Original article

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Body mass index and complications following major gastrointestinal surgery: a prospective, international cohort study and meta-analysis

EuroSurg Collaborative[1]

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Abstract

Aim Previous studies reported conflicting evidence on the effects of obesity on outcomes after gastrointestinal surgery. The aims of this study were to explore the relationship of obesity with major postoperative complications in an international cohort and to present a meta-analysis of all available prospective data.

Methods This prospective, multicentre study included adults undergoing both elective and emergency gastrointestinal resection, reversal of stoma or formation of stoma. The primary end-point was 30-day major complications (Clavien–Dindo Grades III–V). A systematic search was undertaken for studies assessing the relationship between obesity and major complications after gastrointestinal surgery. Individual patient meta-analysis was used to analyse pooled results.

Results This study included 2519 patients across 127 centres, of whom 560 (22.2%) were obese. Unadjusted major complication rates were lower in obese *vs* normal weight patients (13.0% *vs* 16.2%, respectively), but this did not reach statistical significance ($P = 0.863$) on multivariate analysis for patients having surgery for either malignant or benign conditions. Individual patient meta-analysis demonstrated that obese patients undergoing surgery for malignancy were at increased risk of major complications (OR 2.10, 95% CI 1.49–2.96, $P < 0.001$), whereas obese patients undergoing surgery for benign indications were at decreased risk (OR 0.59, 95% CI 0.46–0.75, $P < 0.001$) compared to normal weight patients.

Conclusions In our international data, obesity was not found to be associated with major complications following gastrointestinal surgery. Meta-analysis of available prospective data made a novel finding of obesity being associated with different outcomes depending on whether patients were undergoing surgery for benign or malignant disease.

Keywords Postoperative complications, obesity, digestive tract, gastrointestinal tract, body mass index, body weight

What does this paper add to the literature?
There is conflicting evidence regarding the impact of obesity after gastrointestinal surgery. Our international data did not identify obesity as an independent risk factor for postoperative complications. Individual patient meta-analysis with previous data identified obesity to be associated with increased risk in cancer surgery but decreased risk in benign surgery.

Introduction

Obesity has reached epidemic levels in high income countries, with its prevalence expected to increase further over the coming decades [1]. With one-third of patients undergoing gastrointestinal surgery in the UK being obese [2], an understanding of the relationship between obesity and surgical outcomes is needed to optimize preoperative assessment and perioperative care. Whilst obesity is a recognized risk factor for cardiovascular and metabolic disease, there is conflicting evidence on its impact on postoperative complications after gastrointestinal surgery [3].

There is wide variation on the impact of obesity after gastrointestinal surgery in published reports. In some patient groups, no association [4,5] is identified between obesity and postoperative complications, whereas other studies have identified obesity as a risk factor for increased postoperative complications [6,7]. An 'obesity paradox' has been proposed suggesting that obese patients

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may be at decreased risk of complications in some settings [8]. Most previous evidence relies on retrospective analyses of registry data, which are limited by a high risk of bias. Inconsistent and selective outcome reporting are also key challenges in interpreting these results.

The primary aim of this study was to explore prospectively the relationship between obesity and major postoperative complications after gastrointestinal surgery in an international cohort, with a secondary aim to identify and meta-analyse all available prospective data regarding the relationship between obesity and major postoperative complications.

Method

Study design

This was a prospective, multicentre, observational study delivered by an established network of students and trainees [9]. A systematic search for previous evidence, followed by individual patient meta-analysis of pooled data, was also performed. The results are reported with consideration to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) and Preferred Reporting for Systematic Reviews and Meta-Analyses (PRISMA) statements [10,11].

EuroSurg Collaborative

The EuroSurg Collaborative is a medical-student- and surgical-trainee-led research network. The collaborative was established in September 2015 at the tenth meeting of the European Society of Coloproctology, by delegates representing six European countries [9]. Inspired by the medical student collaborative model developed by the Student Audit and Research in Surgery (STARSurg) network in the UK [12], the group sought to engage students and trainees across Europe in multicentre surgical research.

Protocol development and dissemination

The pre-specified protocol for this prospective, multicentre observational study was developed based on the STARSurg DISCOVER protocol [13]. Medical students and surgical trainees were invited to work together in their local surgical units, under supervision from a senior surgeon, to collect data over a maximum of three predefined 14-day data collection periods in February–May 2016. Any hospital offering emergency or elective gastrointestinal resection in the Czech Republic, Republic of Ireland, Italy, the Netherlands, Spain, Turkey and the UK was eligible.

Ethics and study approval

Across the seven participating countries, local collaborators and their supervisors registered the study according to national and institutional regulations. In some countries, this required formal research ethics approval with written patient consent. In the UK, this observational study was registered as a re-audit of DISCOVER [2]. At all centres, approval was gained to collect anonymized patient data using a secure online Research Electronic Data Capture (REDCap) system [14].

Inclusion criteria

Adult patients aged 18 years or older undergoing gastrointestinal resection, reversal of ileostomy or colostomy, or creation of a stoma as a primary procedure were included. Both elective and emergency procedures using open, laparoscopic or robotic operative approaches were eligible. Patients undergoing appendicectomy alone were excluded. As the primary aim was to assess the effect of being overweight or obese, underweight patients [body mass index (BMI) < 18.5 kg/m^2] were excluded.

Outcome measures

The primary outcome measure was the 30-day major adverse event rate, defined as Clavien–Dindo Grade III–V complications [15]. These include the need for unplanned surgical, endoscopic or radiological procedures under local or general anaesthetic (Grade III), the need for organ support in an intensive care setting or stroke (Grade IV) and death (Grade V). The secondary outcome was 30-day mortality.

Explanatory variables

The main explanatory variable was preoperative BMI, calculated as weight divided by the square of height. Patients were stratified by BMI into three groups: normal weight (BMI 18.5–24.9 kg/m^2), overweight (BMI 25.0–29.9 kg/m^2) and obese (BMI ≥ 30.0 kg/m^2). Preoperative variables were collected to risk adjust clinical outcomes. These included demographic parameters such as age and sex as well as American Society of Anesthesiologists (ASA) and Revised Cardiac Risk Index scores [16].

Data validation

A selection of participating hospitals identified independent data validators who had not been involved in the

original data collection. These validators assessed their site's case ascertainment by independent review of theatre logbooks and operating lists. The case ascertainment rate was the proportion of all eligible patients who had been included in the original data collection. Validators also reviewed the data submitted from their site to determine data accuracy. This was based on validation of the primary outcome (30-day major adverse events) and 11 other predefined data fields (age; gender; ASA grade; history of ischaemic heart disease, congestive heart failure, cerebrovascular disease, insulin dependent diabetes or chronic kidney disease; urgency of operation; pathology; operation performed). The data accuracy rate was the proportion of validated data fields that had been correctly completed by the original data collection team.

Systematic review

A systematic search of bibliographical databases (PubMed, Scopus and Web of Science) was undertaken on 30 September 2017 by two independent reviewers to identify previous studies investigating the relationship between BMI and major postoperative complications after gastrointestinal surgery (Table S1). Eligible studies involved adult patients undergoing oesophagogastric, colorectal or liver surgery using any surgical approach. Case–control studies, cohort studies and randomized controlled trials whose primary aim was to compare outcomes between normal weight *vs* overweight and obese patients using the standardized Clavien–Dindo classification for complications were included. Study abstracts were initially screened for suitability followed by inspection of full text papers. Additional studies, not included in the database search, were identified by searching the reference lists of retained articles.

Statistical analysis

Simple summary statistics were used to summarize characteristics and outcomes across BMI categories, with categorical variables expressed as percentages and continuous variables as mean averages alongside the corresponding standard deviation (SD). Differences between categorical demographic groups were tested using the Kruskal–Wallis test, Welch's t test was used for continuous data, and the chi-squared test for proportions. Two-sided statistical significance was defined as $P < 0.05$ *a priori*. To account for centre level variation, multilevel models were constructed using clinically plausible explanatory variables [11], with patient level factors considered as a level 1 fixed effects and hospital as a level 2 random effect. First order interactions were explored within the model, including interactions between indication (malignant or benign) and BMI which have been previously described [2]. Effect estimates are presented as odds ratios with 95% confidence intervals and P values to indicate statistical significance.

To assess the results of this study in relation to previous work, meta-analysis was pre-planned for all prospective studies identified in the systematic review; an individual patient level meta-analysis was performed. Only the DISCOVER study met the criteria to be included in the meta-analysis. Individual data from the DISCOVER study for patients matching the EuroSurg study's inclusion criteria were pooled with the EuroSurg dataset. Briefly, a mixed-effects model was fitted with patient level explanatory variables as level 1 fixed effects, hospital as level 2 random effects and study as a level 3 random effect. Models were fitted and interactions checked as above. All statistical analyses were performed using R 3.2.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Data were collected across 35 hospitals in the Netherlands, 30 hospitals in Spain, 23 hospitals in Italy, 20 hospitals in Turkey, 14 hospitals in the UK, four hospitals in the Republic of Ireland and one hospital in the Czech Republic. Following exclusion of ineligible patients, a total of 2519 patients were included in the analysis (Fig. 1).

Data validation

Independent data validation was performed in 74 centres across six countries. The case ascertainment rate was 96.6% (1508/1561). Amongst the 17 052 data fields that were validated, the overall data accuracy rate was 99.2%.

Demographics

Overall, 41.4% (1044/2519) patients had a normal BMI, 36.3% (915/2519) were overweight and 22.2% (560/2519) were obese. In the six countries that entered more than 50 patients into the study, rates of obesity varied from 17.7% to 30.9% (Table 1). Overall, overweight and obese patients were older than normal weight patients (Table 2). Overweight patients were more likely to be men, whereas obese patients were more likely to have Grade III–V ASA. There was no difference between the groups in the Revised Cardiac Risk Index scores. Malignancy was most commonly the

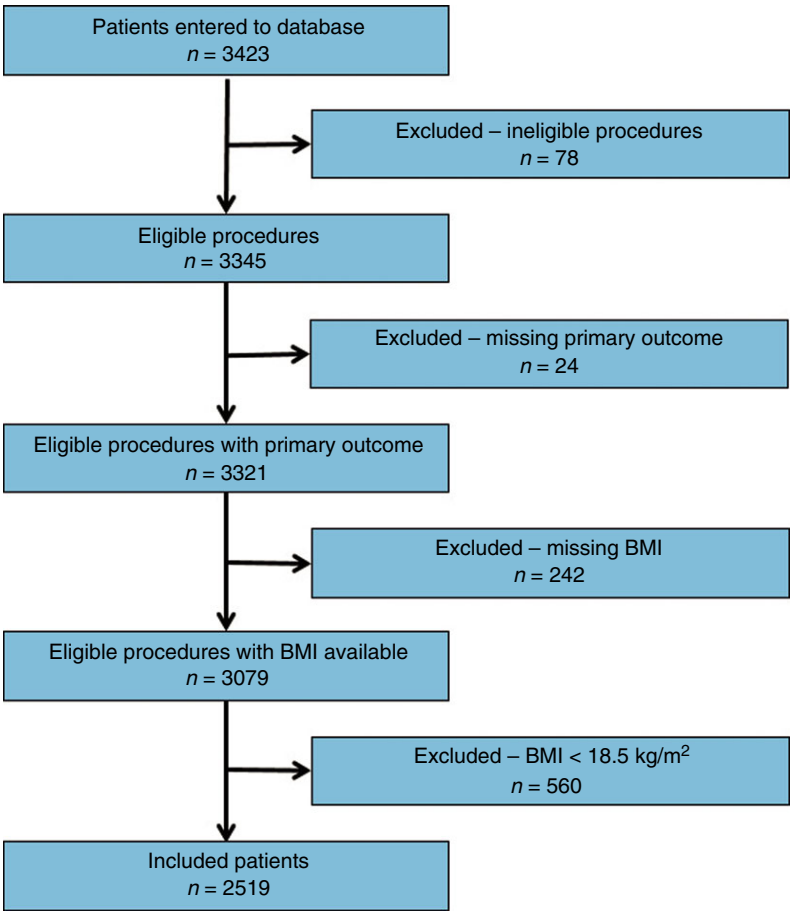


Figure 1 Flowchart of patient inclusion in the observational study.

indication for surgery for overweight and obese patients, whereas a greater proportion of normal weight patients underwent surgery for inflammatory bowel disease. Whilst there was no difference between groups in the proportion of procedures completed on an emergency basis, overweight patients were more likely to undergo open surgery than either normal weight or obese patients. Overweight and obese patients more frequently underwent gastrointestinal resection than normal weight patients (Table 3).

Postoperative major complications

The overall unadjusted 30-day major complication rate was 14.5% (365/2519). This varied from 13.0% (73/560) for obese patients to 16.2% (169/1044) for normal weight patients (Table 4). Overall unadjusted 30-day mortality was 2.4%. Univariate analysis (Table 5) identified that overweight (OR 0.80, 95% CI 0.62–1.03, $P = 0.089$) and obese (OR 0.78, 95% CI 0.57–1.01, $P = 0.093$) patients overall were not at an increased risk of 30-day major complications. Multilevel modelling found that amongst patients undergoing surgery for malignancy neither overweight (OR 0.73, 95% CI 0.43–1.25, $P = 0.257$) nor obese (OR 1.06, 95% CI 0.56–1.99, $P = 0.863$) patients were at increased risk of serious complications.

Table 1 Prevalence of overweight and obese patients by country in the EuroSurg cohort study.

Country	Normal weight (%) ($N = 1044$)	Overweight (%) ($N = 915$)	Obese (%) ($N = 560$)
A	0 (0.0)	0 (0.0)	30 (5.4)
B	28 (2.7)	19 (2.1)	21 (3.8)
C	182 (17.4)	116 (12.7)	64 (11.4)
D	290 (27.8)	256 (28.0)	137 (24.5)
E	176 (16.9)	220 (24.0)	113 (20.2)
F	153 (14.7)	122 (13.3)	72 (12.9)
G	215 (20.6)	182 (19.9)	123 (22.0)

A, Czech Republic; B, Republic of Ireland; C, Italy; D, Netherlands; E, Spain; F, Turkey; G, United Kingdom.

Table 2 Patient demographics in the EuroSurg cohort study split by body mass index group.

	Normal weight ($N = 1044$)	Overweight ($N = 915$)	Obese ($N = 560$)	P
Age, mean (SD)	62.1 (16.3)	65 (13.2)	63.9 (12.2)	0.001
Sex (%)				
Male	561 (53.7)	577 (63.1)	298 (53.2)	< 0.001
Female	483 (46.3)	338 (36.9)	262 (46.8)	
Body mass index (kg/m^2), mean (SD)	22.4 (1.7)	27.1 (1.4)	34 (5.1)	< 0.001
ASA grade (%)				
I	150 (14.4)	108 (11.8)	35 (6.2)	< 0.001
II	579 (55.5)	521 (56.9)	299 (53.4)	
III	257 (24.6)	245 (26.8)	198 (35.4)	
IV	50 (4.8)	31 (3.4)	22 (3.9)	
V	2 (0.2)	2 (0.2)	1 (0.2)	
Missing	6 (0.6)	8 (0.9)	5 (0.9)	
Revised Cardiac Risk Index (%)				
No predictors	819 (78.4)	688 (75.2)	401 (71.6)	0.086
One predictor	170 (16.3)	166 (18.1)	121 (21.6)	
Over 2 predictors	51 (4.9)	58 (6.3)	37 (6.6)	
Missing	4 (0.4)	3 (0.3)	1 (0.2)	
Urgency (%)				
Elective	866 (83.0)	776 (84.8)	490 (87.5)	0.134
Emergency	177 (17.0)	139 (15.2)	70 (12.5)	
Missing	1 (0.1)	0 (0.0)	0 (0.0)	
Operative approach (%)				
Open	621 (59.5)	497 (54.3)	325 (58.0)	0.014
Laparoscopic/robotic	423 (40.5)	418 (45.7)	233 (41.6)	
Missing	0 (0.0)	0 (0.0)	2 (0.4)	
Smoking status (%)				
Non-smoker	899 (86.1)	779 (85.1)	466 (83.2)	0.382
Current smoker	145 (13.9)	135 (14.8)	94 (16.8)	
Missing	0 (0.0)	1 (0.1)	0 (0.0)	
Indication for surgery (%)				
Cancer	637 (61.0)	619 (67.7)	387 (69.1)	< 0.001
Inflammatory bowel disease	125 (12.0)	59 (6.4)	37 (6.6)	
Other benign disease	282 (27.0)	237 (25.9)	136 (24.3)	
Procedure type (%)				
Minor GI operation	218 (20.9)	147 (16.1)	93 (16.6)	0.012
Major GI resection	826 (79.1)	768 (83.9)	467 (83.4)	

Systematic review

A total of six studies [2,17–21] were identified in the systematic review that presented primary data comparing major postoperative complications between healthy weight *vs* overweight and obese patients following gastrointestinal surgery (Fig. 2). Five studies were retrospective, single centre studies that only included elective patients, leaving one prospective multicentre study, the DISCOVER study (Table 6). Of the four studies reporting outcomes in patients undergoing surgery for malignancy (Table 7), only the DISCOVER study found obesity to be an independent risk factor on multivariate analysis for major complications [2], with the other three studies finding no association [19–21]. Only the DISCOVER study reported outcomes in the sub-group of patients undergoing surgery for benign indications, finding no relationship between obesity and major complications. Two studies did not stratify patient outcomes according to whether the indication for surgery was benign or malignant; one found obesity to be independently associated with major complications [17], whilst the other study found no such association [18].

Individual patient data meta-analysis

Individual patient meta-analysis was performed on a combined DISCOVER and EuroSurg study dataset (Table 8). From the multilevel models, independent

Table 3 Procedures included in the EuroSurg cohort study split by body mass index group.

Operation	Normal weight (%) ($N = 1044$)	Overweight (%) ($N = 915$)	Obese (%) ($N = 560$)
Oesophagogastric resections			
Oesophagogastrectomy	9 (0.9)	9 (1.0)	6 (1.1)
Total oesophagectomy	14 (1.3)	6 (0.7)	9 (1.6)
Partial oesophagectomy	6 (0.6)	9 (1.0)	5 (0.9)
Total gastrectomy	29 (2.8)	25 (2.7)	11 (2.0)
Partial gastrectomy	42 (4.0)	35 (3.8)	20 (3.6)
Gastroduodenectomy	3 (0.3)	2 (0.2)	0 (0.0)
Small bowel resections			
Total excision of duodenum	0 (0.0)	1 (0.1)	0 (0.0)
Partial excision of duodenum	4 (0.4)	0 (0.0)	0 (0.0)
Total jejunectomy	2 (0.2)	0 (0.0)	0 (0.0)
Partial jejunectomy	15 (1.4)	12 (1.3)	6 (1.1)
Ileectomy	48 (4.6)	35 (3.8)	23 (4.1)
Ileo-caecal/ileo-colic resection	39 (3.7)	21 (2.3)	11 (2.0)
Colonic resections			
Right hemicolectomy	172 (16.5)	183 (20.0)	101 (18.0)
Transverse colectomy	6 (0.6)	5 (0.5)	2 (0.4)
Left hemicolectomy	44 (4.2)	55 (6.0)	28 (5.0)
Sigmoid colectomy	99 (9.5)	112 (12.2)	52 (9.3)
Rectosigmoidectomy	37 (3.5)	34 (3.7)	34 (6.1)
Subtotal colectomy	33 (3.2)	26 (2.8)	17 (3.0)
Total colectomy	20 (1.9)	12 (1.3)	9 (1.6)
Rectal resections			
Abdominoperineal excision	27 (2.6)	28 (3.1)	24 (4.3)
Proctectomy	14 (1.3)	14 (1.5)	7 (1.2)
Anterior resection	108 (10.3)	105 (11.5)	79 (14.1)
Panproctocolectomy	7 (0.7)	5 (0.5)	1 (0.2)
Completion proctocolectomy and IPAA	11 (1.1)	6 (0.7)	4 (0.7)
Formation/reversal of stoma			
Formation of colostomy	53 (5.1)	33 (3.6)	18 (3.2)
Formation of ileostomy	29 (2.8)	16 (1.7)	13 (2.3)
Closure of colostomy	38 (3.6)	33 (3.6)	16 (2.9)
Closure of ileostomy	88 (8.4)	61 (6.7)	42 (7.5)
Other procedures			
Other unlisted procedure	46 (4.4)	32 (3.5)	22 (3.9)
Missing	1 (0.1)	0 (0.0)	0 (0.0)

IPAA, ileal pouch anal anastomosis.

predictors for increased major postoperative complications included male gender, ASA Grades III–V and emergency timing of surgery. In the overall dataset, being overweight (OR 0.81, 95% CI 0.64–1.02, $P = 0.070$) was not associated with any change to risk of major postoperative complications compared to normal weight patients, whereas being obese (OR 0.59, 95% CI 0.46–0.75, $P < 0.001$) was overall associated with a reduced likelihood of complications. Amongst patients undergoing surgery for malignancy, being overweight (OR 1.30, 95% CI 0.95–1.79, $P = 0.102$) was not associated with a higher risk of major postoperative complications, but obese patients were at increased risk (OR 2.10, 95% CI 1.49–2.96, $P < 0.001$). Overweight patients undergoing surgery for benign indications had no change in their risk of major complications (OR 0.81, 95% CI 0.64–1.02, $P = 0.070$), whereas obese patients were at decreased risk of complications compared to normal weight patients (OR 0.59, 95% CI 0.46–0.75, $P < 0.001$).

Discussion

This prospective international cohort study explored the relationship between obesity and major postoperative complications after gastrointestinal surgery. Following

Table 4 Unadjusted 30-day outcomes by body mass index in the EuroSurg cohort study.

	Normal weight ($N = 1044$)	Overweight ($N = 915$)	Obese ($N = 560$)	P
Major complications (Clavien–Dindo Grades III–V) (%)				
No	875 (83.8)	792 (86.6)	487 (87.0)	0.123
Yes	169 (16.2)	123 (13.4)	73 (13.0)	
30-day mortality (%)				
Alive	1021 (97.8)	886 (96.8)	552 (98.6)	0.092
Died	23 (2.2)	29 (3.2)	8 (1.4)	

adjustment, no difference was found between complication rates in normal weight, overweight or obese patients. However, individual patient level meta-analysis of prospective studies showed that in patients undergoing cancer surgery obesity was associated with an increased risk of major complications, whereas in patients undergoing surgery for benign indications obesity was associated with decreased risk.

The physiology of obesity and its impact on postoperative recovery is complex. Excess secretion of adipocytokine and macrophage recruitment are features of obesity-related systemic inflammation which lead to low-grade chronic inflammation [22]. Even in early disease

Table 5 EuroSurg cohort study univariate and multilevel analyses with major complications (Clavien–Dindo Grades III–V) as outcome.

	Univariable		Multilevel	
	Odds ratio	P	Odds ratio	P
BMI				
Normal	1.00 (reference)	–	1.00 (reference)	–
Overweight	0.80 (0.62–1.03)	0.089	0.88 (0.59–1.31)	0.525
Obese	0.78 (0.57–1.04)	0.093	0.74 (0.45–1.22)	0.237
Age	1.01 (1.00–1.02)	0.079	1 (0.99–1.01)	0.847
Sex				
Male	1.00 (reference)	–	1.00 (reference)	–
Female	0.70 (0.55–0.88)	0.002	0.65 (0.51–0.83)	0.001
Previous surgery				
Yes	1.00 (reference)	–	1.00 (reference)	–
No	0.89 (0.71–1.11)	0.292	0.85 (0.66–1.08)	0.186
Smoking				
Non-smoker	1.00 (reference)	–	1.00 (reference)	–
Current smoker	1.26 (0.93–1.69)	0.120	1.3 (0.96–1.78)	0.094
ASA grade				
I–II	1.00 (reference)	–	1.00 (reference)	–
III–V	2.02 (1.61–2.53)	< 0.001	1.81 (1.38–2.38)	< 0.001
Revised Cardiac Risk Index score				
0	1.00 (reference)	–	1.00 (reference)	–
1	1.17 (0.88–1.55)	0.277	0.92 (0.67–1.26)	0.584
2	1.79 (1.17–2.67)	0.006	1.23 (0.77–1.96)	0.383
Diagnosis				
Benign	1.00 (reference)	–	1.00 (reference)	–
Malignant	0.82 (0.66–1.03)	0.092	1.02 (0.7–1.48)	0.932
Operative urgency				
Elective	1.00 (reference)	–	1.00 (reference)	–
Emergency	2.69 (2.07–3.48)	< 0.001	2.49 (1.85–3.35)	< 0.001
Operative approach				
Open	1.00 (reference)	–	1.00 (reference)	–
Laparoscopic/robotic	1.09 (0.87–1.36)	0.474	1.07 (0.84–1.35)	0.592
Interaction variables				
BMI group by diagnosis				
Overweight by malignancy	–	–	0.73 (0.43–1.25)	0.257
Obese by malignancy	–	–	1.06 (0.56–1.99)	0.863

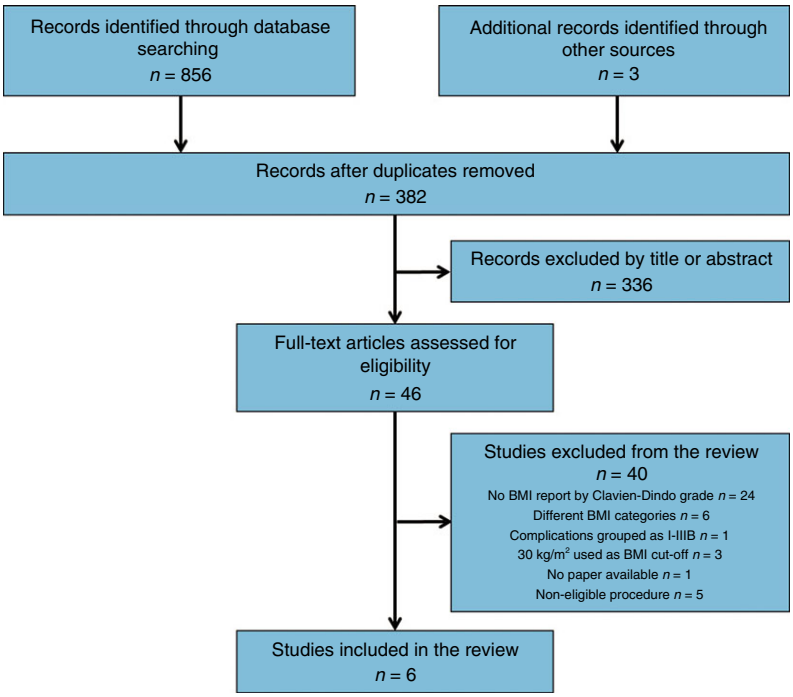


Figure 2 Flowchart of study inclusion in the systematic review.

Table 6 Studies included in the systematic review.

Study, first author	Country	Study type	Patient population	Indication		Urgency	
				Benign	Malignant	Elective	Emergency
Balzan [17]	France	Retrospective single centre	Liver resection	219	465	684	0
Pata [21]	Italy	Retrospective single centre	Gastrectomy for gastric cancer	0	191	191	0
STARSurg [2]	UK	Prospective multicentre	Gastrointestinal and liver surgery	5442	2129	4295	3038
Tanaka [19]	Japan	Retrospective single centre	Hepatic resection for HCC	0	202	202	0
Wiggans [18]	UK	Retrospective single centre	Liver resection	40	464	504	0
Xia [20]	China	Retrospective single centre	Laparoscopic colorectal cancer resection	0	527	527	0

HCC, hepatocellular carcinoma.

stages visceral fat surrounding diseased non-malignant bowel, such as in Crohn's disease patients, has been shown to contain localized inflammation [23–25]. These complex relationships between obesity and inflammation may explain the different associations in patients undergoing cancer surgery and those having surgery for benign conditions. Distinct preoperative patient pathways for benign and malignant disease may also contribute to these differences. For example, cancer patients' risk of complications may be increased by neoadjuvant chemoradiotherapy, whereas inflammatory bowel disease patients may be at higher risk if immunosuppressant drugs have been administered in the preoperative and perioperative periods. Although the exclusion of these factors from our models may be a limitation, this ensured we followed a predefined statistical plan based on the model previously developed in the DISCOVER study.

Of the studies identified in our systematic review, five focused on well-defined groups of elective patients [17–21], limiting their generalizability. Only the DISCOVER study reported prospective data, finding in a cohort of 7965 patients across 163 UK and Irish

Table 7 Major complication (Clavien–Dindo Grades III–V) rates reported in studies included in the systematic review.

Study, first author	Normal weight, %	Overweight, %	Obese, %
Balzan [17]	5.8 (21/359)	9.6 (22/228)	13.4 (13/97)
Pata [21]	11.1 (7/63)	23.3 (17/73)	12 (3/25)
STARSurg [2]	12.1 (307/2545)	12 (322/2673)	10.2 (279/2747)
Tanaka [19]	23.9 (33/138)	20 (11/55)	11.1 (1/9)
Wiggans [18]	16.8 (28/167)	20.1 (42/209)	19.5 (24/123)
Xia [20]	5.9 (22/371)	5.6 (8/142)	14.3 (2/14)

Table 8 Individual patient data meta-analysis with major complications (Clavien–Dindo Grades III–V) as outcome.

	Univariable model		Multivariate model	
	Odds ratio	*P*	Odds ratio	*P*
Age	1.01 (1.01–1.02)	< 0.001	1.00 (1.00–1.01)	0.079
Sex				
Male	1.00 (reference)	–	1.00 (reference)	–
Female	0.69 (0.60–0.78)	< 0.001	0.72 (0.62–0.82)	< 0.001
ASA grade				
I–II	1.00 (reference)	–	1.00 (reference)	–
III–V	2.13 (1.87–2.43)	< 0.001	1.79 (1.54–2.07)	< 0.001
Revised Cardiac Risk Index score				
0	1.00 (reference)	–	1.00 (reference)	–
1	1.32 (1.13–1.54)	0.001	1.06 (0.89–1.25)	0.522
2	1.82 (1.45–2.27)	< 0.001	1.23 (0.96–1.57)	0.102
Diagnosis				
Benign	1.00 (reference)	–	–	–
Malignant	1.05 (0.93–1.20)	0.424	0.86 (0.68–1.08)	0.196
Operative urgency				
Elective	1.00 (reference)	–	1.00 (reference)	–
Emergency	2.33 (2.02–2.69)	< 0.001	2.19 (1.86–2.58)	< 0.001
Body mass index				
Normal weight	1.00 (reference)	–	–	–
Overweight	0.93 (0.80–1.08)	0.359	–	–
Obese	0.78 (0.66–0.92)	0.003	–	–
Interaction variables				
BMI group by diagnosis				
Overweight by malignancy	–	–	1.30 (0.95–1.79)	0.102
Obese by malignancy	–	–	2.10 (1.49–2.96)	< 0.001
Overweight by benign	–	–	0.81 (0.64–1.02)	0.070
Obese by benign	–	–	0.59 (0.46–0.75)	< 0.001

centres [2] that obesity was independently associated with an increased risk of major complications in overweight and obese patients undergoing surgery for malignancy, but not for benign indications [2]. The current study's primary data failed to identify any association between obesity and major complications. This may be because it captured a broader and more heterogeneous international population, with lower rates of obesity than in DISCOVER's predominantly UK patients. Our primary data may also be underpowered to identify differences in complication rates between the BMI groups. The pooling by pre-planned meta-analysis attempted to address this limitation and identified a novel differential relationship between obesity and major complications, in that obese patients undergoing cancer surgery are at increased risk of major

complications whereas obese patients undergoing surgery for benign indications are at decreased risk compared to normal weight patients.

The differential relationships identified in patients with malignancy and benign disease may also be partly related to selection biases. Surgery in high risk patients with benign conditions may be delayed or avoided altogether, whereas most cancer patients require timely surgical intervention, regardless of comorbid status. Whilst preoperative weight loss and pre-habilitation might offer a means of improving obese patients' outcomes, implementation of these programmes is complicated by the strict targets set by some health services for commencing definitive cancer treatment.

A limitation of this study was the reliance on the snapshot of BMI taken at the time of surgery, with no data collected on preoperative weight loss for example. Unintentional preoperative weight loss is associated with increased cardiac complications, ventilator dependency and mortality [26]. Inclusion of preoperative weight loss may have enhanced our models, but it was not feasible to collect these data within the constraints of this observational, student-driven study. Furthermore, whilst BMI is in routine clinical use because it is based on readily available non-invasive measurements, a meta-analysis of 32 000 patients across 32 studies found a pooled sensitivity of 0.42 for the commonly applied BMI cut-off of $\geq$ 30 kg/m^2 for obesity [27], suggesting that BMI might fail to identify more than half of patients with high body fat. Moreover, an inverse relation has been observed between BMI performance and age, with BMI being less reliable in older individuals [28], who may exhibit 'sarcopenic obesity' whereby lean mass is lost, with increased inter/intramuscular fat [29]. A further limitation of BMI is that it does not account for the relative distribution of visceral and subcutaneous fat. Although some studies have identified that only patients with high visceral fat are at significantly increased risk of complications, there is conflicting evidence regarding the significance of the visceral to subcutaneous fat ratio [30,31].

In the UK, the STARSurg model of student-driven research increases students' understanding and confidence in clinical research [12], but in many countries research opportunities for medical students are limited [32]. The EuroSurg Collaborative was founded with the aim of engaging students across Europe in high quality research [9]; it has already catalysed the foundation by Italian trainees of an independent trainee research network in Italy [33]. The next EuroSurg study [34] will stimulate the development of further research networks across Europe.

Conclusion

Although in our international cohort study there was no association between obesity and postoperative complications following gastrointestinal surgery, we made a novel finding of obesity being associated with different outcomes depending on underlying pathology. In patients undergoing cancer surgery obesity was associated with an increased risk of major complications, whereas in patients undergoing surgery for benign indications it was associated with decreased risk. Further research is required to understand the underlying pathophysiology of this effect, in order to inform improved management and preoperative optimization of patients undergoing surgery.

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Ethical approval

Ethical approval was obtained from local ethical committees or institutional review boards by each local team in accordance with country-specific regulations.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:
Appendix S1. Collaborators.
Table S1. PubMed search strategy.