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ORIGINAL CONTRIBUTION

A Comparative Study Evaluating the Incidence of Colorectal Neoplasia(s) in Candidates for Bariatric Surgery by Screening Colonoscopy, 40–49 Versus 50–65 Years Old: a Preliminary Study

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Abstract

Introduction Obesity and metabolic syndrome (MetS) are associated with colorectal neoplasia (CRN) and carcinoma (CRC). Whether such subjects must undergo screening colonoscopy (SC) earlier, is unknown. Incidences of CRNs in 40–49- versus 50–65-year-old bariatric patients were compared by SC. No prospective data on SC is available in morbidly obese/MetS.

Material and Methods Surgical weight loss candidates over 39 years of age, asymptomatic, and average-risk for CRC offered SC. Those giving written informed consent were enrolled. Colonoscopies were done by the same surgeon. Smoking/drinking history, fasting blood glucose (FBG), insulin, C-peptide, triglyceride, high density lipoprotein, vitamin D, HbA1c, and insulin resistance parameters were recorded. CRN rate and the distribution of variables in patients 40–49 years of age were compared with 50–65. Student's *t* and Chi-square tests were used as appropriate. $P < 0.05$ was regarded as statistically significant.

Results Among 168 SCs, 47 had CRNs (27.9%). Including carcinoma, 15 had an advanced CRN (aCRN) (8.9% aCRN and 0.6% CRC). CRN rate was 35.6% in ≥ 50 years old whereas 22.1% in 40–49 ($p = 0.053$). aCRN rates (8.4% in 40–49 versus 9.6% in 50–65) were similar ($p = 0.792$). Metabolic parameters and smoking-drinking history were equally distributed between the groups except FBG and HbA1c as their mean levels were slightly higher in the 50–65 age group ($p < 0.05$).

Conclusions Presented results warrant routine SC in the 40–49-year-old morbidly obese and/or MetS patient population with average risk, and in aged > 50, it certainly must be enforced and included in the preoperative check-list if not done before.

Keywords Screening colonoscopy · Obese · Metabolic syndrome · Morbid obesity

Introduction

Obesity is a risk factor for many solid tumors and colorectal carcinoma (CRC) is no exception [1]. Most CRCs develop through the adenoma-carcinoma sequence, and meta-analyses have also pointed out obesity as a risk factor for the development of adenomas, the so-called colorectal neoplasia (CRN) [2, 3]. Metabolic syndrome (MetS) is also reported as a risk factor for CRNs [4–7] and prospective studies showed increase in the incidence of CRCs and related mortality in patients with MetS [8–13]. Therefore, candidates for surgical weight loss, who are either morbidly obese or have MetS, frequently both, represent a challenging group with special reference to increased CRC risk.

Currently, the initial screening colonoscopy (SC) in average-risk patients is advised to be undertaken at the age of 50 and no specific guidelines are available for the obese or metabolically unhealthy [14–16]. However, during an obesity pandemic which increases colonic carcinogenesis, the questions whether obese with average-risk must have their first SC earlier, and if yes, how early, became extremely valid. Hypothetically, it seems reasonable to assume that decreasing the age limit to 40 may allow better CRC prevention in the average-risk morbidly obese and/or MetS patients. To test this hypothesis, we prospectively compared the incidence of CRNs by SC in our bariatric surgery candidates in two consecutive age groups. Furthermore, the distribution of sex, body mass index (BMI kg/m^2), various metabolic factors, and smoking/drinking history were compared.

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No trial is available about the SC in a bariatric patient population.

Material and Methods

The study protocol was approved by our institutional ethics committee.

Inclusion Criteria Candidates for weight reduction surgery who were > 39 years of age, and having only average-risk for CRC, were the primary subjects. Average risk defines asymptomatic individuals lacking high-risk medical conditions (polyposis syndromes, inflammatory bowel disease) and a personal/family history of CRN/CRCs. Patients were specifically informed about the increased risk for CRNs and CRCs in obesity/MetS and offered SC. All were informed about the probable complications of colonoscopy. Age 40–49 patients were further informed about the experimental nature of their part of the study. All participants who gave written informed consent had SC.

Exclusion Criteria Patients who had previous SC were excluded for standardization. Patients who were symptomatic (i.e., bleeding, positive fecal occult blood test, changed bowel habits, iron deficiency anemia) or in "high-risk" category for CRC were also excluded as those who did not want to comply.

Colonoscopy

Medications associated with increased bleeding were stopped a week before. Cleansing was achieved with polyethylene glycol or a phosphate-based solution depending on renal function. Endoscopies were done by the senior author (M.A.Y.) who had done over 2000 colonoscopies. Gastroscopy a routine and colonoscopy were performed in sequence (Olympus, GIF-H180J and CF-H180AL Tokyo, Japan) in the presence of an anesthetist. Under monitoring, deep sedation was achieved with propofol 1-2 mg/kg after the patients were premedicated with midazolam 0.05 mg/kg and fentanyl 1 μg/kg. All polyps were removed utilizing forceps or snares and sent for histological examination to two pathologists. Polyp size was measured at pathology and also colonoscopically, by comparison with a 6-mm forceps. Location of polyps was recorded as proximal or distal with respect to the splenic flexure. Multiple polyps in both proximal and distal colon were evaluated in diffuse category.

Definitions

CRN was defined as the presence of components of adenoma or adenocarcinoma. Non-neoplastic lesions such as hyperplastic, inflammatory, lymphoid polyps were regarded as normal. Advanced CRN (aCRN) was defined as the presence of either high-grade dysplasia, villous components, adenoma size ≥ 1 cm, multiple adenomas ≥ 3, or adenocarcinoma. For patients with multiple neoplasms, the most advanced lesion was reported. The Paris classification of superficial neoplastic lesions was used to categorize the lesions according to their endoscopic appearance [17].

Non-smokers defined as who never smoked and smokers included current smokers and quitters. An alcohol consumption of > 1 drink per week defined as drinkers.

BMI, smoking/drinking history, levels of fasting blood glucose (FBG mg/dl), insulin (MU/ml), C-peptide (ng/ml), triglyceride (TG mg/dl), high density lipoprotein (HDL mg/dl), vitamin D (ng/ml), HbA1c, and homeostatic model assessment for insulin resistance (HOMA-IR) were recorded.

MetS defined the presence of at least three of the following parameters: abdominal obesity; FBG ≥ 100 or taking glucose lowering medications; diastolic or systolic blood pressures ≥ 85 or ≥ 130 mmHg, respectively, or taking anti-hypertensive medications; TG ≥ 150; HDL < 40 in men, and < 50 in women.

Statistical Analysis

All statistics were done using SPSS version 24.0 (Armonk, NY: IBM corp., USA). Continuous variables were expressed as mean ± standard deviation. The incidence of CRNs and the distribution of other variables in patients 40–49 years of age were compared with the data obtained from patients who were 50–65 years old. Chi-square test was used to compare the categorical variables. Student's *t* test was used to compare the continuous variables. $P < 0.05$ was regarded as statistically significant.

Results

Between January 2014 and October 2018, 199 patients aged > 39 were referred to us for weight loss surgery. Five who had a SC elsewhere, 18 who were symptomatic or in "high-risk" category, and 8 non-compliers were excluded. After exclusions, 168 have undergone SC without any complications.

Cleansing was good or reasonable and caecum was reached in all. No polypoid lesion was found in 76, whereas in 92 occasions, 1 to 9 polyps were removed. Among this 92, 45 had only non-neoplastic lesions which were regarded as normal findings.

Histopathology confirmed CRNs in 47 patients giving a CRN detection rate of 27.9% ($n = 47/168$) (Table 1). Including the single carcinoma, 15 had an aCRN, giving an overall aCRN and CRC detection rates of 8.9% and 0.6%, respectively. CRNs were single in 37, whereas 10 had 2 to 5

Table 1 Distribution of demographics, adenoma status, and measured variables between the groups

	$N = 168$	Age < 50, $N = 95$	Age ≥ 50, $N = 73$	p
Age (range)	48.9 ± 5.9 (40–65)	44.6 ± 2.7 (40–49)	54.7 ± 3.7 (50–65)	*< .001*
Male *n* (%)	74 (44)	41 (43.2)	33 (45.2)	.791
Female *n* (%)	94 (56)	54 (56.8)	40 (54.8)	
BMI (range)	43.7 ± 6.6 (31.1–70.5)	43.2 ± 5.8 (31.1–57)	44.3 ± 7.6 (32.8–70.5)	.254
CRN *n* (%)	47 (28)	21 (22.1)	26 (35.6)	.053
aCRN *n* (%)	15 (8.9)	8 (8.4)	7 (9.6)	.792
CRC *n* (%)	1 (0.6)	0	1(1.4)	.435
Smoking *n* (%)	63 (37.5)	41 (43.2)	22 (30.1)	.084
Alcohol *n* (%)	67 (39.9)	43 (45.3)	24 (32.9)	.104
MetS *n* (%)	125 (74.4)	71 (74.7)	54 (74)	.910
FBG	112.7 ± 38.9	106.5 ± 30	120.7 ± 47.2	*.019*
Insulin	21.2 ± 12.2	21.7 ± 13.1	20.6 ± 10.9	.545
HOMA-IR	6 ± 4.4	6 ± 4.8	6.1 ± 3.9	.977
HbA1c	6.1 ± 1.2	5.9 ± 0.9	6.4 ± 1.5	*.016*
C-peptide	3.5 ± 1.5	3.5 ± 1.4	3.6 ± 1.7	.818
Vitamin D	20.1 ± 13.1	18.8 ± 9.8	21.8 ± 16.3	.126
Triglyceride	174.2 ± 87.3	178 ± 81	169.1 ± 95.7	.534
HDL	45.4 ± 12.6	44.1 ± 11.3	47.2 ± 14.1	.132

BMI body mass index, *CRN* colorectal neoplasia, *aCRN* advanced colorectal neoplasia, *CRC* colorectal carcinoma, *MetS* metabolic syndrome, *FBG* fasting blood glucose, *HOMA-IR* homeostatic model assessment for insulin resistance, *HDL* high density lipoprotein

adenomas. Table 2 summarizes the pathology, location, size, and endoscopic appearance data of CRNs. Details of the aCRNs in two consecutive age groups are presented in Table 3.

All patients have undergone laparoscopic sleeve gastrectomy (LSG). The patient having adenocarcinoma was diagnosed as stage 1 CRC and referred for laparoscopic left hemicolectomy which was successfully accomplished elsewhere. Pathology confirmed the curative potential of the operation as a T1N0M0 tumor was removed. This 60-year-old man with 41 BMI and MetS had a LSG, 8 months later. He is metabolically healthy with 24.6 BMI, tumor free, since 4 years.

Table 2 Features of 47 colorectal neoplasias

		N (%)
Histopathology	Tubular/SSA	35 (74.5)
	Villous component	11 (23.4)
	Carcinoma on villous CRN	1 (2.1)
Location	Proximal	9 (19.2)
	Distal	33 (70.2)
	Diffuse	5 (10.6)
Size	< 1 cm	40 (85.1)
	≥ 1 cm	7 (14.9)
Multiplicity	Single adenoma	37 (78.8)
	2 adenomas	5 (10.6)
	Adenoma number ≥ 3	5 (10.6)
Paris Classification	0-Is	35 (74.5)
	0-Ip	10 (21.3)
	0-Ip + 0-Is	1 (2.1)
	0-III	1 (2.1)

SSA sessile serrated adenoma, *CRN* colorectal neoplasia

The demographics and the distribution of CRNs in patients 40–49 years of age vs ≥ 50 are summarized in Table 1. The mean BMI and genders were equally distributed ($p > 0.05$). The prevalence of CRNs was 35.6% in patients ≥ 50 years old whereas 22.1% in the younger group ($p = 0.053$). The distribution of aCRNs (8.4% in 40–49 and 9.6% in 50–65 groups) was similar ($p = 0.792$). All measured metabolic parameters and smoking-drinking history were equally distributed between the groups except FBG and HbA1c as their mean levels were slightly higher in the 50–65 age group ($p < 0.05$).

Discussion

CRC very commonly originates from an adenoma. The adenoma-carcinoma sequence, lasting over a decade, allows many patients to be diagnosed and treated by SC which allows adenoma removal. Thus, proper use of SC resulted in improvements in the incidence and related mortality of CRC [18]. But, still being the 2nd and 3rd most common cancer in females and males, respectively, and the 4th cause of

Table 3 Characteristics of advanced colorectal neoplasias in consecutive age groups

Age group	Sex	Age	BMI	Smoking	MetS	Adenoma number	Diameter ≥ 1 cm	Villous component	HGD
40–49	F	40	54,0	Yes	Yes	1	No	Yes	No
	F	44	50,0	Yes	No	2	Yes	Yes	No
	M	47	47,0	Yes	Yes	2	Yes	Yes	No
	M	47	45,0	Yes	Yes	1	Yes	Yes	Yes
	M	47	37,4	Yes	Yes	4	Yes	Yes	Yes
	F	47	47,9	Yes	Yes	4	No	Yes	Yes
	M	47	31,1	Yes	Yes	1	No	Yes	No
	M	47	49,5	Yes	Yes	3	No	Yes	No
≥ 50	M	50	41,2	Yes	Yes	3	No	No	No
	M	54	45,0	No	Yes	1	Yes	Yes	No
	M	54	34,0	No	Yes	1	No	Yes	No
	M	54	56,6	No	No	5	Yes	No	No
	F	58	43,0	No	Yes	1	Yes	Yes	No
	M	60	38,0	No	Yes	2	Yes	Yes	Yes/CRC
	M	61	43,4	Yes	Yes	3	No	No	No

BMI body mass index, *MetS* metabolic syndrome, *HGD* high-grade dysplasia, *CRC* colorectal carcinoma

cancer-related deaths worldwide [19], despite the benefits of SC, we are still far from being done as far as better prevention is concerned.

The common indication to start screening at 50 in average-risk patients is based on the available evidence [14–16] but many investigators from different continents have already argued current recommendations and suggested that black race [15], smoking [20], male-sex status [21], and obesity/MetS [22] to be taken into account. Studies that specifically sought for an answer whether to start screening at 40 in average-risk, asymptomatic subjects is presented in Table 4 [21–36]. Few studies could not find any significant yield of SC in the 40–49 category but it is noteworthy that no obesity or MetS data was given [23, 24, 30]. Other studies showed interesting results because of the differences in racial status, risk definition, and inclusion/exclusion criteria among the selected patient populations. In most of those studies, SC had a positive yield in 40–49 category and this was especially true in males [25, 29, 32, 33, 36], obese [33], and if a combination of several metabolic factors [22, 33] were present. Interestingly, no previous study on SC was conducted in bariatric patients who were all obese either morbidly, or had MetS, which both are associated with increased risk for CRC.

The most striking finding of this study is the exceedingly high rate of aCRNs detected. It is arguable that the concomitant presence of three CRNs as a criterion for inclusion as an aCRN, but this is beyond the scope of this study. As only two cases, both from the 50–65 age group, were regarded as an aCRN for this reason, the rates in the 40–49 age group remains un-effected and does not statistically change even in the 50–65 age group, even if those two aCRNs related to multiplicity are excluded (Table 3). Reported aCRN rates in 40–49-year-old subjects vary between 1.2 and 3.7%, and our 8.4% aCRN detection rate was over 3-fold (2.3 to 7) more than that it was reported previously (Table 4). It is also noteworthy that many studies in Table 4 had even included some high-risk individuals and the male/female ratio was higher, but still reported at least 3-fold less aCRN rates.

Reported rate of CRNs varies between 9.5 and 28.5% in the 50–59 age group (Table 4). Our 22% CRN detection rate was around 2-fold more than that was reported in eight previous studies (Table 4) and similar to the rest.

Due to unknown factors, obese are already known to undergo less SC [37–39]. The extremely low rate of SC that obese undergo, even required, was also striking as only five patients have had SC previously in our 50–65 age group which comprises 73 patients. Hence, this finding must alert bariatric surgeons. In the ≥ 50 group, a 35.6% CRN, almost 10% aCRN and 1.4% carcinoma rates emphasize the importance of SC which possibly saved the life of the cancer patient in this trial. CRC, if detected early, is curable and SC should be a routine during the preoperative preparation for LSG in patients older than 50 and must be enforced. It must be remembered that, after a LSG, colonoscopy will be very difficult for a certain period of time.

Almost 30% of the CRNs and 20% of the aCRNs were detected in the proximal colon but the single cancer was in the distal colon (Tables 2 and 3). Further studies will help to clarify whether sigmoidoscopy would have sufficed, but this is also beyond our scope. Any obese who is eligible for a LSG can undergo full colonoscopy safely as shown in this series.

As all colonoscopies were done by a single person, all specimens were evaluated by two pathologists, all enrolled were upper or upper-middle class white Caucasians, and all

Table 4 Studies specifically reported on screening colonoscopy in average-risk, asymptomatic patients 40–49 years of age in chronologic order

Author	Year	Country	Study design	Inclusion criteria	Male %	(*N*) and age range of evaluated groups	CRN/aCRN/CRC (%)
Toydemir	2019	Turkey	P	AA	44	(95) 40–49 (73) 50–65	22.1/8.4/0 35.6/9.6/0.6
Wong [35]	2017	China	P	AA + high risk	38	(1133) 40–49	20.5/2.6/0.2
Park [34]	2017	S. Korea	R/CS	AA + high risk	58.7	(2781) 40–49	20.2/2.5/0.4
Leshno [33]	2016	Israel	P	AA	52.3	(505) 40–49 (1245) 50–59	9.5/1.2/0.2 16.3/2.6/0.2
Jung [32]	2015	S. Korea	R	AA + high risk	81	(12507) 40–49 (2319) 50–59	18 /2.4/0.1 30.1/6.7/0.2
Hemmasi [31]	2015	Iran	R	AA	52.6	(333) 40–49 (407) 50–59	11.7/1.2/0 16.4/2.9/0
Ko [30]	2012	S. Korea	R/CS	AA	60.9	(1200) 40–49 (1038) 50–59	28.5/3.7/0.6 42.7/7.5/0.7
Thoma [29]	2011	USA	R	AA + diagnostic	51.6	(247) 40–49 (747) 50–59	12.1/2/0 22.6/5.3/0.4
Hong [21]	2010	S. Korea	R/CS	AA	63.2	(1049) 40–49 (712) 50–59	17.3/2.5/0 22.2/4.4/0.3
Chung [28]	2010	S. Korea	R/CS	AA + high risk	67.2	(1930) 40–49 (2716) 50–59	22.2/2.7/0.2 32.8/4.1/0.3
Choi [27]	2010	S. Korea	R	AA	50.1	(2775) 40–49	24/1.7/0.1
Boursi [26]	2009	Israel	P	AA	52	(262) 40–49 (1218) 50–75	10.7/3.1/0.4 17.4/5.1/0.7
Rundle [25]	2008	USA	R	AA	75	(553) 40–49 (352) 50–59	14.3/2/0 15.9/4/0.3
Eisele [24]	2007	Germany	P	AA	100	(285) 40–49 (333) 50–59	26.7/3.2 /0 35.7/10.2/0
Strul [23]	2006	Israel	R	AA	47.2	(183) 40–49 (917) 50–75	9.8/2/0 22.5/5.5/1.2
Regula [20]	2006	Poland	R/CS	AA + high risk	35.9	(7106) 40–49 (43042) 50–66	9.5/3.4/0.4 14.9/5.9/0.9
Imperiale [22]	2002	USA	R/CS	AA + high risk	61	(906) 40–49	11/3.5/0

CRN colorectal neoplasia, *aCRN* advanced colorectal neoplasia, *CRC* colorectal carcinoma, *P* prospective, *R/CS* retrospective and cross-sectional, *R* retrospective, *AA* average risk and asymptomatic

data is strictly collected according to protocol prospectively, regarding bias, the present study is strong. The most important limitation of our study, however, is the small number of patients. The extremely high rate of aCRNs detected during the study period, especially in the 40–49 group, had prompted us to publish our results rather prematurely.

Therefore, our study cannot provide sufficient data to assess the probable effect of the incremental increase in the level of any particular metabolic measurement on the rate of CRNs because of the limited number of patients (unpublished data). As 75% of the patients had MetS, and all were obese (BMI range: 31.1–70.5, mean BMI = 43.7), the study population was highly selected, besides being small, making meaningful data collection impossible. Although the older age group was slightly more metabolically unhealthy and a bit more hyperglycemic compared to the younger group, in a regression model, the significance of FBG and HbA1c disappears (unpublished data) and all measured factors and also MetS were always equally distributed. As we are still collecting data, once the number of patients allow, the effect of metabolic variables on the rate of CRNs will be the subject of a future report.

In conclusion, we believe that our results warrant routine SC in the 40–49-year-old morbidly obese and/or MetS patient population with average-risk and in aged > 50, SC must be enforced. Further assessments on larger number of patients are certainly needed to be able to change current recommendations which is under scrutiny. Given the fact that obesity is increasingly becoming a pandemic and still on the rise, the number of individuals that might be affected if any new recommendation prevails is actually very high emphasizing the urgency of larger, well-designed, prospective studies.

Compliance with Ethical Standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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

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