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Higher Serrated Polyp Detection Rates are Associated with Lower Risk for Post Colonoscopy Colorectal Cancer: Data From the New Hampshire Colonoscopy Registry

Joseph C Anderson, M.D.[1,2], **Douglas K Rex**[5], **Todd A Mackenzie, PhD**[1], **William Hisey, M.Sc.**[3,4], **Christina M Robinson, M.S.**[3,4], **Lynn F Butterly, M.D.**[1,3,4,*]

[1]Geisel School of Medicine at Dartmouth, Hanover, NH

[2]White River Junction VAMC, White River Junction VT

[3]Department of Gastroenterology and Hepatology, Dartmouth-Hitchcock Medical Center, Lebanon, NH;

[4]NH Colonoscopy Registry, Lebanon, NH

[5]Indiana University School of Medicine, Department of Medicine, Division of Gastroenterology and Hepatology, Indianapolis, Indiana

Abstract

Background—We used New Hampshire Colonoscopy Registry (NHCR) data to examine the association between Post-colonoscopy colorectal cancer (PCCRC) and sessile serrated detection rates (SSLDR).

Methods—We included patients with either a colonoscopy or a CRC diagnosis in the NH State Cancer Registry. PCCRC, was any CRC diagnosed >/= 6 months after index exam.

Results—Of 26,901 patients, 162 were diagnosed with PCCRC. The hazard ratio for PCCRC was lowest for patients whose endoscopists had the highest SSLDR quintile (≥6%) (HR=0.29;95%CI:0.16–0.50)

Discussion—Endoscopists with higher SSLDR had lower risks for PCCRC. These data validate SSLDR as a clinically relevant quality measure.

*Corresponding author: Joseph C Anderson, M.D. Joseph.Anderson@Dartmouth.edu; White River Junction VAMC White River Junction, VT, Phone: 603-653-3427; fax: 603-727-7919.

Author Contributions

Conception and design: J.C.A., W.H., T.A.M., L.F.B., C.M.R., D.K.R.
Data Curation: J.C.A., W.H., T.A.M., L.F.B., C.M.R.
Analysis and interpretation of the data: J.C.A., W.H., T.A.M., L.F.B., C.M.R., D.K.R.
Drafting of the article: J.C.A., L.F.B., C.M.R., W.H., T.A.M., D.K.R.
Critical revision of the article for important intellectual content: J.C.A., L.F.B., C.M.R., W.H., T.A.M., D.K.R.
Statistical analysis; J.C.A., W.H., T.A.M., L.F.B., C.M.R.
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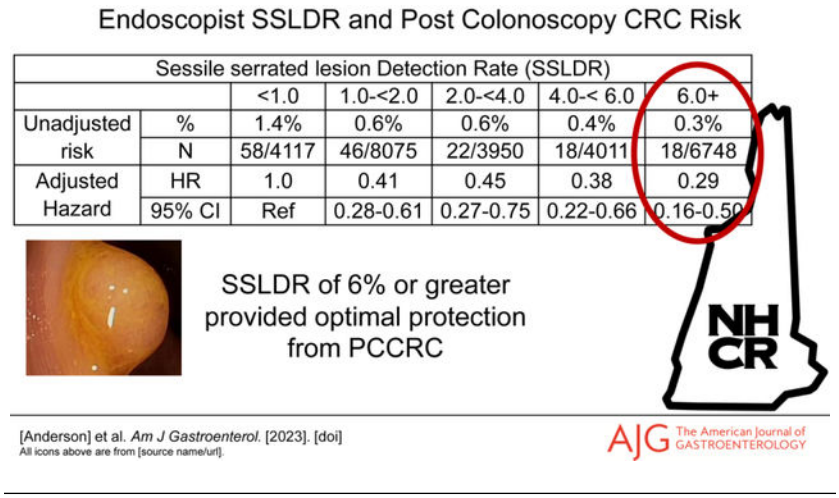
Graphical Abstract



Introduction

Colorectal cancers (CRC) may arise through the serrated pathway, which accounts for a large proportion of CRC.[1–3] Similar to adenoma detection rates (ADR), higher serrated detection rates (SDR) may be associated with a lower incidence of PCCRC.[4, 5] Unlike ADR, there are little data examining potential SDR benchmarks. We used data from the New Hampshire Colonoscopy Registry (NHCR) to examine the association between PCCRC risk and SDR.

Methods

As previously described and approved by the Committee for the Protection of Human Subjects at Dartmouth College (CPHS#00015834), NHCR patients consent to data collection from their initial and subsequent colonoscopies.[6–8]

We included patients with an index colonoscopy plus a follow-up of at least one colonoscopy performed ≥6 months after the index exam, or a diagnosis of CRC recorded in the NH State Cancer Registry. The follow-up time was calculated (months) from index exam to first follow-up colonoscopy or CRC diagnosis. Exclusion criteria included a history of inflammatory bowel disease, familial genetic cancer syndromes, or CRC diagnosed at or within 6 months of the index exam.

Our outcome was post colonoscopy colorectal cancer (PCCRC), CRC diagnosed ≥6 months after index exam. Our exposure of interest was endoscopist-specific sessile serrated lesions detection rates (SSLDR) calculated as the proportion of all an endoscopist's *screening colonoscopies* with at least 1 sessile serrated lesion. We divided the SSLDR into quintiles.[9]

Covariates included age, sex, index findings of clinically significant serrated polyps[7] (traditional serrated adenomas, sessile serrated lesions, large or proximal hyperplastic polyps > 5 mm) or conventional advanced adenomas (≥ 1cm, villous, high grade dysplasia), the

indication, bowel preparation quality, and year of index exam, and whether the patient had > 1 surveillance exam.

Means and standard deviations were calculated for continuous variables while numbers and percents were derived for proportions. We used the chi squared test for trend and Fisher's exact test to evaluate categorical variables. T-tests were used to compare continuous variables and Mann-Whitney U tests were used for continuous variables with non-Gaussian distributions. Cox regression was used to model the hazard of PCCRC controlling for covariates (SPSS27, IBM).

Results

26,901 patients had index colonoscopies performed by 148 endoscopists (2004–21) and a follow-up event. As compared to patients with no PCCRC, those with PCCRC (n=162) were more likely to be older, have a shorter follow-up time, and have an endoscopist with a lower SSLDR (Table 1).

Endoscopists with higher SSLDR had lower unadjusted risks for PCCRC (Q5:6.0%+; 0.3%) and hazard ratio (HR:0.29;95%CI0.16–0.50) (Table 2). There was a significant reduction in PCCRC for each 1% increase in SSLDR (HR:0.86; 95% CI: 0.80–0.93). We stratified by ADR of 25 and median SSLDR of 3; 1) ADR < 25, 2) ADR ≥ 25 and 3) SDR < 3 and ADR ≥ 25 and SDR ≥ 3. PCCRC risk was lowest for endoscopists with ADR≥25 and SSLDR≥3% (0.3% and HR:0.58;95%CI:0.39–0.86)(Table 3). When stratifying by highest SSLDR quintile, approximately one-third of endoscopists had adequate ADR but SSLDR <6% (33.8%;50/148) (data not shown).

To examine the impact of patients without a follow up event, we conducted a sensitvity analysis by censoring all NHCR patients (with and without follow up) at 6 months prior to the last linkage date between the NHCR and the NH State Cancer Registry. An additional 87,296 patients (45.5% male, average age 58.1 (±S.D.11.4)) had an average time to censoring of 59.8 months (S.D.±33.9). As in the primary analysis, higher SSLDRs were associated with lower unadjusted risks of PCCRC and HRs but the point estimates for the hazards were more modest (0.06% and HR:0.36;95%CI 0.21–0.62)(Table 2).

Discussion

Our data demonstrate that higher SSLDRs are protective of post colonoscopy CRC (PCCRC). The most optimal protection was observed in the highest quintile of SSLDR. The HRs were lower for higher quintiles, though 95% CIs overlapped. Currently there are few data regarding risk of PCCRC and SSLDR. A recent paper examining SDRs observed a trend for lower hazard of PCCRC death with higher SSLDR (HR:0.97;95%CI:0.89–1.06).[10] van Toledo et al demonstrated a lower risk of PCCRC for endoscopists with higher SSLDR.[11] Similarly, we observed a 14% reduction in PCCRC for each 1% increase in SSLDR. Thus, endoscopists should strive to achieve the highest SSLDR rate, perhaps with the use of artificial intelligence.[12]

Similar to our results, van Toledo et al observed that superior serration detection added to the existing ADR benchmark. Specifically, those who had the highest ADR and SSLDR had a lower HR than those with lower ADR or those with high ADR but lower SSLDR. This finding is important for the ongoing effort to reduce PCCRC because approximately one-third of endoscopists had an adequate ADR,[13] yet had an SSLDR less than the most protective SSLDR of 6%. As compared to the Dutch study, our data calculated from screening exams may be more generalizable to US practices; our patients had longer follow up, 5 versus 3 years.

Although the population of New Hampshire includes substantial ethnic, socioeconomic and rural/urban diversity, it has limited racial diversity[14]. It will be helpful to assess these results in other more racially diverse settings. Use of additional detection rates may increase the burden on endoscopists. One solution might be to document all serrated polyps (with artificial intelligence), through phtotography.[15] We also acknowledge that there may be differences in serrated polyp detection in other populations with more high risk groups such as smokers,[16, 17] and there may be significant variation of SSLDR due to variation in pathological interpretation.[18]

In terms of choosing the best SDR to evaluate quality, although SSLDR may be pathologist dependent it is more difficult to game since it is independent of size and location. In addition, it measures detection for the entire colon. Our data suggest that an SSLDR benchmark of 6% would offer optimal protection. It is reassuring that the GI Quic Registry, demonstrate population-based estimates of 6% for SSL.[19] In summary, our data linking low SSLDR to increased PCCRC support development of recommendations to measure SDR in clinical practice, and development of educational platforms, techniques and devices to improve low SDR.

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Table 1.

Characteristics of the patients and colonoscopies with and without PCCRC.

Characteristic	Follow up with no PCCRC	Patients with PCCRC	P value (With PCCRC versus no PCCRC)
Patients	N=26,739	N=162	
Sex (% male)	48.1% (12,846)	43.8% (71)	0.28
Age (average, ±S.D.)	58.0 (9.7)	65.5 (11.0)	0.0001
Exam			
Cecal intubation	98.6% (26,355)	96.9% (157)	0.09
Bowel Prep (% poor)	2.2% (586)	2.5% (4)	0.78
Follow up time to 1st exam or diagnosis (average months, ±S.D.)	62.5 (31.4)	53.4 (32.6)	0.0001
SSLDR detection rate (average, +S.D.)	3.8 (3.1)	2.4 (2.5)	0.0001

Table 2

Detection rates and unadjusted risks and adjusted hazard ratios for post colonoscopy colorectal cancer (PCCRC) in patients with* and without# follow up event

Sessile serrated lesion Detection Rate (SSLDR) (with at least 1 follow up event)* (n=26,901)						
		< 1.0	1.0 – < 2.0	2.0 – < 4.0	4.0 – < 6.0	6.0+
Unadjusted risk PCCRC	%	1.4%	0.6%	0.6%	0.4%	0.3%*
	N	58/4117	46/8075	22/3950	18/4011	18/6748
***Adjusted Hazard	HR	1.0	0.41	0.45	0.38	0.29
	95% CI	Reference	0.28–0.61	0.27–0.75	0.22–0.66	0.16–0.50
Sessile serrated lesion Detection Rate (SSLDR) (with/without follow up event)(n= 114,197)**						
		< 1.0	1.0 – < 2.0	2.0 – < 4.0	4.0 – < 6.0	6.0+
Unadjusted risk PCCRC	%	0.31%	0.18%	0.11%	0.09%	0.06%*
	N	58/18793	46/25824	22/19693	18/19518	18/30369
***Adjusted Hazard	HR	1.0	0.46	0.53	0.49	0.36
	95% CI	Reference	0.31–0.68	032–0.88	0.29–0.85	0.21–0.62

* $p < 0.0001$

*** Cox regression was used to model the hazard of PCCRC on SSLDR controlling for age, sex, presence of CSSPs, presence of advanced adenomas, year of index exam, indication of index exam, bowel prep quality, and having more than 1 surveillance exam.

** Censored at 1st follow up or 6 months prior to last linkage date with the NH State Cancer Registry

Table 3

Serrated Detection rates as stratified by ADR of 25 and SSLDR of 3%

		ADR < 25	ADR ≥ 25 & SSLDR < 3%	ADR ≥ 25 & SSLDR ≥ 3%	P value
SSLDR	Unadjusted Risk	0.9% (85/9784)	0.6% (31/4801)	0.4% (46/12316)	0.0001
	**Adjusted HR (95% CI)	1.0 (Reference)	0.81 (0.53–1.23)	0.58 (0.39–0.86)	0.02

** Cox regression was used to model the hazard of PCCRC on SSLDR controlling for age, sex, presence of CSSPs, presence of advanced adenomas, year of index exam, indication of index exam, bowel prep quality, and having more than 1 surveillance exam.