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ORIGINAL CONTRIBUTIONS

Incidence of Colorectal Adenomas After Bariatric Surgery: Pre-operative Super Morbid Obesity Is Independently Associated with Increased Risk

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Abstract

Purpose The impact of pre-bariatric surgery BMI on the incidence of colorectal adenomas in the post-operative period is unknown. Here we aim to evaluate the incidence of colorectal adenomas after bariatric surgery and to assess super morbid obesity (SMO) as a risk factor for post-operative colorectal adenomas.

Materials and Methods An inception cohort of 1639 patients that underwent bariatric surgery between 2011 and 2019 in a referral center was retrospectively analyzed. SMO was defined as BMI > 50.0 kg/m^2. Cox regression analysis was performed to assess the influence of pre-operative BMI on the primary outcome.

Results A total 381 patients (23.2% of the cohort) underwent colonoscopy and included in the analysis. Mean age was 51.1 years (± 10.6) with mean BMI of 42.2 kg/m^2 (± 6.2), and 49 patients (12.9%) had SMO. Median time to colonoscopy was 3.5 years. One hundred nine patients (28.6%) had colorectal polyps, and 38/109 (34.8%) had advanced adenoma. Two patients had colorectal cancer (CRC). Pre-procedural SMO was associated with diagnosis of colorectal polyp (HR 2.4, 95% CI 1.5–3.9, $p < 0.001$) and advanced adenomas (HR 4.2, 95% CI 2.0–8.9, $p < 0.001$) upon adjustment to previously reported risk factors of CRC.

Conclusion Pre-procedural SMO is associated with increased risk of colorectal adenomas after bariatric surgery compared to obese and morbidly obese individuals. Pre-operative BMI should be incorporated into post-operative screening plan in this population.

Keywords Colorectal polyps · Obesity · Metabolic surgery · Bariatric surgery · Colorectal cancer

Key points

- The effect of weight loss associated with bariatric surgery on the incidence of colorectal adenomas after the surgery is a matter of debate.
- In this study, we found that BMI above 50 kg/m^2 prior to surgery is associated with higher incidence of colorectal adenomas compared to patients with lower baseline BMI.
- These findings should be incorporated in the screening plan of patients that underwent bariatric surgery.

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Introduction

Colorectal cancer (CRC) is one of the most common cancers in the western world, with increased prevalence in CRC diagnosis in young individuals [1]. Obesity and the metabolic syndrome are well-known risk factors for CRC and colorectal adenomas [2, 3]. It is reported that the relative risk of the development of CRC attributable to obesity is 1.2 for men, and ranges between 1.04 and 1.13, depending on country [4, 5]. In addition, previous data well-documented an association between obesity and prevalence of both colorectal adenoma and adenoma recurrence following polypectomy [6, 7].

Bariatric procedures are an effective way to reduce weight in obese, morbidly obese, and super morbidly obese (SMO) individuals [8, 9]. Nevertheless, although more patients elect to undergo bariatric procedures as a means for sustained weight loss, there is lack of definitive evidence to show a protective effect of bariatric procedures on future development of CRC and its precursors [10]. In addition, data on the incidence of colorectal adenomas after bariatric surgery and the effect of pre-operative body mass index (BMI), and specifically SMO, on post-operative development of CRC and colorectal adenomas in patients undergoing bariatric procedure are scarce.

In this study, we aimed to define the incidence of colorectal adenomas after bariatric surgery and to assess whether pre-operative SMO is a risk factor for future, post-operative development of colorectal adenoma and CRC, even after surgery-related weight loss.

Methods

This retrospective study was approved by the local institutional review board of Rabin Medical Center in Israel (IRB) according to the local regulations (RMC-007918).

Patients

All adult patients that underwent bariatric surgery, including sleeve gastrectomy, Roux and Y gastric bypass (RYGB), one anastomosis gastric bypass (OAGB), and biliopancreatic diversion with duodenal switch (BPD-DS), in a tertiary referral center between January 2011 and December 2019 were identified retrospectively. Patients' demographic data, BMI, type 2 diabetes mellitus (DM) and hypertension prior to bariatric surgery, and smoking status were captured from the computerized patients' medical records which included hospitalization summaries, surgery reports, gastroenterology, bariatric and nutrition clinics, and outpatient visits at the primary care centers. SMO was defined as BMI > 50.0 kg/m^2 before the surgery, whereas obesity was defined as 30.0 < BMI < 39.9 and morbid obesity was defined as 40.0 < BMI < 49.9 according to previously accepted definitions [11].

Data Collection and Outcome Parameters

The primary outcome was the comparative incidence of colorectal polyps between SMO and other obese and morbidly obese populations that underwent bariatric surgery. Secondary outcome was the incidence of CRC and advanced adenomas defined as follows: any adenoma ≥ 10 mm in size, tubulovillous or villous histology regardless of size, or any adenoma with high-grade dysplasia [12].

Patient's weight, height, and BMI were captured at surgery and 1 year after the surgery. The indications for colonoscopy and full endoscopic report were identified from the electronic records. Diagnoses of colorectal polyp or CRC were identified through patients' electronic records, with access to endoscopic report and pathology report even if patients were treated outside our institution. Bowel preparation was graded as adequate and inadequate.

Percentage excess weight loss (%EWL) was defined as (weight loss/baseline excess weight) × 100, and percentage total weight loss (%TWL) was defined as (weight loss/baseline weight) × 100. Weight loss was defined as 1-year post-operative weight − baseline weight, and baseline excess weight was the baseline weight − ideal body weight [13].

Exclusion criteria included (i) patients with a personal or family history of CRC and (ii) patients with known inflammatory bowel disease (IBD).

Statistical Analysis

Statistical analysis was performed using SPSS version 25 (SPSS Inc., Chicago, IL). Categorical and continuous variables were examined using the Student *t*-test, Mann-Whitney *U* test, chi-square, or Fisher exact tests, as appropriate. A 2-sided *p*-value of less than 0.05 was considered statistically significant. The probability of polyp detection in super obese and general bariatric population was graphically displayed according to the Kaplan-Meier analysis, with a comparison of cumulative rate of events by the log-rank test. Follow-up was defined as the time from bariatric surgery to colonoscopy. A Cox proportional hazards regression analysis was conducted to assess the effect of SMO and pre-operative BMI on the primary outcome. The model contained potential confounders, a priori agreed upon, that were defined based on an assumed association on either polyp formation or on BMI. The variables included age, gender, type 2 DM and hypertension at baseline, smoking status, and %EWL. Since personal history of colorectal polyp is also a risk factor for the formation of future colorectal lesions, we performed a sensitivity analysis, excluding all patients with history of colorectal polyp of any kind.

Results

A total of 1639 patients underwent bariatric surgery between January 2011 and December 2019, 1080 patients underwent laparoscopic sleeve gastrectomy, 434 had RYGB, 104 had OAGB, and 21 patients underwent BPD-DS (65.9%, 26.5%, 6.3%, and 1.3%, respectively, Figure 1). Mean age at surgery was 44.2 years with most of the patients being females (1077 patients, 65.7%) with mean BMI of 42.4 kg/m^2 at baseline. One hundred and seventy-six individuals (10.7%) had SMO at baseline.

Of the total cohort, 402 patients (24.5%) underwent colonoscopy at least 1 year from the surgery. Twenty-one of the patients were excluded; 14 patients had family or personal history of colon cancer and 7 patients had diagnosis IBD prior

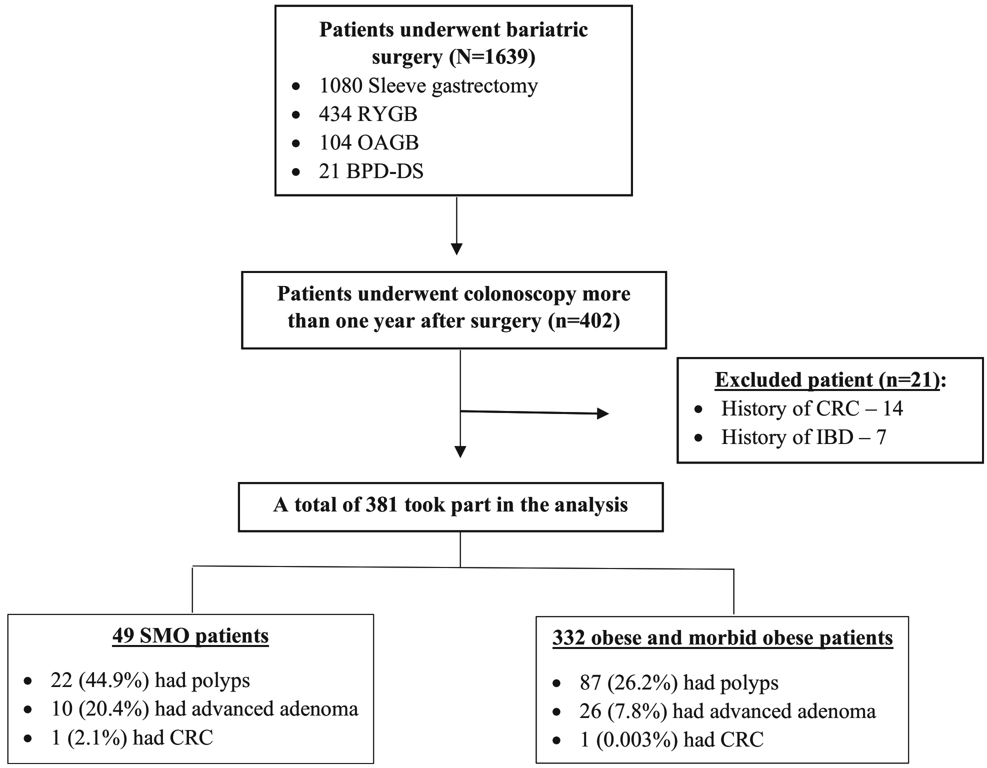

Figure 1 Study flow chart describing patients' disposition and reasons for exclusion

to colonoscopy. Correspondingly, 381 patients were part of the cohort, with mean age of 51.1 years (± 10.6) and mean BMI of 42.2 kg/m^2 (± 6.2). Forty-nine patients (12.9%) were SMO at baseline.

Baseline characteristics of the study cohort are reported in Table 1. Patients with SMO at baseline (group 1) did not differ from obese and morbidly obese patients (group 2) regarding age, gender, type of surgery, comorbidity proportions, and

Table 1 Baseline characteristics of the study cohort according to pre-operative BMI groups

	Group 1 BMI > 50 kg/m^2 (n = 49)	Group 2 BMI < 50 kg/m^2 (n = 332)	p value
Age, years (SD)	50.6 (12.3)	51.5 (10.4)	0.64
Gender—male, *n* (%)	14 (28.6)	121 (36.4)	0.33
Pre-operative BMI, kg/m^2 (SD)	53.8 (± 3.8)	40.5 (± 4.5)	< 0.001
Type 2 DM, *n* (%)	16 (32.6)	146 (44.0)	0.16
Hypertension, *n* (%)	21 (42.8)	152 (45.8)	0.76
Ever smoke, *n* (%)	7 (14.3)	69 (20.8)	0.28
Type of surgery *n* (%)			0.78
Sleeve gastrectomy	30 (61.2)	179 (53.9)	
RYGB	16 (32.7)	126 (37.9)	
OAGB	2 (4.1)	15 (4.5)	
BPD-DS	1 (2.0)	12 (3.6)	
%EWL at 12 months (SD)	− 61.8 (17.9)	− 66.8 (22.0)	0.09
%TWL at 12 months (SD)	− 33.8 (10.5)	− 28.6 (9.3)	0.01
Time to colonoscopy, years (SD)	3.3 (1.5)	3.6 (1.9)	0.31

Group 1—patients with SMO at baseline. Group 2—obese and morbidly obese individuals at baseline. The data for continuous variable includes mean (standard deviation)

BMI body mass index, *DM* diabetes mellitus, *RYGB* Roux and Y gastric bypass, *OAGB* one anastomosis gastric bypass, *BPD-DS* biliopancreatic diversion with duodenal switch, *%EWL* percent of excess weight loss. *%TWL* percent of total weight loss

%EWL. %TWL was higher in SMO compared to obese and morbidly obese individuals (− 33.8% vs. − 28.6%, $p = 0.01$). Time to colonoscopy was comparable in both groups (3.3 years in group 1 compared to 3.6 years in group 2, $p = 0.31$).

Primary Outcome

The most common indication for colonoscopy in both groups was change in bowel habits (30.6% in group 1 and 29.5% in group 2, Supplementary Material Table 1). Seven patients (1.8% of the cohort) had inadequate preparation; all were part of group 2. A total of 175 polyps were detected in 109 patients during the study (22 patients in group 1 and 87 patients in group 2, Table 2), and 52 polyps (29.7%) were advanced adenomas. Polyp size, location, histologic types, and dysplasia grades were comparable in both groups. Two patients developed CRC during follow-up (one case of CRC in each study group). When allocated according to surgery type, there was no difference in the incidence of polyps ($p = 0.42$) or advanced adenoma ($p = 0.50$, Supplementary Material).

Kaplan-Meier analysis of the primary outcome of polyp detection as a function of obesity status at baseline is shown in Figure 2A. SMO was associated with the primary outcome, with higher cumulative rates of diagnosis of colorectal polyp at 3 years in group 1 (28.2% compared to 12.3% in group 2, log-rank $p < 0.001$). Further evaluation of SMO and incidence of advanced adenomas is depicted in Figure 2B. Patients in group 1 had a higher cumulative incidence of advanced adenomas at 3 years compared to patients in group 2 (12.7% vs. 3.2%, respectively, log-rank $p < 0.001$).

Predictors of Colorectal Polyps

The results of a Cox regression analysis are shown in Table 3. SMO was associated with the primary outcome, with more than twofold increase in polyp detection (HR 2.4, 95% CI 1.5–3.9, $p < 0.001$). Additional independent predictor of the primary outcome was age at baseline. In addition, SMO was associated with higher incidence of advanced adenomas (HR 4.2, 95% CI 2.0–8.9, $p < 0.001$, Supplementary Material Table 2). Pre-operative BMI was also significantly associated with the formation of colorectal polyp (HR 1.05, 95% CI 1.02–1.08, $p < 0.001$) and advanced adenomas (HR 1.08, 95% CI 1.03–1.12, $p = 0.001$, Supplementary Material Table 3).

Sensitivity Analysis

Since prior diagnosis of colorectal lesion is a risk factor for future polyp detection, we excluded 15 patients with prior history of colorectal polyps. Six out of these 15 patients (40%) had 10 colorectal polyps found after the surgery, and two of these were advanced adenomas. In a Cox regression analysis, even upon adjustment to age, gender, type 2 DM, hypertension, smoking status, and %EWL, SMO prior to bariatric surgery was associated with higher risk of diagnosis of

Table 2 Characteristics and classification of polyps detected during follow-up

	Group 1 BMI > 50 kg/m^2 (41 polyps)	Group 2 BMI < 50 kg/m^2 (134 polyps)	p value
Total number of advanced adenomas, n (%)	13 (31.7)	39 (29.1)	0.23
Polyp size, mean, mm (SD)	8.51 (5.2)	7.28 (4.5)	0.14
Location, n (%)			0.29
Right colon	16 (39.1)	56 (41.8)	
Transverse colon	5 (12.2)	15 (11.2)	
Left colon	11 (26.8)	18 (13.4)	
Sigmoid colon and rectum	9 (21.9)	45 (33.6)	
Histologic type, n (%)			0.34
Tubular adenoma	33 (80.5)	91 (67.9)	
Villus adenoma	0 (0)	2 (1.5)	
Tubulovillous adenoma	3 (7.3)	24 (17.9)	
Sessile serrated adenoma	1 (2.4)	1 (0.7)	
Hyperplastic polyp	4 (9.7)	16 (11.9)	
Dysplasia, n (%)			0.62
Low-grade dysplasia	35 (85.4)	115 (85.8)	
High-grade dysplasia	0 (0)	2 (1.5)	
Adenocarcinoma	1 (2.4)	1 (0.7)	

Group 1—patients with SMO at baseline. Group 2—obese and morbidly obese individuals at baseline

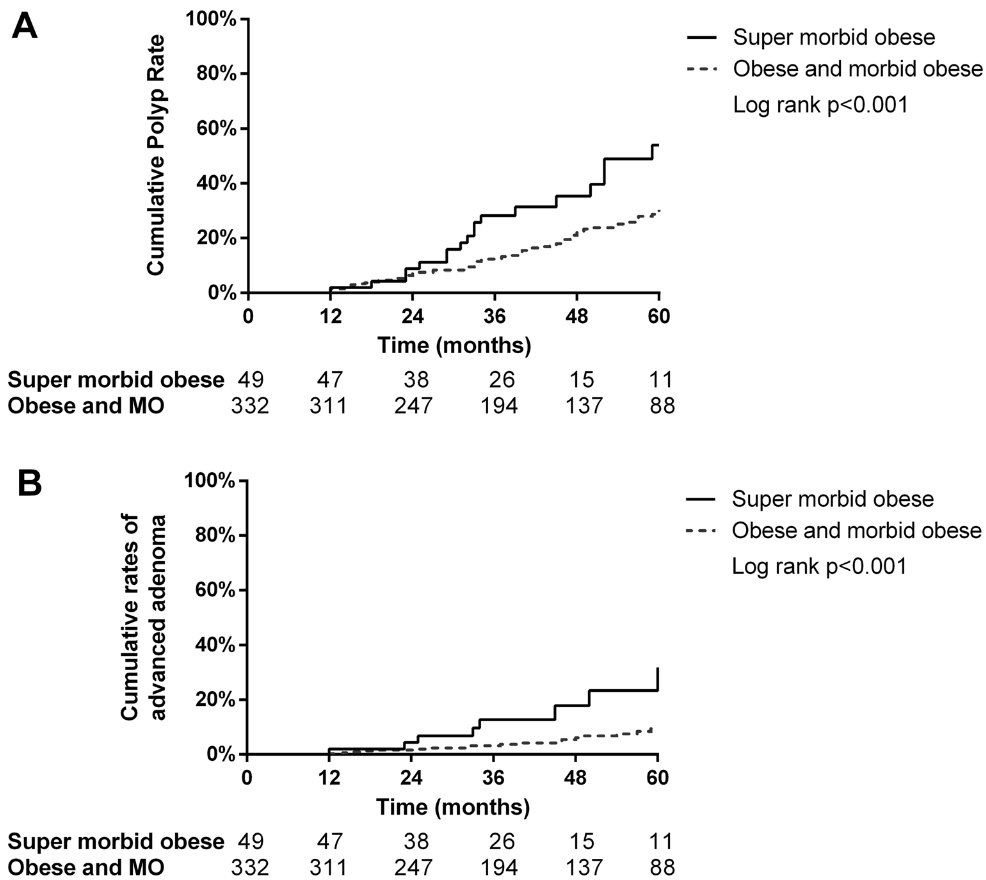

Figure 2 Risk of colorectal adenomas in super morbidly obese vs. obese and morbidly obese patients. **A** A Kaplan-Meier analysis of the primary outcome of colorectal polyps during the follow-up period, as a function of baseline BMI category. **B** A Kaplan Meier's analysis of advanced adenomas during the follow-up period, as a function of BMI category.

colorectal polyps (HR 2.3; 95% CI 1.4–3.8, p = 0.001) and advanced adenoma (HR 3.8; 95% CI 1.8–8.4, p = 0.001) compared to obese and morbidly obese individuals (Supplementary Material Table 4). Finally, we replaced %EWL with the covariate of %TWL and re-execute Cox regression analysis. This did not change the results, and SMO was associated with 2-fold increase in the diagnosis of colorectal polyp (HR 2.1, 95% CI 1.25–3.51, p = 0.004) and almost 4-fold increase in the diagnosis of advanced adenoma (HR 3.8, 95% CI 1.7–8.4, $p < 0.001$) upon adjustment to age, gender, type 2DM, HTN, and %TWL.

Table 3 Cox regression analysis: predictors of the primary endpoint of detection of polyp

	HR	95% CI	p value
Super morbid obesity	2.4	1.5–3.9	< 0.001
Age	1.03	1.01–1.04	0.04
Gender	0.9	0.6–1.4	0.86
Type 2 DM	1.4	0.8–2.1	0.17
Hypertension	0.8	0.5–1.2	0.27
Ever smoke	1.1	0.7–1.8	0.60
%EWL	0.6	0.2–1.6	0.34

DM diabetes mellitus, *%EWL* percent excess weight loss

Discussion

In this large cohort of patients that underwent bariatric surgery and colonoscopy, we found that SMO is associated with higher incidence of colonic polyps, with more than 2-fold increase in the incidence of polyps and 4-fold increase incidence in advanced adenomas, even upon adjustment of well-known CRC risk factors and metabolic factors. These findings underscore the heterogeneity of the bariatric population and suggest that SMO individuals might have excess risk of CRC compared to obese and morbidly obese populations.

Obesity and the metabolic syndrome are known risk factors for CRC and colorectal adenomas, and the biomechanism behind this phenomena is related to insulin resistance and elevated IGF-1 levels which in turn promote cell proliferation and a carcinogenesis-favorable milieu [14, 15]. Nevertheless, several studies have shown the positive and long-lasting effect of bariatric surgeries on insulin resistance, systemic inflammation, and oxidative stress [16–18] in obese, morbidly obese, and SMO individuals [19–21]. In addition, some weight-independent protective mechanisms were suggested, like influence on gut microbiome and post-operative change in the gastrointestinal anatomy.

Bariatric Surgeries and CRC

As bariatric surgeries can create a protective effect from CRC and its precursors by weight loss and metabolic improvement, the role of the long period of pre-procedural obesity in patients that underwent bariatric surgeries is not yet clear, and it is possible that its impact might last even after the surgery.

To date, only a few studies evaluated the effect of bariatric surgeries on the diagnosis of CRC and colorectal polyps after surgery, with conflicting results [10, 22–25]. None of these studies has addressed the sub-population of SMO individuals, and several studies originate from the same registry-based Swedish cohort [25, 26], which might cause a bias. Our cohort is based on heterogeneous population of bariatric patients, with prevalence of more than 10% of SMO at baseline.

Polyp Detection Rates in SMO Individuals

Previous reports have shown wide range of polyp detection rates in western population, which extends from 20 to 40% [27–29]. In our cohort, the polyp detection rates were 28.61% which corresponds with the previously reported rates; nevertheless, in the sub-population of SMO individuals, the polyp detection rates were as high as 44.89% compared to 26.20% in obese and morbidly obese cases. Although obesity is a known risk factor of CRC and colorectal adenoma [2, 3], previous studies did not address specifically the unique population of SMO individuals; hence, our observation needs to be revalidated with future prospective studies.

In addition, in our cohort, there was no association between diagnosis of polyps or advanced adenomas and the type of bariatric surgery. Although previous study demonstrated higher rates of serrated polyps after RYGB, other retrospective cohorts found no association between the type of bariatric surgery and polyp detection [24, 30].

Our study is based on a large cohort of patients that underwent bariatric surgery with a relatively long term of follow-up period. We acknowledge several limitations. First, our study is limited by its retrospective design and only minority of patients that had bariatric surgery have had colonoscopy after it. However, the relatively large cohort and the use of regression and sensitivity analysis act to minimize any bias effect. Second, there was no a priori protocol for the decision of surgery for each patient's prototype. Nevertheless, there was no difference between the type of surgery in the SMO group compared to obese and morbidly obese group which may reduce this bias. In addition, since colonoscopy prior to bariatric surgery is not indicated, we do not have pre-procedural endoscopic baseline, and we could not adjust our findings to baseline polyp status for each individual. However, we believe that our observation is still important, since many patients and caregivers might think that surgery-related weight loss convey a protective effect from colorectal neoplasia. Our findings suggest that pre-procedural BMI, and specifically pre-procedural SMO, should be incorporated into decision-making regarding colorectal polyps in post-bariatric surgery population. Finally, most patients that underwent colonoscopy were symptomatic during the examination, and the number of screening colonoscopy is relatively small. Nevertheless, indications for colonoscopy were comparable in both groups.

In conclusion, SMO prior to bariatric surgery is associated with higher incidence of polyps compared to obese and morbidly obese bariatric population. Our findings should be incorporated in the screening plan in this bariatric population and prompt colonoscopy in symptomatic individuals. Further prospective studies are needed in order to understand the biomechanism of this observation and fully validate preoperative BMI role in polyp formation and CRC detection.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11695-021-05567-8.

Declarations

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

For this type of study formal consent is not required.

Conflict of Interest The authors declare no competing interests.

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