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Review

Concomitant cholecystectomy during bariatric surgery: The jury is still out

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ABSTRACT

Background: We sought to compare clinical outcomes of concomitant cholecystectomy during four different types of bariatric surgery vs. bariatric surgery alone.
Data sources: A systematic literature search of PubMed and Cochrane databases was conducted in accordance with the PRISMA guidelines. Thirty studies were included in this study, reporting data on 13,675 patients. Our findings suggest a higher rate of anastomotic leak/stricture in the case of concomitant cholecystectomy with gastric bypass compared to those who had gastric bypass alone. The scarcity of data concerning sleeve gastrectomy, adjustable gastric banding and biliopancreatic diversion prevented us from quantifying possible difference of outcomes between the examined treatment groups.
Conclusions: This study highlights the small number and poor quality of available studies referring to the role of simultaneous cholecystectomy during bariatric surgery.

Introduction

Obesity pandemic is one of the most serious public health issues of our century.[1] The high prevalence of obesity worldwide has led to a more invasive treatment approach resulting, thus, in the rapid inflation of bariatric surgery to such an extent that it is currently considered the gold standard of treatment for morbid obesity.[1] Bariatric surgical procedures, namely Roux en Y gastric bypass (RYGB), laparoscopic sleeve gastrectomy (LSG), biliopancreatic diversion with duodenal switch (BPD-DS), and laparoscopic adjustable gastric band (LAGB) apart from ameliorating the "weight problem" per se, are also beneficial in minimizing comorbidities for the bariatric patient.[2]

Despite this ideal portrait encircling the term "bariatric surgery", it is well documented that the severe loss of weight in most surgically treated patients is associated with an increased risk in developing cholelithiasis.[3] Namely, the formation of gallstones after a bariatric surgery exceeds 35% in the first year.[4] Routine administration of ursodeoxycholic acid, simultaneous cholecystectomy during a bariatric surgery procedure and performance of cholecystectomy following a bariatric surgery operation are the main ways these patients are being treated.[5]

Although performing concomitant cholecystectomy (CC) has been adopted by a part of the surgical community, no specific guidelines exist to date. We sought to systematically review the literature in order to compare clinical outcomes of concomitant cholecystectomy during bariatric surgery to bariatric surgery alone with the aim to answer the question whether concomitant cholecystectomy during bariatric surgery is beneficial to bariatric patients.

Materials and methods

Search strategy and article selection

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and in line with the protocol agreed by all authors.[6] Eligible studies were identified by a

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meticulous search of PubMed and Cochrane bibliographic databases (last search: September 19th, 2016). Two investigators (G.M. and I.D.) working independently executed the search using the following MeSH-term algorithm: "(bariatric OR obesity surgery OR metabolic surgery OR sleeve gastrectomy OR gastric bypass OR biliopancreatic diversion OR adjustable gastric band OR LSG OR RYGB OR BPD) AND (cholecystectomy OR cholelithiasis OR gallstones OR gallbladder disease OR ERCP OR ursodeoxycholic acid)". In addition, all references of relevant reviews and eligible articles were hand-searched for potentially missed eligible studies following a snowball procedure. A study was deemed eligible for our analysis if the authors reported clinical data on patients who underwent RYGB, LSG, AGB or BPD for obesity and their studied cohort of patients was followed-up for a period of more than 3 months for gallbladder disease and possible subsequent CC. We also included articles reporting clinical data on patients who underwent concomitant CC during one of the above types of bariatric surgery. Only original studies written in English were included. Studies reporting on more than one type of bariatric surgery were separately analyzed.

Data extraction

Data were extracted regarding study design, study origin, study timeframe, score in Newcastle-Ottawa Quality Scale (NOS), type of bariatric surgery performed, surgical approach used and number of patients included. As far as patient data are concerned, demographic data (gender, age, body mass index (BMI), gallbladder pathologies, prior abdominal operations) and co-morbidities (diabetes mellitus (DM), hyperlipidemia, hypertension, gastroesophageal reflux disease (GERD), sleep apnea) were gathered. Operative data consisted of postoperative complications (anastomotic leak/stricture, bleeding, re-operation, conversion to open, intestinal obstruction, hernia formation, renal failure, cardiovascular disease (CVD), respiratory failure, wound and overall infection, deep vein thrombosis (DVT)), duration of surgery, length of hospital stay and mortality.

Statistical analysis

All data extracted from eligible studies were tabulated and outcomes were analyzed cumulatively. A descriptive approach was adopted in all parameters when a meta-analysis was not possible.

Whenever the data were sufficient, a meta-analysis was performed. Odds ratio (ORs) and 95% confidence intervals (CI) were calculated by means of 2×2 tables for each categorical outcome; $OR > 1$ denoted outcome more frequently present in the concomitant cholecystectomy during bariatric surgery group. Weighted mean difference (WMD) with its 95% CI were calculated for each continuous outcome; $WMD > 0$ corresponded to larger values in the concomitant cholecystectomy during bariatric surgery group. Random-effects (DerSimonian-Laird) models were appropriately used to calculate pooled effect estimates. Between-study heterogeneity was assessed through Cochran Q statistic and by estimating I^2.[7]

Assessment of study quality

The quality of the included studies was evaluated using the NOS.[8] In the item assessing whether the follow-up period was long enough for outcomes to occur, the cut-off value was *a priori* set at 30 postoperative days, whereas regarding the item about the adequacy of follow-up, a 90% rate was also *a priori* adopted. Evidently, items pertaining to the comparability of groups were marked as "not applicable" in the non-comparative studies. Two reviewers (ID and GM) working independently rated the studies and final decision was reached by consensus with a third reviewer (KPE).

Although our initial purpose was to evaluate the existence of publication bias using the Egger's formal statistical test, statistical evaluation was performed only when the number of included studies was adequate (10 or more) given that the power of the test is otherwise substantially compromised.[9] For the interpretation of Egger's test, statistical significance was defined as $p < 0.1$[10] Statistical analysis was performed using STATA/SE version 13 (Stata Corp, College Station, TX, USA).

Protocol registration

This study is registered with the Research Registry (http://www.researchregistry.com/) and the unique identifying number is: reviewregistry255.

Results

Study characteristics and patient demographics

The initial literature search generated 9,048 studies. The trial flow is shown on Fig. 1. A total of 30 studies were determined eligible for this systematic review. They were published between 1988 and 2016 and their patient enrollment started in 1982. The majority of the studies (66.6%) took place in the United States, while the rest were mainly conducted in Europe. The largest proportion of studies was of retrospective nature, while only 7 studies were labeled as prospective cohorts. Due to absence of randomized control trials (RCTs) relevant to our topic, evaluation of the included studies in compliance with NOS was performed and exhibited an average of 5.8 stars. With respect to the type of bariatric surgeries, 21 studies included RYGB, 4 LSG, 6 AGB and 2 BPD (Tables 1 and 2).

A total of 13,765 patients were included in our analysis. Of them, 12,119 underwent bariatric surgery alone, while 1,646 underwent concomitant CC along with the bariatric surgery. Individualized reports for each type of surgery are depicted in Tables 1 and 2. Male gender represents the minority of the population; ranging from 20% to 58%, presenting the highest prevalence in AGB + CC subgroup and the lowest one in AGB subgroup, while the remaining percentages were mainly fluctuating between 20 and 30%. Morbid obesity was a constant finding in all studies, with the highest BMI being noted in patients undergoing either RYGB or BPD with or without concomitant CC (approximate mean BMI $= 50$ kg/m^2). Mean age ranged between 40 and 50 years. The majority of the patients (>85%) who did not receive concomitant CC had a normal gallbladder, while none of the patients who underwent simultaneous CC had a normal gallbladder (Tables 1 and 2).

Major co-morbidities and clinical assessment

Major co-morbidities of the patients are summarized in Table 3. With respect to the type of surgery, 1 out of 5 patients who underwent RYGB had DM, while approximately 1 out of 3 had dyslipidemia, hypertension and GERD. Average rate of comorbidities was higher in BPD group, whereas LSG patients exhibited the lowest frequencies. The three most common comorbidities were hypertension, GERD and hyperlipidemia for RYGB; hypertension, DM and dyslipidemia for LSG; dyslipidemia, hypertension and sleep apnea for LSG and BPD (Table 3).

Peri-operative data

Most common indication for both concomitant and subsequent CC was cholelithiasis, except for BPD subgroup in which 66.6% of

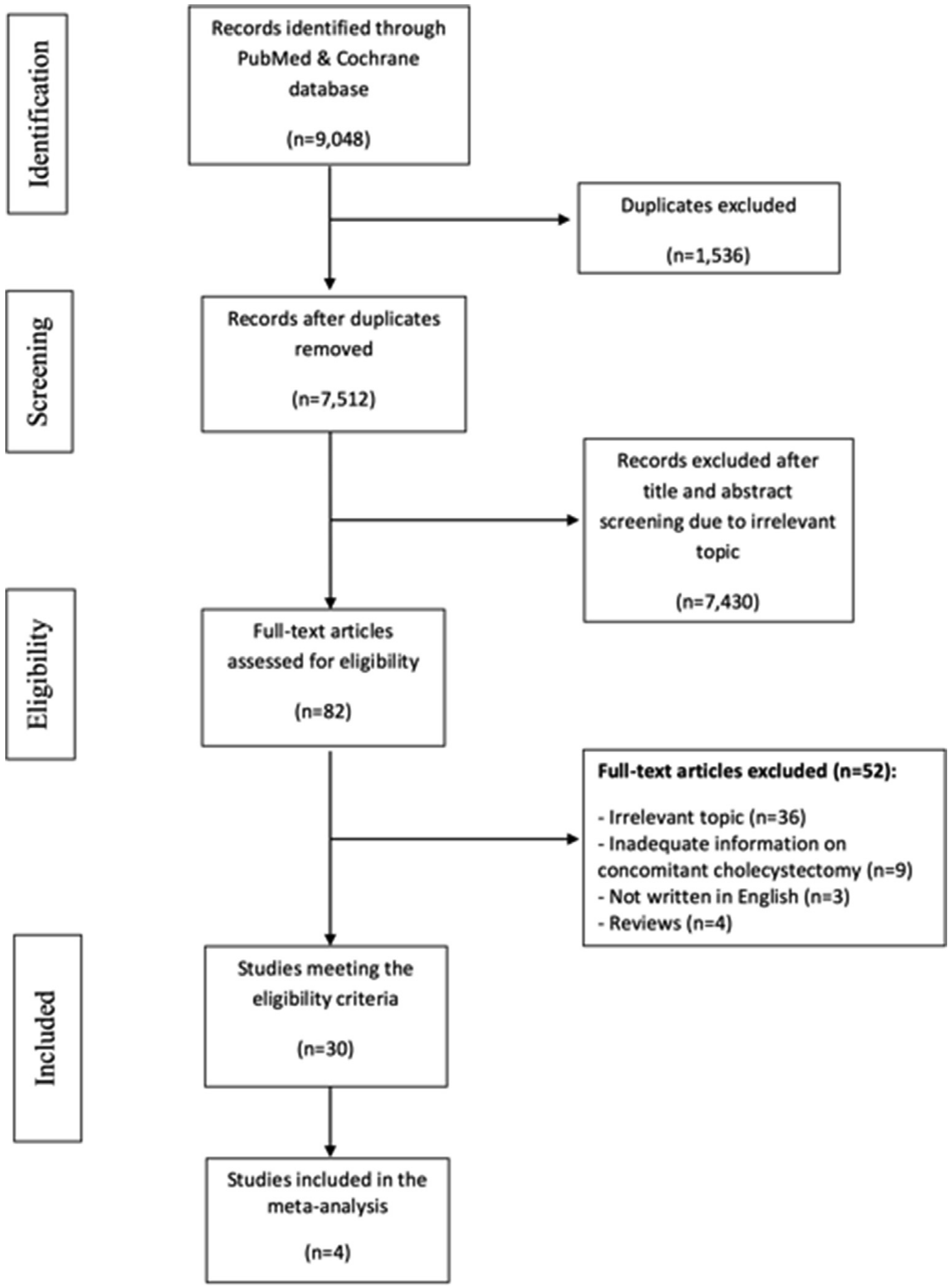

Fig. 1. Flow diagram of studies selection according to PRISMA Statement.

patients underwent subsequent CC because of biliary colic or dyskinesia. Treatment with ursodeoxycholic acid was offered in half of the patients that underwent RYGB and in all patients who underwent BPD, while none of the patients who underwent LSG or AGB received respective treatment. A relatively low percentage of patients (7–18%) had undergone CC previous to bariatric surgery. Almost 10% of the patients that underwent RYGB developed gallbladder-associated symptoms and 6.4% of them required CC. Less than 3.5% of the LSG patients developed gallbladder pathology and 3.1% required CC, while 4.4% of AGB and 17.9% of BPD developed gallbladder symptoms, which led to surgery in all occasions. The average time to subsequent CC ranged between 8.3 and 17.7 months. Almost 20% of the RYGB group and 38.2% of the RYGB + CC group were performed via open surgery, while all other types of surgeries were performed laparoscopically (Table 4).

Post-operative complications

The most frequently presented complications in each type of surgery are illustrated in Table 5. Number of studies included in the meta-analysis examining the differences between RYGB and RYGB + CC with regard to post-operative outcomes, pooled ORs, I^2, and p values of heterogeneity for all outcomes are provided in Table 6.

Table 1
Study characteristics and patients' demographics regarding Roux En Y gastric bypass.

Trial ID[a]	Journal	Years of enrollment	Type of study	Stars in ottawa	No of patients		Gender		Age (years)		Preoperative BMI		Gallbladder status, n (%)			
							Male, n (%)		Mean ± SD		Mean ± SD		Normal		Asymptomatic cholelithiasis	
					RYGB	RYGB + CC	RYGB	RYGB + CC	RYGB	RYGB + CC	RYGB	RYGB + CC	RYGB	RYGB + CC	RYGB	RYGB + CC
Fuller	Obes Surg	2003	R	5	135	9	–	–	–	45	–	46	93 (68.8)	–	135 (100)	–
Tarantino	Obes Surg	12/2000–03/2008	R	5	140	134	39 (27.9)	33 (24.6)	43 ± 10.2	40.7 ± 9.8	47.7 ± 6.4	46.1 ± 5.6	–	0	–	–
Amstutz	Obes Surg	05/2003–01/2008	R	5	64	26	17 (25.6)	–	–	–	43.8 ± 6.2	–	–	–	–	–
Caruana	Surg Obes Relat Dis	06/2000–07/2003	R	6	125	98	23 (18.4)	–	39 ± 11	–	52 ± 9.8	–	125 (100)	0	125 (100)	0
Coupaye	Surg Obes Relat Dis	01/2004–10/2013	P	5	117	37	11 (9.4)	–	41.4 ± 11.5	–	44.9 ± 5	–	–	–	–	–
D'Hondt	J Gastrointest Surg	08/2003–11/2009	–	5	625	16	194 (31)	–	38.1 ± 12.7	–	41.5 ± 10.5	–	521 (82.2)		104 (17.8)	–
Hamad	Obes Surg	12/1997–05/2001	–	8	462	94	85 (18.4)	18 (19.1)	42.2 ± 9.3	44.8 ± 9.3	48.8 ± 7.3	48.6 ± 6.9	462 (100)	0	462 (100)	89 (94.6)
Karadeniz	Ulus Cerrahi Derg	10/2006–03/2011	R	6	46	6	–	0	39 ± 10.8	39.4 ± 7.1	31.6	30.6	46 (100)	0	46 (100)	–
Kim	Surg Obes Relat Dis	1996–2006	R	7	454	298	76 (16.7)	76 (25.5)	42.6 ± 9.3	42.7 ± 9.2	53.4 ± 9.3	55.5 ± 10.4	454 (100)	0	454 (100)	–
Papasavas	Surg Obes Relat Dis	07/1999–09/2004	R	5	624	20	–	–	–	–	–	–	614 (98.4)	0	624 (100)	0
Portenier	Surg Obes Relat Dis	2000–2005	P	5	984	73	–	–	–	–	–	–	379 (38.5)	0	524 (53.3)	–
Patel	Am Surg	01/2003–01/2005	R	6	199	1	28 (14)	–	43 ± 11	–	50.1 ± 11.9	–	–	–	–	–
Scott	Surg Endosc	01/2000–08/2001	P	5	129	21	14 (10.9)	1 (4.7)	38.7 ± 7.7	42 ± 7.2	48.7 ± 5.8	48.3 ± 4.2	128 (99.9)	0	129 (100)	–
Swartz	Surg Obes Relat Dis	04/2003–03/2004	R/P	5	319	6	–	–	–	–	–	–	319 (100)	0	319 (100)	0
Taylor	Obes Surg	–	R	5	412	80	–	–	–	–	–	–	–	–	–	–
Tucker	Surg Endosc	02/2000–08/2006	R	5	1590	123	–	–	–	–	–	–	1508 (94.8)	0	–	–
Villegas	Obes Surg	11/1999–05/2002	P	7	151	40	–	–	–	–	–	–	151 (100)	0	151 (100)	–
Puzziferri	Ann Surg	05/1999–03/2001	P	7	99	17	–	–	–	–	–	–	–	–	–	–
Moon	Surg Obes Relat Dis	01/2009–08/2011	R	7	367	36	88 (24)	–	42.6 ± 11.9	–	47.1 ± 7.7	–	367 (100)	0	0	0
Shiffman	Am Col of Gastroenterology	–	R	5	81	24	15 (18.5)	16 (66.6)	34.8 ± 8.7	38 ± 7.8	–	–	81 (100)	0	0	20 (83.3)
Schimdt	Am Surg	03/1982–09/1984	R	6	63	30	–	–	–	–	–	–	63 (100)	0	0	30 (100)
Total or Average					**7186**	**1189**	**590 (21.4)**	**144 (24.9)**	**40.8**	**42.4**	**47.2**	**51.4**	**5311 (86.3)**	**0**	**3073 (67.3)**	**139 (45.1)**

RYGB: Roux-en-Y Gastric Bypass; CC: Cholecystectomy; R: Retrospective; P: Prospective; SD: Standard Deviation.
[a] For the references of the included studies, please see Supplemental Table 1.

Table 2
Study characteristics and patients' demographics regarding laparoscopic sleeve gastrectomy, adjustable gastric banding and biliopancreatic diversion.

Trial ID[a]	Journal	Years of enrollment	Type of study	Stars in ottawa	No of patients		Gender		Age (years)		Preoperative BMI		Gallbladder status, n (%)			
							Male, n (%)		Mean ± SD		Mean ± SD		Normal		Asymptomatic cholelithiasis	
					LSG	LSG + CC	LSG	LSG + CC	LSG	LSG + CC	LSG	LSG + CC	LSG	LSG + CC	LSG	LSG + CC
Coupaye	Surg Obes Relat Dis	01/2004–10/2013	P	6	43	12	4 (9.3)	–	42.5 ± 10.1	–	44.9 ± 8.6	–	–	–	–	–
Raziel	Surn Endosc	01/2006–07/2014	–	8	2383	180	906 (38)	38 (20)	43 ± 15.5	46 ± 12	42.9	43.1	2340 (98.2)	0	43 (1.8)	0
Sioka	J Obes	08/2006–12/2011	P	5	129	9	–	–	–	–	–	–	106 (82.2)	0	23 (17.8)	0
Moon	Surg Obes Relat Dis	01/2009–08/2011	R	7	115	16	32 (27.8)	–	43.7 ± 11.9	–	46 ± 7.9	–	115 (100)	0	0	0
Total or Average					**2670**	**217**	**942 (37)**	**38(20)**	**43**	**46 ± 12**	**43**	**43.1**	**2561 (97.5)**	**0**	**66 (2.5)**	**0**
					AGB	**AGB + CC**	**AGB**	**AGB + CC**	**AGB**	**AGB + CC**	**AGB**	**AGB + CC**	**AGB**	**AGB + CC**	**AGB**	**AGB + CC**
Obeid	Surg Endosc	07/2013–04/2015	R	6	84	28	15 (18)	19 (67)	46.4 ± 12.5	46.6 ± 12.4	43.6 ± 4.7	44.1	84 (100)	0	0	0
O'Brien	Arch Surg	07/1994–10/2001	R	5	990	10	–	–	–	–	–	–	809 (81.7)	0	0	0
Sakcak	Eur J Gastroenterol Hepatol	09/2006–05/2009	R	6	137	8	29 (21.2)	2 (25)	29.6 ± 6.1	28.2 ± 5.8	46.8 ± 6.6	44.1 ± 6.8	–	–	–	–
Myers	Surg Obes Relat Dis	11/2001–07/2004	R	5	261	7	–	–	–	–	–	–	261 (100)	0	0	0
Zilberstein	Obes Surg	01/2000–01/2004	–	6	291	17	–	–	–	–	–	–	–	–	–	–
Moon	Surg Obes Relat Dis	01/2009–08/2011	R	7	104	7	20 (19.2)	–	45.8 ± 11	–	41.5 ± 4.9	–	104 (100)	0	0	0
Total or Average					**1867**	**77**	**64 (19.7)**	**21 (58.3)**	**39.1**	**42.5**	**44.3**	**44.1**	**1258 (87.4)**	**0**	**0**	**0**
					BPD	**BPD + CC**	**BPD**	**BPD + CC**	**BPD**	**BPD + CC**	**BPD**	**BPD + CC**	**BPD**	**BPD + CC**	**BPD**	**BPD + CC**
Bardaro	Surg Obes Relat Dis	01/1999–01/2003	R	5	157	10	–	–	–	–	–	–	157 (100)	–	–	–
Sucandy	Obes Surg	2006–2012	R	7	239	63	72 (30)	17 (27)	44.4 ± 10.3	45.1 ± 10.3	50.4 ± 11.4	51.1 ± 7.3	239 (100)	–	–	–
Total or Average					**396**	**73**	**72(30)**	**17(27)**	**44.4**	**45.1**	**50.4**	**51.1**	**396 (100)**	**-**	**-**	**-**

LSG: Laparoscopic Sleeve Gastrectomy, CC: Cholecystectomy; P: Prospective; R: Retrospective; AGB: Adjustable Gastric Banding; BPD: Biliopancreatic Diversion; SD: Standard Deviation.
[a] For the references of the included studies, see Supplemental Table 1.

Table 3
Patients' comorbidities.

Comorbidities, n (%)	RYGB	RYGB + CC	LSG	LSG + CC	AGB	AGB + CC	BPD	BPD + CC
DM	168 (15.8)	2 (22.2)	8 (19)	–	38 (17.2)	12 (33.3)	115 (48)	33 (52.4)
Dyslipidemia	266 (28.3)	3 (33.3)	7 (16)	–	71 (32.1)	19 (52.8)	–	–
CHF	26 (4.2)	0	–	–	0	0	12 (5)	2 (3.2)
Hypertension	181 (41.4)	3 (33.3)	11 (26)	–	54 (24.4)	16 (44.4)	133 (55.6)	39 (61.9)
GERD	96 (48)	3 (33.3)	–	–	37 (16.7)	2 (5.6)	–	–
COPD	0	0	–	–	8 (3.6)	0	–	–
Sleep Apnea	0	2 (22.2)	–	–	29 (13.1)	9 (25)	145 (60.7)	32 (50.8)
Arthritis	0	6 (66.6)	–	–	12 (5.4)	1 (2.8)	–	–
Stress Incontinence	0	0	–	–	0	0	–	–

DM: Diabetes Mellitus; CHF: Congestive Heart Failure; GERD: Gastroesophageal Reflux; COPD: Chronic Obstructive Pulmonary Disease; RYGB: Roux-en-Y Gastric Bypass; CC: Cholecystectomy; LSG: Laparoscopic Sleeve Gastrectomy; AGB: Adjustable Gastric Banding; BPD: Biliopancreatic Diversion.

Table 4
Peri-operative characteristics.

Peri-operative Characteristics	RYGB	RYGB + CC	LSG	LSG + CC	AGB	AGB + CC	BPD	BPD + CC
Indication for CC, n (%)								
CD	66 (30)	10 (1.6)	3 (3.6)	0	0	0	47 (66.2)	–
CL	81 (37)	536 (83.4)	7 (8.3)	9 (100)	10 (100)	39 (86.7)	21 (30)	–
CY	54 (24.7)	93 (14.5)	5 (6)	0	0	6 (13.3)	0	–
CDL	8 (3.6)	0	5 (6)	0	0	0	0	–
BP	10 (4.7)	0	4 (4.8)	0	0	0	1 (1.4)	–
Ursodeoxycholic Acid Therapy, n (%)	1298 (49.4)	–	0	–	0	–	393 (100)	–
Previous CC, n (%)	1211 (18.2)	–	192 (7.2)	–	272 (18.2)	–	59 (14.9)	–
Gallbladder Disease Post-op, n (%)	700 (9.7)	–	91 (3.4)	–	65 (4.4)	–	71 (17.9)	–
Subsequent CC, n (%)	459 (6.4)	–	84 (3.1)	–	65 (4.4)	–	71 (17.9)	–
Time to Subsequent CC (mo)	17.7	–	11	–	8.3	–	–	–
Open, n (%)	806 (19.2)	54 (38.2)	0	1 (0.4)	0	0	0	0
Subsequent CC								
Open, n (%)	25 (8.7)	–		–	0	–	3 (5.8)	–

RYGB: Roux-en-Y Gastric Bypass; CC: Cholecystectomy; LSG: Laparoscopic Sleeve Gastrectomy; AGB: Adjustable Gastric Banding; BPD: Biliopancreatic Diversion; CD: Colic or Dyskinesia; CL: Cholelithiasis; CY: Cholecystitis; CDL: Choledocholithiasis; BP: Biliary Pancreatitis.

Anastomotic leak/stricture

Two trials[11,12] reported the incidence of anastomotic leak/stricture. There was an increased anastomotic leak/stricture rate in RYGB + CC (8.7%) compared with RYGB (2.5%) group (OR: 3.080, 95%CI: 1.970–4.818).

Other post-operative complications

Two trials[11,12] reported the incidence of bleeding, intestinal obstruction, cardiovascular events, respiratory failure, wound infection and DVT. There was no significant difference between RYGB and RYGB + CC with respect to bleeding (1.6% vs. 2.4%, OR: 1.320, 95% CI: 0.629–2.770), intestinal obstruction (2.3% vs. 5.9%,

Table 5
Post-operative complications.

Complications, n (%)	RYGB	RYGB + CC	LSG	LSG + CC	AGB	AGB + CC	BPD	BPD + CC
Anastomotic Leak/Stricture	32 (2.5)	56 (8.7)	23 (0.9)	2 (1)	0	0	1 (0.4)	0
Nausea	0	0	0	0	0	0	0	0
Bleeding	21 (1.6)	13 (2.4)	54 (2)	4 (2.1)	15 (2.4)	0	4 (1.7)	0
Re- operation	0	3 (0.5)	0	0	15 (2.4)	4 (7.5)	0	0
Adjacent Structures Injury	0	1 (0.3)	2 (0.1)	0	0	0	0	0
Conversion	12 (1.2)	6 (2.2)	0	0	0	0	4 (1.7)	1 (1.6)
Intestinal Obstruction	30 (2.3)	26 (5.9)	0	0	0	0	0	0
Hernia	69 (4.8)	84 (19.2)	7 (0.3)	2 (1)	0	0	0	0
Tachycardia	2 (0.1)	0	0	0	0	0	0	0
Renal Failure	7 (0.5)	4 (0.9)	0	0	0	0	0	0
Cardiovascular	2 (0.2)	0	0	0	0	0	0	0
Respiratory Failure	47 (3.7)	17 (3.9)	1 (0.01)	0	1 (0.01)	0	0	0
Band Slippage	0	0	0	0	5 (0.8)	1 (1.9)	0	0
Chest Pain	0	0	0	0	0	0	0	0
Septic Shock	0	0	0	0	0	0	0	0
Wound Infection	41 (3.2)	26 (4.6)	0	0	8 (1.3)	1 (1.9)	0	0
Infection (other)	5 (0.4)	2 (0.4)	6 (0.2)	1 (0.5)	1 (0.1)	0	0	0
DVT	1 (0.1)	3 (0.7)	1 (0.01)	0	0	0	8 (3.3)	0
Marginal Ulcer	5 (0.4)	13 (2.9)	0	0	0	0	0	0
Complications of Subsequent CC, n (%)	5 (2.9)	–	0	–	0	–	5 (26.3)	–

RYGB: Roux-en-Y Gastric Bypass; CC: Concomitant Cholecystectomy; LSG: Laparoscopic Sleeve Gastrectomy; AGB: Adjustable Gastric Banding; BPD: Biliopancreatic Diversion; DVT: Deep Vein Thrombosis.

Table 6
Results of the meta-analyses examining the differences between Roux En Y Gastric Bypass alone and with concomitant cholecystectomy.

	RYGB (%)	RYGB + CC (%)	No of studies	OR (95% CI)	Heterogeneity, I^2, p
Categorical outcomes					
Anastomotic Leak/Stricture	2.5	8.7	2	3.080 (1.970–4.818)	0.0%, 0.682
Bleeding	1.6	2.4	2	1.320 (0.629–2.770)	0.0%, 0.831
Conversion	1.2	2.2	2	1.024 (0.346–3.028)	0.0%, 0.542
Intestinal Obstruction	2.3	5.9	2	1.476 (0.855–2.549)	0.0%, 0.659
Cardiovascular	0.2	0	2	0.842 (0.088–8.104)	0.0%, 0.611
Respiratory Failure	3.7	3.9	2	0.984 (0.546–1.771)	0.0%, 0.995
Wound Infection	3.2	4.6	2	1.449 (0.850 2.472)	0.0%, 0.478
DVT	0.1	0.7	2	5.607 (0.816–38.510)	0.0%, 0.384
Early Mortality	0.1	1.1	2	0.349 (0.096–1.270)	0.0%, 0.678
Continuous outcomes					
Operative time (min)	229	227	4	0.336 (−0.045–0.718)	90.4%, 0.000
EWL%	58	65	2	−0.001 (−0.163–0.161)	0.0%, 0.365
LoS (d)	4	5	4	−0.025 (−0.466–0.416)	92.9%, 0.000
Follow-up (mo)	26.7	24.2	3	−0.508 (−1.377–0.361)	98.1%, 0.000

OR: odds ratio; DVT: deep vein thrombosis; EWL%: % excess weight loss; LoS: length of stay.

OR: 1.476, 95% CI: 0.855–2.549), cardiovascular events (0.2% vs. 0%, OR: 0.842, 95% CI: 0.088–8.104), respiratory failure (3.7% vs. 3.9%, OR: 0.984, 95% CI: 0.546–1.771), wound infection (3.2% vs. 4.6%, OR: 1.449, 95% CI: 0.850–2.472) and DVT (0.1% vs. 0.7%, OR: 1.024, 95% CI: 0.346–3.028).

Two trials[11,13] reported the conversion to open rate. There was no significant difference between RYGB (1.2%) and RYGB + CC (2.2%) groups (OR: 1.024, 95% CI: 0.346–3.028). (Figs. 2 and 3).

Peri-operative data and mortality

Data concerning operative time, length of hospital stay, weight loss, time to follow-up, early and overall mortality are explicitly tabulated in Table 7 for each type of surgery. Four trials[11–14] reported the mean operative time. There was no difference between RYGB (229 min) and RYGB + CC (227 min) groups (OR: 0.336, 95% CI: −0.045 to +0.718). Four trials[11–14] reported the mean operative time. There was no difference between RYGB (4 days) and RYGB + CC (5 days) groups (OR: −0.025, 95%CI: −0.466 to +0.416). Two trials[11,13] referred to % of extra weight loss. There was no difference between RYGB (58%) and RYGB + CC (65%) groups (OR: −0.001, 95%CI: −0.163 to +0.161). Seven studies reported on early mortality,[11,12,15–19] however only two were[11,12] included in the analysis. There was no difference between RYGB (0.1%) and RYGB + CC (1.1%) groups (OR: 0.349, 95% CI: 0.096–1.270). Three trials[11–13] mentioned the follow-up period. There was no difference between RYGB (26.7 mo) and RYGB + CC (24.2 mo) groups (OR: −0.508, 95%CI: −1.377 to +0.361).

Discussion

The performance of cholecystectomy concomitantly with bariatric surgery remains a clinical question with no clear answer to date. In this systematic review and meta-analysis, we sought to investigate the need, feasibility and efficacy for concomitant cholecystectomy. A total of 13,765 patients were included in our analysis and 4 types of bariatric operations (RYGB, LSG, AGB, BPD) were examined. To our knowledge, this the first attempt for a head-to-head comparison between bariatric surgery and concomitant CC versus bariatric surgery alone, in terms of complications, mortality and effectiveness of the bariatric surgery. Our results show that there is an increased risk for anastomotic leak/stricture in patients undergoing RYGB + CC compared with RYGB alone. Additionally, there is a risk for gallstone or sludge formation after bariatric surgery, ranging from 3.4% to 17.9% and a risk for complicated CC (defined as CC with the presence of bile duct injuries, bleeding, cardiovascular events, respiratory failure, infection or death) after a bariatric operation ranging from 0%[20–22] to 26.3%.[23]

The debate for the optimal timing of CC arises from the fact that bariatric surgery leads to higher risk for gallbladder pathologies due to the massive weight reduction and it is also associated with altered gastrointestinal anatomy, making, thus, the CC more

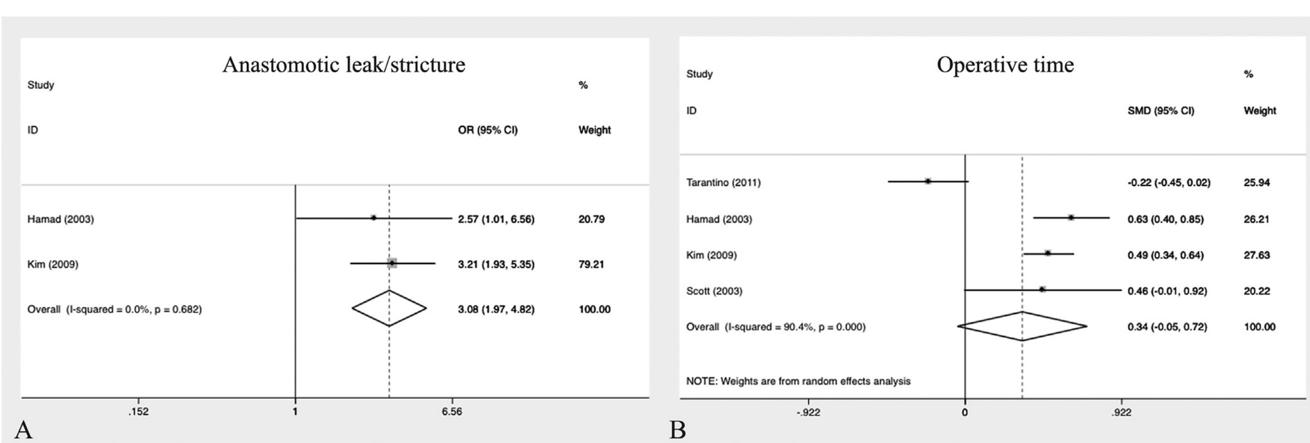

Fig. 2. Forest plot describing the differences in the rate of (a) anastomotic leak/stricture and (b) operative time between Roux En Y Gastric Bypass (RYGB) and RYGB with concomitant cholecystectomy (CC).

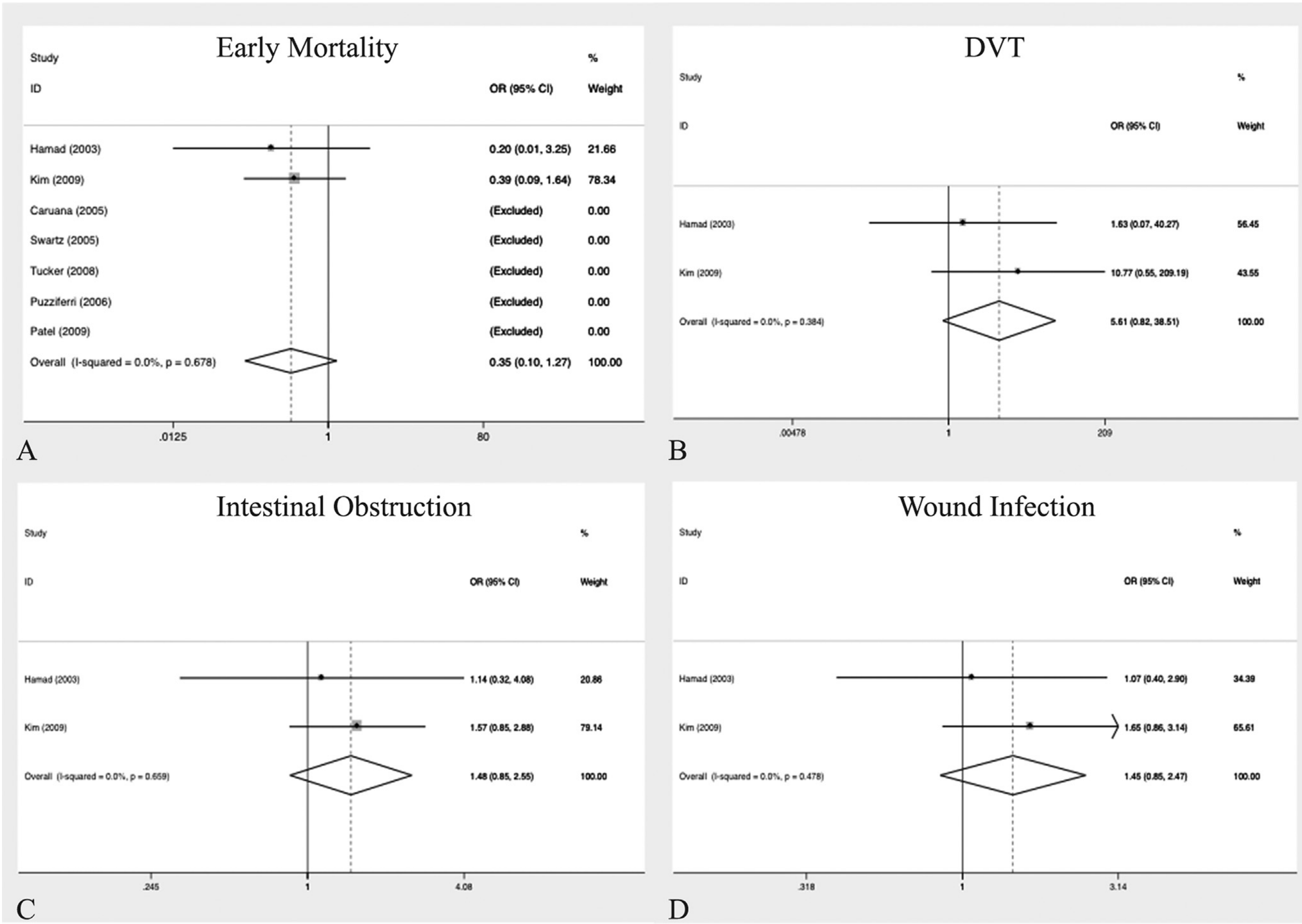

Fig. 3. Forest plot describing the differences in rates of (a) early mortality, (b) deep vein thrombosis (DVT), (c) intestinal obstruction and (d) wound infection between Roux En Y Gastric Bypass (RYGB) and RYGB with concomitant cholecystectomy (CC).

changeling in operated patients. On the other hand, adding CC to a bariatric surgery poses certain risks due to the increased morbidity of the obese patients. The risk factors for gallstone formation include diminished bile acid and phospholipid secretion, high biliary cholesterol secretion and gallbladder stasis.[24,25] This imbalance is magnified in persons with obesity undergoing rapid weight loss, since an important amount of cholesterol is mobilized from visceral adipose tissue. Dieting and fasting also lead to greater gallbladder stasis due to resistance to cholecystokinin and decreased stimuli for its secretion.[26] Additionally, the low sensitivity (50–75%) of the transabdominal ultrasound in obese populations, hinders the exact estimation of the incidence of gallbladder disease.[19,27] On these grounds, there have been made attempts to reach a consensus regarding the optimal management of bariatric patients with respect to gallbladder disease/complications and CC. Various options of addressing this issue have been proposed over the last decade.[28] Prophylactic CC,[13,29] CC in the case of gallbladder disease[18,30,31] and conservative management with ursodeoxycholic acid[26,28,31] have been investigated. Each approach presents with certain pros and cons, but the superiority of a specific approach has not been proved. Yet, there is tendency towards a more conservative approach suggesting initial medical treatment and subsequent CC when indicated.[31]

The lowest risk for subsequent CC was observed in patients undergoing LSG, while the highest in patients undergoing BPD. Morais et al., published a 3-year follow-up of bariatric patients, and

Table 7
Post-operative data and mortality.

Post-operative Data	RYGB	RYGB + CC	LSG	LSG + CC	AGB	AGB + CC	BPD	BPD + CC
EWL, %	58	65	58.3	–	31.2	–	–	–
Weight Loss (kg)	32.6	–	26.9	–	–	–	–	–
Post-operative BMI (kg/m2)	37.4	36.4	–	–	–	–	–	–
LoS (d)	4	5	2	2	1.2	1.5	3.5	3
Duration of Surgery (min)	229	227	–	–	74.7	69	290.8	302.8
Mortality, %								
Early	4 (0.1)	6 (1.1)	0	0	0	0	0	0
Late	0	0	0	0	0	–	–	–
Follow-up (mo)	26.7	24.2	27.2	28	27.1	33.3	31	–

RYGB: Roux-en-Y Gastric Bypass; CC: Cholecystectomy; LSG: Laparoscopic Sleeve Gastrectomy; AGB: Adjustable Gastric Banding; BPD: Biliopancreatic Diversion; EWL: Excess Weight Loss = [(Operative Weight Loss – Follow-up Wight)/Operative Excess Weight] x 100%; BMI: Body Mass Index; LoS: Length of Stay.

showed that 3.3% presented with gallbladder disease and only one third of them led to subsequent CC.[32] Intriguingly, although treatment with ursodeoxycholic acid has been suggested to be associated with lower incidence of gallbladder pathology (8.8% vs. 27.7% for placebo),[26] none of the LSG patients received ursodeoxycholic acid after the operation, while all of the BPD patients did so. Upon this oxymoron, a proposed hypothesis regarding the association between the amount of weight loss, the duration of obesity state, the type of surgery and the risk for gallstone formation may be of interest.[32–34] It should not be neglected, though, that the adherence of patients to treatment with ursodeoxycholic acid is not strict due to its adverse effects - namely constipation, headache, dizziness, diarrhea and upper respiratory infections - and its relatively high cost.[35–37] Chang et al., reported that in a retrospective study of 3,765 patients, only age was found to be significantly correlated with the risk of gallbladder complications after bariatric surgery in a multivariate regression model of analysis.[38] Although, this hypothesis has not been widely accepted, it should merit consideration, since there is not a well-documented consistency between the interrelationship of obesity-weight loss-cholelithiasis.

Moreover, the reason for CC either during or after bariatric surgery is cholecystitis and it seems to be consistent in all subgroups, maybe due to its higher prevalence, in general. Exception to this, are the patients who underwent BPD and received subsequent CC mainly because of biliary colic or dyskinesia. This could be due to the nature of this surgical technique or by the fact that these different diagnoses are semantics used by the authors of those papers. Another interesting point is that patients who underwent RYGB required CC 17.7 months after the surgery, on average, while this period was much shorter for LSG and AGB (11 months and 8.3 months, respectively). Although, it is proposed that the peak of gallbladder disease incidence is at 12 months post-operatively,[3,39] it has been reported that one out of five patients that underwent RYGB developed gallstones 17 months after surgery.[29] As it has been mentioned, these differences may be owned to the different intrinsic characteristics of each surgical technique or to the different demographic and post-operative characteristics of each patient.

Complications, albeit uncommon, were shown to be more frequent when concomitant CC was performed. Meta-analysis of the studies was applicable only in RYGB, due to the scarcity of available studies regarding the other techniques. Only anastomotic leak/stricture was found to be firmly associated with concomitant CC, while operative time, early mortality, DVT, intestinal obstruction and wound infection had a marginal correlation. (Figs. 2 and 3). It is speculated that the higher pre-operative BMI in the RYGB + CC group could be merely responsible for the creation of a smaller gastric pouch, and thus a technically more challenging anastomosis with subsequent increased rates of leak and/or stricture. Moreover, the fact that the operative time did not differ between the RYGB and RYGB + CC groups could mean that less time was spent on the construction of the anastomosis in the group of the concomitant CC. However, these results were generated only from two studies due to the major absence of data on the rest of the studies. Current literature suggests that there is not a significant increase in the complication rate when performing CC simultaneously with a bariatric operation.[12,40,41] On the other hand, Worni et al. analyzed the National Inpatient Sample in the USA, which contains 70,287 patients, and reported that concomitant CC was associated with increased complication rate and early mortality.[5] Undisputedly, complication rate is firmly dependent on surgeon's and hospital's experience −a parameter known as volume/outcome relationship. It is significant to underline that subsequent CC can be challenging for the surgeon, due to the altered anatomy and the possibility of complicated gallstones. More specifically, our study showed that even though complication rate of subsequent CC was zero after LSG or AGB, there was a 2.9% risk after RYGB, which climbed up to 26.3% after BPD. Although a slight increase in the total duration of the operation is anticipated by the concomitant CC, such findings were not robustly supported by our observations. However, a small increase in the length of stay was noted, which may not be significant as suggested by Ahmed et al.[40] With respect to the weight loss per se, concomitant CC did not seem to interfere with the efficacy of the bariatric surgery.

We would like to acknowledge some limitations of our study. The majority of the data were retrieved from retrospective cohort studies. The included studies differed considerably in their study design, particularly in the indication for concomitant CC, the postoperative ursodeoxycholic acid therapy, and the primary study outcome. Moreover, the small amount of studies included in the meta-analysis may prevent us from drawing strong conclusions.

It is imperative need to highlight that the limitations of our study reflect the current level of evidence. The lack of randomized controlled trials, the inconsistency between available studies, the limited availability of studies reporting on techniques other than RYGB and the heterogeneity of the studies cumulatively lead to the decision that yet, no definitive conclusion can be made. Taking into consideration that the majority of the eligible studies reported laparoscopic procedures, it should not be neglected that the feasibility, efficacy and utilization have been enhanced since then, therefore amelioration of clinical outcomes may be expected nowadays. Intervening at the time of bariatric surgery may offer some reassurance, however it is an option that comes at a certain price. The performance of concomitant cholecystectomy addresses the risk for subsequent gallbladder pathologies -in untreated cases-which may require a challenging surgery; however, it is accompanied by an increased risk of post-operative complications that should not be neglected.

Conclusions

Our results suggest that, on the one hand, there is an increased risk for gallstone formation after bariatric surgery, while on the other hand there is an established risk for anastomotic leak/stricture during concomitant CC in RYGB. Nonetheless, large randomized controlled trials examining the optimal timing of CC in bariatric patients is required in order to extract stronger conclusions.

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Appendix A. Supplementary data

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