasia was similar in both the subgroups (3.8% vs. 1.9%, $P = 0.302$).

Correlation between adenoma and SSL detection rates among endoscopists

This study involved seven endoscopists (endoscopists A–G). Their adenoma detection rates ranged from 17.1% to 43.8%, whereas their SSL detection rates ranged from 2.0% to 11.0%. The corresponding data are presented in **Supplementary Figure 1**. Two endoscopists (endoscopists E and G) had the highest SSL detection rates (7.7% and 11.0%, respectively). These two endoscopists were responsible for conducting 90.7% of the health checkup colonoscopy examinations and 44.5% of outpatient colonoscopy examinations, which may explain the relative higher performance observed in the health check-up subgroup. Interestingly, our analysis did not reveal a significantly correlation between the prevalence of adenomas and SSL detection rate ($P = 0.083$).

Predictors of SSL detection in the younger age group

In our analysis, we investigated the association between the presence of SSLs during colonoscopy among younger individuals. The results of the univariable analysis for predefined clinical factors are presented in **Table 3**. Younger individuals with SSLs tended be older (41.6 ± 5.2 vs. 39.6 ± 6.4 years, $P < 0.001$), be male (55.1% vs. 48.0%, $P = 0.003$) and have longer withdrawal times (10.6 ± 4.3 min vs. 7.3 ± 3.3 min, $P < 0.001$). They were also more likely to be asymptomatic (72.7% vs. 56.7%, P

< 0.001) and receive colonoscopy during health checkups (61.0% vs. 46.5%, $P < 0.001$). Because the latter two variables seemed to be highly correlated, and the two higher performers were responsible for the majority of the health check-up exams, we finally took age, sex, withdrawal time and endoscopist performance into the multi-variable analysis.

In the multivariable analysis, we divided the individuals in the younger age group into three subgroups (20–29 years, 30–39 years, and 40–49 years) for finer-grained results on age. The benchmark of SSL detection rate was set at 7% to define high performers and average performers [22]. Consequently, binary logistic regression **(Table 4)** results revealed that increased age (40–49 years, OR = 1.81, 95% CI = 1.01 – 3.23, $P = 0.01$), longer withdrawal time (OR = 1.17, 95% CI = 1.14 – 1.20 per minute increment, $P < 0.001$), and endoscopist performance (high performers vs average performers, OR = 3.35, 95% CI = 2.44 – 4.58 per minute increment, $P < 0.001$) were independent predictors of SSLs among the younger individuals.

Sensitivity analysis and subgroup analysis

The effects of withdrawal time, endoscopist performance and age were further examined using the data from the older age group. Longer withdrawal time (OR = 1.07, 95% CI = 1.05 – 1.09 per minute increment, $P < 0.001$) and endoscopist performance (high performers, OR = 2.41, 95% CI = 1.89 – 3.07, $P < 0.001$) remained significant predictive factors for SSL detection in this group. However, individuals aged 50–59 years exhibited SSL detection rates similar to those aged 40–49 years (OR = 0.91, 95% CI = 0.75–1.11, $P = 0.914$). All other older age subgroups exhibited lower SSL detection rates, implying a potential peak at the age range of 40–49 years in this cohort (**Supplementary Table 1**). Age-based analysis suggested that although adenoma detection was strongly correlated with advanced age, the detection rates of SSLs, SSL with cytological dysplasia, and CSSPs exhibited flatter trends with age increment (**Supplementary Figure 2**). Notably, significant correlation was observed between SSLs and cytological dysplasia per 10-year age increment (partial correlation: 0.19, $P < 0.001$).

Finally, we analyzed the data of individuals had their SSLs detected in a health checkup; we did so to identify additional predictors of younger age SSLs (**Supplementary Table 2**). In this subgroup, younger individuals with SSLs tended to have a slightly higher mean age (41.4 ± 5.2 vs. 39.5 ± 6.4 years, $P < 0.001$). They were also more likely to be obese (24.5% vs. 17.7%, $P = 0.015$), have metabolic syndrome (16.8% vs. 11.9%, $P < 0.001$), and have diabetes mellitus (7.2% vs. 2.8%, $P < 0.001$). Additionally, current tobacco use (22.1% vs. 15.4%, $P = 0.011$) was more prevalent among individuals with SSLs, and they had longer colonoscopy withdrawal times (9.7 ± 3.5 vs. 7.1 ± 2.8 mins, $P < 0.001$). However, the multivariate logistic regression revealed that only colonoscopy withdrawal time was a significant factor (**Supplementary Table 3**).

Discussion

To date, the recommended starting age for CRC screening is now set at 45 years in response to the increasing incidence of early onset CRC, which occurs before the age of 50 [25, 26]. Although SSLs are less likely to be associated with early onset CRC, effective screening for SSLs may lead to further cancer prevention given its long indwelling time.

This study explored SSL prevalence among younger adults by using a cohort with a high detection rate. The findings highlight that SSL prevalence is not negligible among individuals aged <50 years. Moreover, by the age of 40, the prevalence becomes comparable to that observed in older individuals. The association of age and SSL for younger people have only been explored by few studies [20, 21]. Our findings were in line with these literatures that SSLs exhibit more stable prevalence with age compared to that of adenomas. However, several differences exist between and current and previous studies. The primary outcome in Kim et al. [21] was serrated lesions which was predominantly hyperplastic polyps. Hence, the SSL prevalence was quite low (0.5%) in their cohort. On the other hand, the design of Lall et al. [20] is more similar to our study, and the indifferent SSL detection rate among younger and older age people was concordant to our study. However, they did not exclude patients with prior colonoscopies. Since patients with prior lesions would be suggested for follow-up, the detection rate might be cofounded by metachronous lesions, and consequently affect the analysis results. Moreover, some technical issues such as withdrawal time and the variation in endoscopist expertise were less explored in the previous study. Lastly, cytological dysplasia, which is considered a critical step in SSL transformation, was not analyzed. While these two studies were important foundations to the current study, we look forward further validation studies for SSL of younger age people.

Since substantial proportion of SSLs may develop in younger adults. Effective detection and management of SSLs among younger individuals might be beneficial in preventing future serrated CRC. However, detecting and completely resecting SSLs may be challenging due to their obscured appearance and indistinct borders [8, 11, 27]. Although the SSL detection rate has been shown to be correlated with adenoma detection rates, endoscopists may considerably differ in their clinical performance [28, 29], as demonstrated in the present study. In the present study, no significant correlation was noted between adenoma detection and SSL detection, which may be attributed to the relatively small number of endoscopists involved, leading to statistically underpowered results. However, our findings revealed that longer withdrawal times were associated with higher SSL detection, which is consistent with the findings of prior studies [30, 31]. Moreover, endoscopist performance independent to withdrawal time was also highlighted in our study. Although the exact factors affect the detection performance remain to be investigated, the expertise may be attributed to recognition of lesion characteristics, examination technique, and the use of image enhanced endoscopy. Inspiringly, the ability may be improved by active training [32]. On the other hand, the assistance of attachment device and artificial intelligence may also aid in better detection of SSL [33, 34]. Overall, detecting SSLs requires considerable level of expertise and meticulous effort. Strategies to improve outcomes should be formulated.

This study is one of the few to explore the prevalence of SSLs in younger adults and has several strengths including a large cohort and a high detection rate. Additionally, we employed a strict definition of SSLs based on histological diagnosis, and considered CSSPs and right-sided hyperplastic polyps, which are highly correlated with SSLs in clinical practice. Moreover, the study population mainly consisted of relatively healthy individuals receiving index colonoscopy, which may reflect a scenario similar to ordinary screening practices. We also underwent meticulous analysis in order to reduce potential cofounding, such as discrepancy in endoscopist performance in subsets of cohorts.

Nevertheless, this study has some limitations. First, though we tried best to include index exams, individuals who received prior colonoscopies may not be reported. However, given the slow growth of SSLs, intervention bias may be considerably low for younger individuals, as indicated by the age-specific prevalence analysis. Second, some key factors such as smoking, obesity, and diabetes mellitus were only available for a subset of study participants that might lead to underpower for these factors. Diabetes mellitus has been reported as an well-known risk factor of CRC by mechanisms including enhanced DNA methylation, which is also an important carcinogenesis pathway of serrated CRC [35]. Thus, further analysis with a larger patient database in the future may provide more insights into these factors. Third, the withdrawal time in our study consisted of both observation and intervention. On the other hand, the association is even more prominent in cases which have withdrawal time ≤ 9-min (OR 1.85, 95% CI 1.68 – 2.04), suggesting minimal intervention bias. Fourth, we did not report the prevalence of serrated polyposis syndrome among younger age people. Lastly, the inter-observer variation among pathologists may not be completely ruled out. Future large-scale studies with expert pathologists are warranted to investigate the role of SSLs in early onset and late-onset CRC in the younger population.

In summary, our study demonstrated that SSLs are not uncommon in younger individuals, with a significant increase in prevalence starting at the age of 40. Longer withdrawal times and endoscopist expertise during colonoscopy appear to be associated with improved SSL detection. However, further research is required to assess the clinical significance of SSLs in younger age groups and its potential implications for future screening practices.

Figure legend

Figure 1. Appearance of a large sessile serrated lesion at hepatic flexure. The white light image showed a thick fold covered by mucus (A). Using narrow band image, there was cloudy surface pattern with lacy vessels (B). Chromoendoscopy with indigo-carmine spray disclosed the border of the whole lesion (C).

Figure 2. Flowchart of participant inclusion and exclusion

Supplementary Figure 1. Detection rates of adenomas and SSLs between the different endoscopists (A–G)

Supplementary Figure 2. Detection rates of adenomas, sessile serrated lesions (SSLs), SSLs with cytological dysplasia (SSLD), and clinically significant serrated polyps (CSSPs), by age

References

1. Arnold M, Sierra MS, Laversanne M et al. Global patterns and trends in colorectal cancer incidence and mortality. Gut 2017; 66: 683-691
2. Cardoso R, Guo F, Heisser T et al. Colorectal cancer incidence, mortality, and stage distribution in European countries in the colorectal cancer screening era: an international population-based study. The Lancet Oncology 2021; 22: 1002-1013
3. Wong MC, Huang J, Lok V et al. Differences in incidence and mortality trends of colorectal cancer worldwide based on sex, age, and anatomic location. Clinical Gastroenterology and Hepatology 2021; 19: 955-966. e961
4. Murcia O, Juárez M, Hernández-Illán E et al. Serrated colorectal cancer: Molecular classification, prognosis, and response to chemotherapy. World J Gastroenterol 2016; 22: 3516-3530. doi:10.3748/wjg.v22.i13.3516
5. Nakanishi Y, Diaz-Meco MT, Moscat J. Serrated colorectal cancer: the road less travelled? Trends in cancer 2019; 5: 742-754
6. Meester RG, van Herk MM, Lansdorp-Vogelaar I et al. Prevalence and clinical features of sessile serrated polyps: a systematic review. Gastroenterology 2020; 159: 105-118. e125
7. Murakami T, Kurosawa T, Fukushima H et al. Sessile serrated lesions: Clinicopathological characteristics, endoscopic diagnosis, and management. Digestive Endoscopy 2022; 34: 1096-1109
8. Nishizawa T, Yoshida S, Toyoshima A et al. Endoscopic diagnosis for colorectal sessile serrated lesions. World J Gastroenterol 2021; 27: 1321
9. Burnett-Hartman AN, Newcomb PA, Phipps AI et al. Colorectal endoscopy, advanced adenomas, and sessile serrated polyps: implications for proximal colon cancer. The American journal of gastroenterology 2012; 107: 1213-1219. doi:10.1038/ajg.2012.167
10. Chang L-C, Shun C-T, Hsu W-F et al. Fecal immunochemical test detects sessile serrated adenomas and polyps with a low level of sensitivity. Clinical Gastroenterology and Hepatology 2017; 15: 872-879. e871
11. Zorzi M, Senore C, Da Re F et al. Detection rate and predictive factors of sessile serrated polyps in an organised colorectal cancer screening programme with immunochemical faecal occult blood test: the EQuIPE study (Evaluating Quality Indicators of the Performance of Endoscopy). Gut 2017; 66: 1233-1240
12. Anderson JC, Hisey W, Mackenzie TA et al. Clinically significant serrated polyp detection rates and risk for postcolonoscopy colorectal cancer: data from the New Hampshire Colonoscopy Registry. Gastrointestinal endoscopy 2022; 96:

310-317

13. van Toledo DEFWM, Ijspeert JEG, Bossuyt PMM et al. Serrated polyp detection and risk of interval post-colonoscopy colorectal cancer: a population-based study. The Lancet Gastroenterology & Hepatology 2022; 7: 747-754. doi:10.1016/S2468-1253(22)00090-5
14. Bettington M, Walker N, Rosty C et al. Clinicopathological and molecular features of sessile serrated adenomas with dysplasia or carcinoma. Gut 2017; 66: 97-106. doi:10.1136/gutjnl-2015-310456
15. Bouwens MWE, Riedl RG, Bosman FT et al. Large Proximal Serrated Polyps: Natural History and Colorectal Cancer Risk in a Retrospective Series. Journal of Clinical Gastroenterology 2013; 47
16. Holme Ø, Bretthauer M, Eide TJ et al. Long-term risk of colorectal cancer in individuals with serrated polyps. Gut 2015; 64: 929-936. doi:10.1136/gutjnl-2014-307793
17. Liu C, Bettington ML, Walker NI et al. CpG island methylation in sessile serrated adenomas increases with age, indicating lower risk of malignancy in young patients. Gastroenterology 2018; 155: 1362-1365. e1362
18. Lieu CH, Golemis EA, Serebriiskii IG et al. Comprehensive genomic landscapes in early and later onset colorectal cancer. Clinical cancer research 2019; 25: 5852-5858
19. Perea J, Rueda D, Canal A et al. Age at onset should be a major criterion for subclassification of colorectal cancer. The Journal of molecular diagnostics : JMD 2014; 16: 116-126. doi:10.1016/j.jmoldx.2013.07.010
20. Lall V, Ismail AGM, Ayonrinde OT. Disparate age and sex distribution of sessile serrated lesions and conventional adenomas in an outpatient colonoscopy population–implications for colorectal cancer screening? International Journal of Colorectal Disease 2022; 37: 1569-1579
21. Kim HY, Kim SM, Seo J-H et al. Age-specific prevalence of serrated lesions and their subtypes by screening colonoscopy: a retrospective study. BMC Gastroenterology 2014; 14: 82. doi:10.1186/1471-230X-14-82
22. Anderson JC, Butterly LF, Weiss JE et al. Providing data for serrated polyp detection rate benchmarks: an analysis of the New Hampshire Colonoscopy Registry. Gastrointestinal Endoscopy 2017; 85: 1188-1194. doi:https://doi.org/10.1016/j.gie.2017.01.020
23. Aronchick CA, Lipshutz WH, Wright SH et al. A novel tableted purgative for colonoscopic preparation: efficacy and safety comparisons with Colyte and Fleet Phospho-Soda. Gastrointest Endosc 2000; 52: 346-352. doi:10.1067/mge.2000.108480

24. Yeh JH, Lin CW, Wang WL et al. Positive Fecal Immunochemical Test Strongly Predicts Adenomas in Younger Adults With Fatty Liver and Metabolic Syndrome. Clinical and translational gastroenterology 2021; 12: e00305. doi:10.14309/ctg.0000000000000305

25. Force UPST. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. JAMA 2021; 325: 1965-1977. doi:10.1001/jama.2021.6238

26. Patel SG, May FP, Anderson JC et al. Updates on Age to Start and Stop Colorectal Cancer Screening: Recommendations From the U.S. Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2022; 162: 285-299. doi:10.1053/j.gastro.2021.10.007

27. Pohl H, Srivastava A, Bensen SP et al. Incomplete Polyp Resection During Colonoscopy—Results of the Complete Adenoma Resection (CARE) Study. Gastroenterology 2013; 144: 74-80.e71. doi:https://doi.org/10.1053/j.gastro.2012.09.043

28. Kahi CJ, Hewett DG, Norton DL et al. Prevalence and Variable Detection of Proximal Colon Serrated Polyps During Screening Colonoscopy. Clinical Gastroenterology and Hepatology 2011; 9: 42-46. doi:https://doi.org/10.1016/j.cgh.2010.09.013

29. Payne SR, Church TR, Wandell M et al. Endoscopic Detection of Proximal Serrated Lesions and Pathologic Identification of Sessile Serrated Adenomas/Polyps Vary on the Basis of Center. Clinical Gastroenterology and Hepatology 2014; 12: 1119-1126. doi:https://doi.org/10.1016/j.cgh.2013.11.034

30. Butterly L, Robinson CM, Anderson J et al. Serrated and adenomatous polyp detection increases with longer withdrawal time: results from the New Hampshire Colonoscopy Registry. The American journal of gastroenterology 2014; 109: 417

31. de Wijkerslooth TR, Stoop EM, Bossuyt PM et al. Differences in proximal serrated polyp detection among endoscopists are associated with variability in withdrawal time. Gastrointestinal endoscopy 2013; 77: 617-623

32. Jennifer T, Lovedeep G, Steven P et al. Higher adenoma detection, sessile serrated lesion detection and proximal sessile serrated lesion detection are associated with physician specialty and performance on Direct Observation of Procedural Skills. BMJ Open Gastroenterology 2021; 8: e000677. doi:10.1136/bmjgast-2021-000677

33. Verheyen E, Castaneda D, Gross SA et al. Increased sessile serrated adenoma detection rate with mechanical new technology devices: a systematic review

and meta-analysis. Journal of Clinical Gastroenterology 2021; 55: 335-342

34. Wu Z, Yao L, Liu W et al. Development and Validation of a Deep Learning–Based Histologic Diagnosis System for Diagnosing Colorectal Sessile Serrated Lesions. American Journal of Clinical Pathology 2023; 160: 394-403. doi:10.1093/ajcp/aqad058

35. Cheng H-C, Chang T-K, Su W-C et al. Narrative review of the influence of diabetes mellitus and hyperglycemia on colorectal cancer risk and oncological outcomes. Translational Oncology 2021; 14: 101089

Supplementary Material

Prevalence and Predictive factors of colorectal sessile serrated lesions in younger individuals (Jen-Hao Yeh et al.)

Supplementary Table 1. Age-specific detection rates of adenomas, sessile serrated lesions with and without cytological dysplasia, and clinically significant serrated polyps

Age	Total, N	Adenoma, N (%)	SSL, N (%)	SSLD, N (%†)	CSSP, N (%)
20-29	376	26 (6.9)	13 (3.5)	0	19 (5.1)
30-39	1638	273 (16.7)	87 (5.3)	5 (5.7)	135 (8.2)
40-49	2698	764 (28.3)	241 (8.9)	4 (1.7)	331 (12.3)
50-59	2346	990 (42.2)	193 (8.2)	11 (5.7)	275 (11.7)
60-69	1949	928 (47.6)	117 (6.0)	4 (3.4)	197 (10.1)
70-79	734	400 (54.5)	23 (3.1)	2 (8.7)	52 (7.1)
80 and above	113	57 (50.4)	2 (1.8)	0	7 (6.2)

SSL: sessile serrated lesion; SSLD: sessile serrated lesion with dysplasia; SP: serrated polyp; CSSP: clinically significant serrated polyp; †: percentage among cases with SSL

Supplementary Table 2. Baseline characteristics of individuals in the younger age group with and without SSLs receiving health checkups

	With SSL (n = 208)	**Without SSL (n = 2034)**	***P* value**
Age (mean ± SD)	41.4 ± 5.2	39.6 ± 6.4	< 0.001*
Sex (female, %)	93 (44.7)	1039 (51.1)	0.08
Obesity (%)	51 (24.5)	357 (17.7)	0.015*
Current smoker (%)	46 (22.1)	309 (15.4)	0.011*
Family history of colorectal cancer (%)	8 (3.8)	128 (6.3)	0.159
Hypertension (%)	10 (4.8)	90 (4.5)	0.814
Diabetes mellitus (%)	15 (7.2)	56 (2.8)	0.001*
Metabolic syndrome (%)	35 (16.8)	241 (11.9)	0.041*
Fatty liver disease (%)	94 (45.2)	800 (39.6)	0.120
Positive fecal occult blood test (%)	12 (5.8)	65 (3.2)	0.141
Intravenous anesthesia (%)	199 (95.7)	1972 (97.0)	0.316
Withdrawal time (min, mean ± SD)	9.7 ± 3.5	7.1 ± 2.8	< 0.001*
Adenoma (%)	53 (25.5)	499 (24.5)	0.762
Advanced adenoma (%)	5 (2.4)	67 (3.3)	0.331
Right-sided adenoma (%)	36 (17.3)	273 (13.4)	0.121
Right-sided advanced adenoma (%)	1 (0.5)	32 (1.6)	0.213
Colorectal cancer (%)	1 (0.3)	2 (0.1)	0.151
Right-sided hyperplastic polyp (%)	6 (2.9)	106 (5.2)	0.142
Traditional serrated adenoma (%)	0	5 (0.2)	0.474

*: $P < 0.05$;

Supplementary Table 3. Logistic regression analysis results of predictive factors for SSLs among individuals in the younger age group who underwent health checkups

	Univariable analysis		Multivariable analysis	
	Odds ratio (95% CI)	***P* value**	**Odds ratio (95% CI)**	***P* value**
Age 20-29	1	NA	1	NA
Age 30-39	1.14 (0.57 – 2.36)	0.721	0.87 (0.41 – 1.82)	0.713
Age 40-49	2.05 (1.02 – 4.12)	0.042*	1.34 (0.66 – 2.73)	0.415
Withdrawal time (per min increment)	1.21 (1.16 – 1.25)	< 0.001*	1.19 (1.14 – 1.24)	< 0.001*
Obesity	1.51 (1.08 – 2.11)	0.015*	1.19 (0.80 – 1.78)	0.381
Diabetes mellitus	2.72 (1.51 – 4.90)	0.001*	1.85 (0.97 – 3.54)	0.060
Metabolic syndrome	1.49 (1.01 – 2.20)	0.041*	0.87 (0.54 – 1.42)	0.602
Current smoker	1.56 (1.10 – 2.21)	0.011*	1.18 (0.81 – 1.72)	0.386

*: $P < 0.05$

Appendix

Obesity was defined as body mass index >27 kg/m^2. Fatty liver disease was defined based on ultrasonography diagnosis. Hypertension was defined as sustained high-abnormal readings such as systolic blood pressure ≥180 mmHg or diastolic blood pressure ≥120 mmHg at two consecutive examination. Diabetes mellitus was defined as fasting glucose ≥126 mg/dL or glycosylated hemoglobin ≥6.5%. Metabolic syndrome was defined as the presence of at least three of the following findings: central obesity (waist circumference ≥90 cm in men or ≥80 cm in women), elevated blood pressure (systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg in two consecutive readings), fasting glucose impairment (>100 mg/dL), elevated triglyceride (≥150 mg/dL), and reduced high-density lipoprotein cholesterol (<40 mg/dL in men or <50 mg/dL in women). In addition, preexisting diagnosis of hypertension, diabetes mellitus, and/or hyperlipidemia under medical treatment by the individual's report was considered valid regardless of the laboratory results.

Table 1. Baseline demographic and endoscopic characteristics of the cohorts

	Younger age group (< 50-years-old)	**Elder age group (≥ 50-years-old)**	***P* value**
Cases (%)	4712 (47.8)	5142 (52.1)	NA
Cases from health check-up (%)	2242 (47.6)	1248 (24.3)	< 0.001*
Symptomatic cases	1985 (42.1)	2763 (53.7)	< 0.001*
Age (mean ± SD)	39.7 ± 6.4	61.3 ± 8.0	< 0.001*
Sex (female, %)	2425 (51.5)	2649 (51.5)	0.958
Family history of CRC (%)	318 (6.7)	164 (3.2)	< 0.001*
Intravenous anesthesia (%)	3875 (82.2)	3579 (69.6)	< 0.001*
Withdrawal time (min, mean ± SD)	7.5 ± 3.5	9.4 ± 5.3	< 0.001*
Adenoma (%)	1063 (22.6)	2375 (46.2)	< 0.001*
Advanced adenoma (%)	188 (4.0)	728 (14.2)	< 0.001*
Right-sided adenoma (%)	526 (11.2)	1399 (27.2)	< 0.001*
Right-sided advanced adenoma (%)	63 (1.3)	336 (6.5)	< 0.001*
Adenoma numbers (mean ± SD)	0.3 ± 0.6	0.7 ± 1.0	< 0.001*
CRC (%)	19 (0.4)	72 (1.4)	< 0.001*
SSL (%)	341 (7.2)	335 (6.5)	0.157
SSL with dysplasia (%)	9 (0.2)	17 (0.3)	0.177
SSLD among SSL (%)	9 (2.6)	17 (5.1)	0.100
Right-sided hyperplastic polyp (%)	181 (3.8)	243 (4.7)	0.031*
Traditional serrated adenoma (%)	8 (0.2)	21 (0.4)	0.029*
CSSP (%)	485 (10.3)	531 (10.3)	0.956
CSSP numbers (mean ± SD)	0.1 ± 0.4	0.1 ± 0.4	0.550

*: $P < 0.05$; SD: standard deviation; CRC: colorectal cancer; SSL: sessile serrated lesion; SSLD: sessile serrated lesion with dysplasia; CSSP: clinically significant serrated polyp

Table 2. Baseline characteristics of younger individuals (age < 50) from outpatient services and younger individuals from health checkup services

	Outpatient	Health check-up	*P* value
Cases (%)	2470 (52.4)	2242 (47.6)	NA
Age (mean ± SD)	39.7 ± 6.6	39.6 ± 6.1	0.575
Sex (female, %)	1293 (52.3)	1132 (50.5)	0.203
Intravenous anesthesia (%)	1704 (69.0)	2171 (96.8)	< 0.001*
Family history of CRC (%)	182 (7.4)	136 (6.1)	0.075
Positive fecal occult blood test (%)	179 (7.2)	11 (0.5)	< 0.001*
Withdrawal time (min, mean ± SD)	7.7 ± 3.8	7.4 ± 3.0	0.001*
Adenoma (%)	511 (20.7)	552 (24.6)	0.001*
Advanced adenoma (%)	116 (4.7)	80 (3.2)	0.009*
Right-sided adenoma (%)	217 (8.8)	309 (13.8)	< 0.001*
Right-sided advanced adenoma (%)	30 (1.2)	33 (1.5)	0.442
Adenoma numbers (mean ± SD)	0.2 ± 0.6	0.3 ± 0.6	0.014*
CRC (%)	16 (0.6)	3 (0.1)	0.005*
SSL (%)	133 (5.4)	208 (9.3)	< 0.001*
SSL with dysplasia (%)	5 (0.2)	4 (0.2)	0.850
SSLD among SSL (%)	5 (3.8)	4 (1.9)	0.302
Right-sided hyperplastic polyp (%)	69 (2.8)	112 (5.0)	< 0.001*
Traditional serrated adenoma (%)	3 (0.1)	5 (0.2)	0.398
CSSP (%)	192 (7.8)	293 (13.1)	< 0.001*
CSSP numbers (mean ± SD)	0.1 ± 0.3	0.1 ± 0.4	< 0.001*

*: *P* < 0.05; SD: standard deviation; CRC: colorectal cancer; SSL: sessile serrated lesion; SSLD: sessile serrated lesion with dysplasia; CSSP: clinically significant serrated polyp

Table 3. Baseline characteristics of younger individuals with and without SSLs

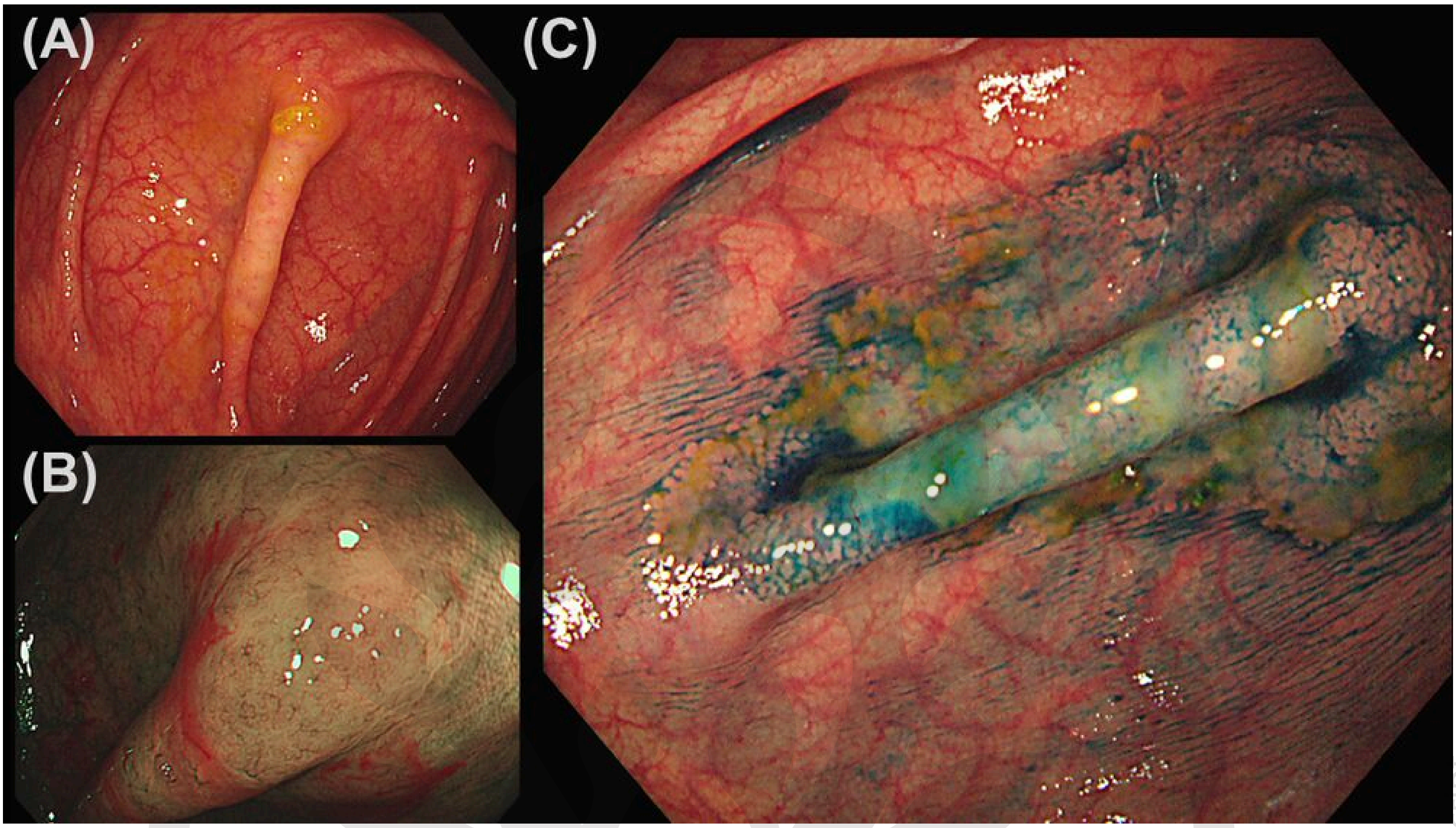
	With SSL (n = 341)	**Without SSL (n = 4371)**	***P* value**
Age (mean ± SD)	41.6 ± 5.2	39.6 ± 6.4	< 0.001*
Age 20-29, n (%)	13 (3.8)	363 (8.3)	
Age 30-39, n (%)	87 (25.5)	1551 (35.5)	
Age 40-49, n (%)	241 (70.7)	2457 (56.2)	
Sex (female, %)	153 (44.9)	2272 (52.0)	0.011*
From outpatient service (%)	133 (39.0)	2337 (53.5)	< 0.001*
Symptomatic cases	93 (27.3)	1892 (43.3)	< 0.001*
Family history of colorectal cancer (%)	26 (7.0)	294 (6.7)	0.825
Positive fecal occult blood test (%)	14 (4.1)	176 (4.0)	0.943
Intravenous anesthesia (%)	278 (81.5)	3597 (82.3)	0.721
Withdrawal time (min, mean ± SD)	10.6 ± 4.3	7.3 ± 3.3	< 0.001*
Adenoma (%)	84 (24.6)	979 (22.4)	0.341
Advanced adenoma (%)	14 (4.1)	174 (4.0)	0.910
Right-sided adenoma (%)	49 (14.4)	477 (10.9)	0.051
Right-sided advanced adenoma (%)	4 (1.2)	59 (1.3)	0.784
CRC (%)	1 (0.3)	18 (0.4)	0.739
Right-sided hyperplastic polyp (%)	9 (2.6)	172 (3.9)	0.230
Traditional serrated adenoma (%)	0	8 (0.2)	0.429

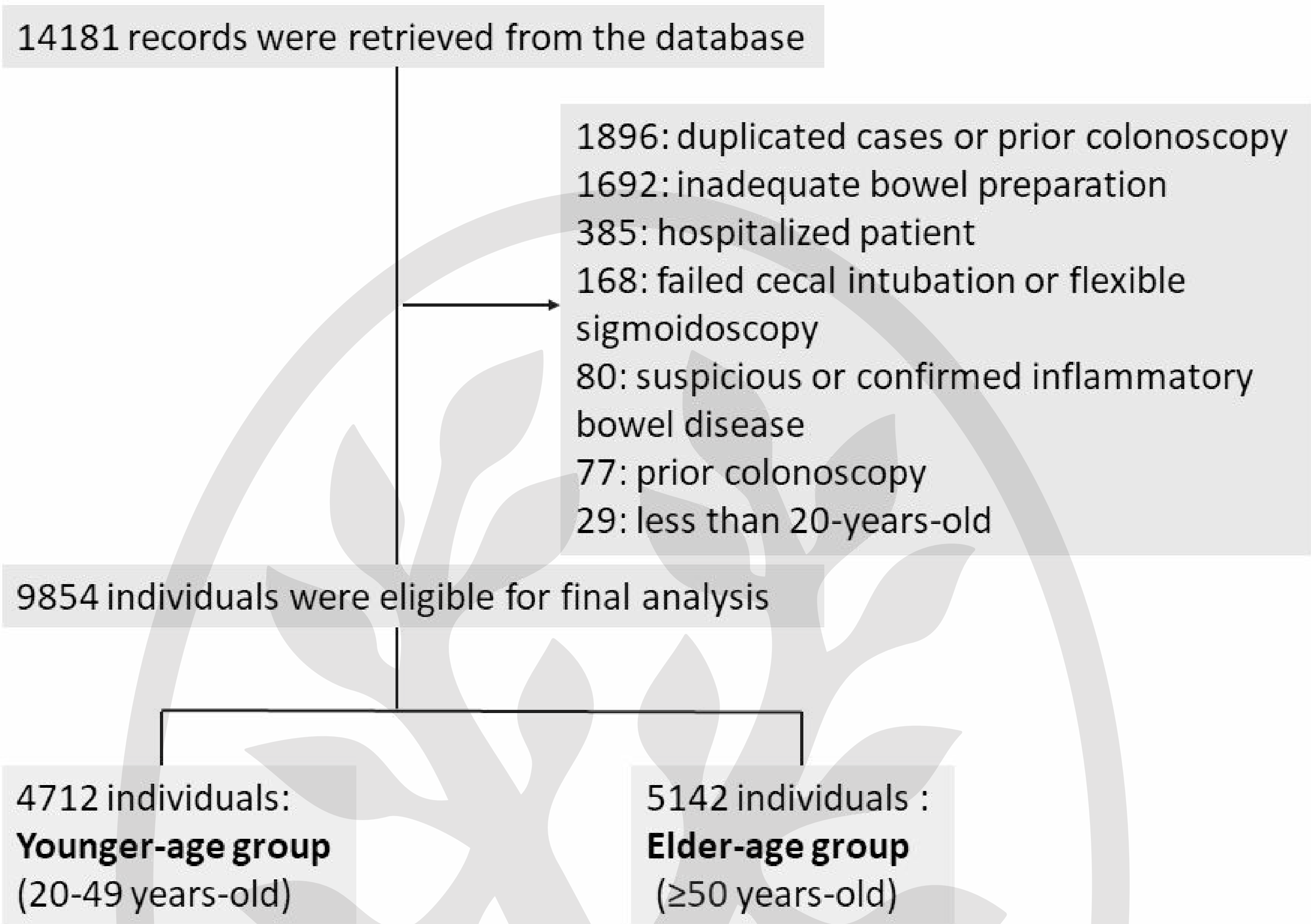
*: $P < 0.05$; SD: standard deviation; SSL: sessile serrated lesion; CRC: colorectal cancer

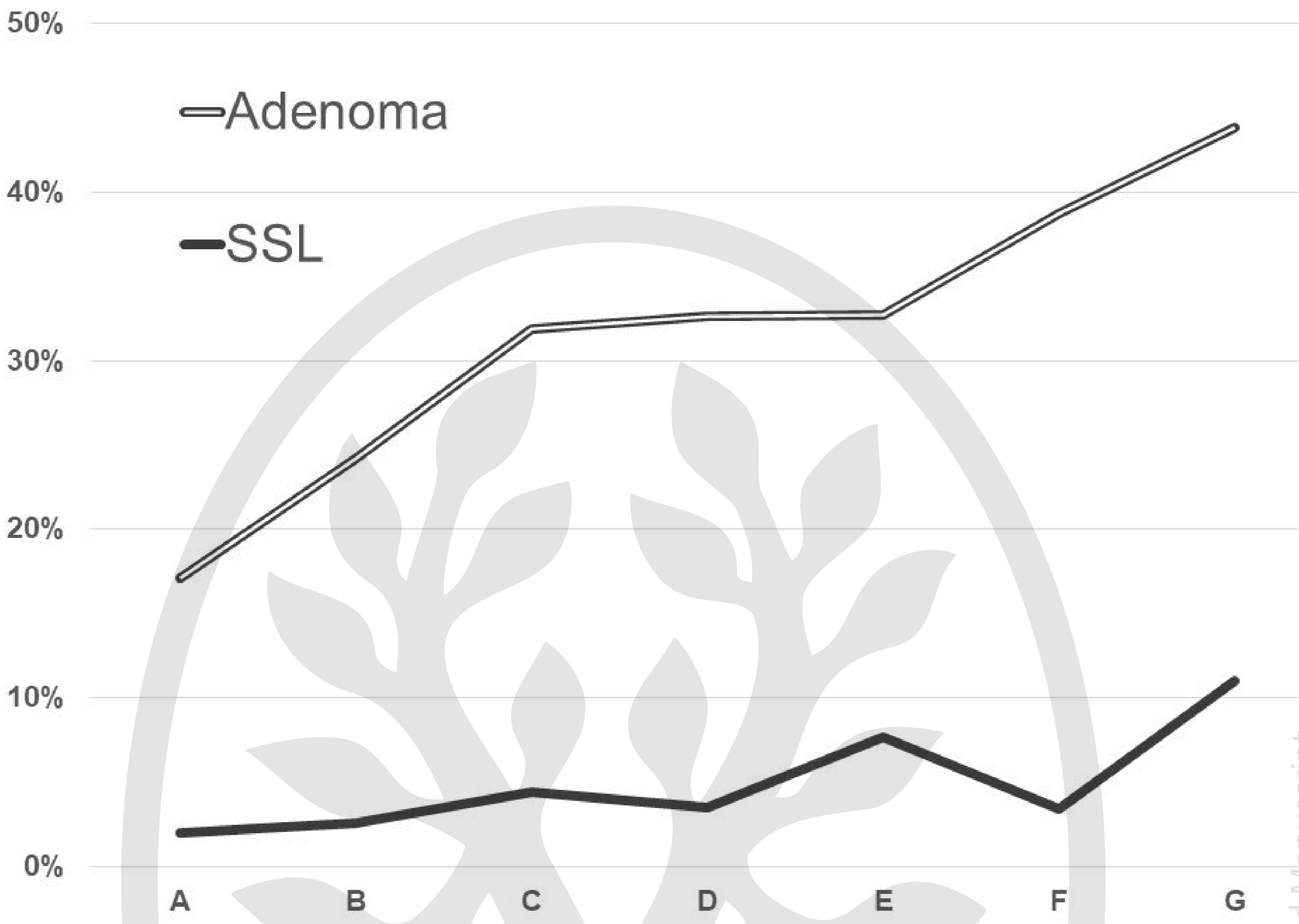
Table 4. Logistic regression analysis results of predictive factors for SSLs in younger age group

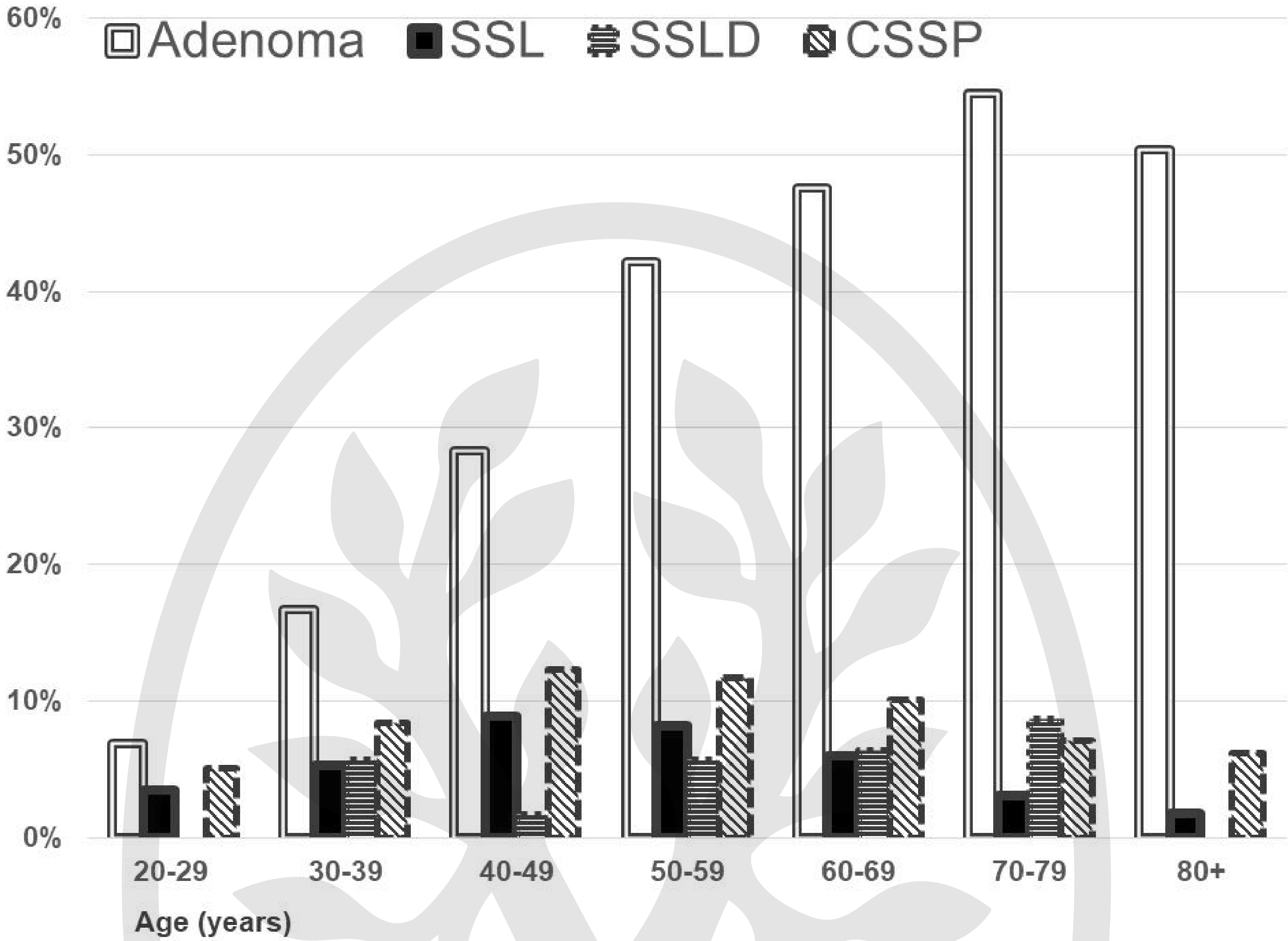
	Univariable analysis		Multivariable analysis	
	Odds ratio (95% CI)	***P* value**	**Odds ratio (95% CI)**	***P* value**
Age				
20-29 years	1	NA	1	NA
30-39 years	1.56 (0.86 – 2.83)	0.139	1.22 (0.67 – 2.24)	0.507
40-49 years	2.73 (1.55 – 4.83)	0.001*	1.81 (1.01 – 3.23)	0.044
Withdrawal time (per min increment)	1.18 (1.15 – 1.21)	< 0.001*	1.17 (1.14 – 1.20)	< 0.001*
Male sex	1.33 (1.06 – 1.66)	0.011*	1.09 (0.87 – 1.38)	0.426
Endoscopist				
Average performers (SSLDR < 7%)	1	NA	1	NA
High performers (SSLDR ≥ 7%)	3.01 (2.24 – 4.05)	< 0.001*	3.35 (2.44 – 4.58)	< 0.001*

*: $P < 0.05$; SSLDR: sessile serrated lesion detection rate


(A)
(B)
(C)


14181 records were retrieved from the database
1896: duplicated cases or prior colonoscopy
1692: inadequate bowel preparation
385: hospitalized patient
168: failed cecal intubation or flexible sigmoidoscopy
80: suspicious or confirmed inflammatory bowel disease
77: prior colonoscopy
29: less than 20-years-old
9854 individuals were eligible for final analysis
4712 individuals: **Younger-age group** (20-49 years-old)
5142 individuals : **Elder-age group** (≥50 years-old)


50%
40%
30%
20%
10%
0%
Adenoma
SSL
A
B
C
D
E
F
G



Adenoma
SSL
SSLD
CSSP
60%
50%
40%
30%
20%
10%
0%
20-29
30-39
40-49
50-59
60-69
70-79
80+
Age (years)