Meta-Analysis



Journal of International Medical Research 2017, Vol. 45(1) 22–37 © The Author(s) 2017 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav DOI: 10.1177/0300060516676411 journals.sagepub.com/home/imr



Shortened preoperative fasting for prevention of complications associated with laparoscopic cholecystectomy: a meta-analysis

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Abstract

Objective: Routine fasting (12 h) is always applied before laparoscopic cholecystectomy, but prolonged preoperative fasting causes thirst, hunger, and irritability as well as dehydration, low blood glucose, insulin resistance and other adverse reactions. We assessed the safety and efficacy of a shortened preoperative fasting period in patients undergoing laparoscopic cholecystectomy. **Methods:** We searched PubMed, Embase and Cochrane Central Register of Controlled Trials up to 20 November 2015 and selected controlled trials with a shortened fasting time before laparoscopic cholecystectomy. We assessed the results by performing a meta-analysis using a variety of outcome measures and investigated the heterogeneity by subgroup analysis.

Results: Eleven trials were included. Forest plots showed that a shortened fasting time reduced the operative risk and patient discomfort. A shortened fasting time also reduced postoperative nausea and vomiting as well as operative vomiting. With respect to glucose metabolism, a shortened fasting time significantly reduced abnormalities in the ratio of insulin sensitivity. The C-reactive protein concentration was also reduced by a shortened fasting time.

Conclusions: A shortened preoperative fasting time increases patients' postoperative comfort, improves insulin resistance, and reduces stress responses. This evidence supports the clinical application of a shortened fasting time before laparoscopic cholecystectomy.

Keywords

Shortened preoperative fasting, complications, laparoscopic cholecystectomy, meta-analysis

Date received: 12 June 2016; accepted: 6 October 2016

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Introduction

Laparoscopic cholecystectomy, which is the treatment of choice for gallbladder stones and cholecystitis, is considered a safe procedure with a low risk of complications compared with traditional cholecystectomy. However, the rate of postoperative nausea and vomiting (PONV) in the first 24 h after laparoscopic cholecystectomy ranges from 38% to 60% and affects the recovery of patients, leading to a prolonged hospital stay.¹ Infection, adverse effects of anaesthesia, and carbon dioxide pneumoperitoneum also affect patients' recovery.²

Routine fasting (12h) is always applied before elective surgery to reduce the gastric volume and acidity, which helps to avoid acute respiratory tract obstruction, aspiration pneumonia and Mendelson syndrome during anesthesia.³ Enhanced recovery after surgery protocols and new guidelines developed by the American Society of Anesthesiologists (ASA) recommend a 6-h preoperative fasting period to reduce operative-related complications. However, some studies have indicated that a long preoperative fasting period causes patient discomfort manifesting as thirst, hunger and irritability as well as adverse reactions such as dehydration, low blood glucose and insulin resistance. Oral administration of carbohydrates 2h before anaesthesia for surgery is safe and reduces both insulin resistance and patient discomfort.⁴ Oral carbohydrates also reduce gluconeogenesis, glycogenolysis, lipolysis and muscle protein catabolism and increase glycogen reserves.⁵ At present, a shortened preoperative fasting period and administration of oral carbohydrates before laparoscopic cholecystectomy remain controversial. This systematic review was performed to provide reliable evidence for the application of this approach in clinical practice.

Three published meta-analyses included studies of paediatric, neoplastic and general surgery, but their results require further investigation. Recently, numerous trials evaluating the impact of preoperative fasting times in patients undergoing laparoscopic cholecystectomy have yielded inconsistent results. Considering the differences in preoperative fasting times, we performed the present meta-analysis of randomized controlled trials to determine the impact of a shortened preoperative fasting period in patients undergoing laparoscopic cholecystectomy. To the best of our knowledge, this is the first meta-analysis of the effects of a shortened preoperative fasting time in patients undergoing laparoscopic cholecystectomy.

Materials and methods

Data sources, search strategies and study selection

We searched the PubMed and Embase databases and the Cochrane Central Register of Controlled Trials using the following core terms: "preoperative fasting," "diet restriction," "perioperative period," and "clinical trial." We applied no language restrictions and included all relevant articles up to 20 November 2015. We also conducted manual searches from the reference lists of identified trials. This study conforms to the PRISMA guidelines for the reporting of systematic reviews and meta-analyses.

Two reviewers independently identified eligible reports. Discrepancies were resolved through group discussion. The eligibility criteria were as follows: treatment by laparoscopic cholecystectomy, randomized controlled design, and use of comparison groups in which one group underwent a shortened preoperative fasting time and the other (control group) underwent routine fasting or water as placebo. The exclusion criteria were as follows: the study did not evaluate the impact of the preoperative fasting time, patients included those who did not undergo laparoscopic cholecystectomy, and data on some investigated outcomes were unavailable (e.g. under risk in operation, gastric volume, pain, PONV, glucose, insulin, insulin resistance/sensitivity, cortisol, C-reactive protein [CRP] and carnitine).

Data extraction and quality assessment

Two authors compiled the data using a predefined information sheet. The following items were extracted from the included articles: author, year, number of patients (experimental), diabetes, ASA level, fasting time in the experimental group, nutrient type, liquid volume, control type and conclusion. Two reviewers also independently assessed the risk of design bias in the included studies using the Cochrane Collaboration tool.⁹ The following outcomes were evaluated in this review: under risk in operation, gastric volume, pain, PONV, glucose, insulin, insulin resistance/ sensitivity, cortisol, CRP and carnitine. These outcome measures were ranked according to the Grading of Recommendations Assessment, Development and Evaluation.¹⁰

Statistical analysis

We used the inverse variance method to pool continuous data and the Mantel-Haenszel method for dichotomous data; the results are presented as the standardized mean difference (SMD) with 95% confidence interval (CI), risk ratio (RR) with 95% CI (under risk in operation) and odds ratio (OR) with 95% CI. The I^2 statistic was calculated to evaluate the extent of variability attributable to statistical heterogeneity between trials. In the absence of statistical heterogeneity $(I^2 < 50\%)$, we used a fixedeffects model; otherwise we used a randomeffects model.¹¹ The median and quartile data were transformed to mean and SD for analysis.¹² We analysed the following predefined subgroups to identify the sources of heterogeneity: nutritional types, control types and intake volume. We investigated

publication bias by visually examining funnel plots and using the Begg–Mazumdar and Egger tests. The nonparametric "trimand-fill" method was used to determine the stability if publication bias was present. Generally, a two-sided *P*-value of < 0.05 was considered statistically significant. Data analysis was performed with Review Manager (Version 5.3) and STATA (Version 12.0).

Results

Literature search and study characteristics

Our database search returned 249 articles after removing duplicates, from which we collected 11 trials for inclusion in our metaanalysis (Figure 1). All included patients underwent laparoscopic cholecystectomy. The ASA class was not described in two articles, while one article included patients with an ASA class of 1 to 3. The preoperative fasting time was 2 h in all studies except one, in which the fasting time was 3 to 4 h. The intake type was carbohydrates (or maltodextrin) and carbohydrates plus protein, glutamine, antioxidants or other nutrients. The intake volume ranged from 200 to 400 ml. The control types were placebo control (water) and blank control (routine fasting). Blank control and placebo control were set parallel in three studies. With respect to the studies' conclusions, one article did not recommend a shortened preoperative fasting period based on the results of glucose metabolism. Others considered a shortened fasting time to be safe, reduce patient discomfort, improve insulin sensitivity and reduce postoperative stress reactions (Table 1). Three studies did not use a blinding method, and four studies used inappropriate blinding methods or the assessor was not blinded to the study group. Overall, the included studies had highquality designs (Figure 2).

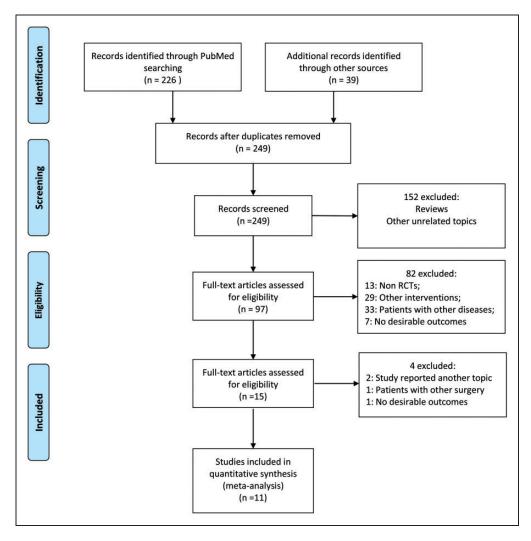


Figure 1. PRISMA flow diagram.

Meta-analysis

For the operative risk and gastric volume index, the fixed-effects model showed that a shortened fasting time reduced the operative risk (lg(RR), -0.74; 95% CI, -1.36 to -0.12; P = 0.019). There was no significant difference in the gastric volume between the shortened fasting and control groups (SMD, -0.31; 95% CI, -0.83 to 0.21) (Figure 3).

For the subjective sensation index, pain assessment using a visual analogue scale

showed that a shortened fasting time significantly reduced postsurgical pain (SMD, -0.89; 95% CI, -1.29 to -0.50; P =0.000). A shortened fasting time also reduced both PONV (lg(OR), -0.24; 95% CI, -0.48 to -0.00; P = 0.046) and operative vomiting (lg(OR), -0.47; 95% CI, -0.71 to -0.22; P = 0.000). However, there was no significant difference in operative nausea between the shortened fasting and control groups (lg(OR), -0.33; 95% CI, -0.72 to 0.06) (Figure 4).

Table 1. Characteristics of included trials.	ics of i	ncluded trials	ċ						
Author	Year	No. of patients (Exp)	Inclusion	ASA	Fasting ASA time (h)	Nutrient type	Intake volume (ml)	Control type	Conclusion
Pedziwiatr M ⁵	2015	46 (22)	No-diabetes 1–3	<u>~</u>	5	Carbohydrate	400	Placebo	CHO-loading is not clinically justified in patients undergoing laparoscopic
de Andrade Gagheggi Ravanini G ¹⁸	2015 38	38 (17)	No-diabetes I–2	1-2	7	33.5% Carbohydrate and 4% protein	200	Blank	Carbohydrate + protein- Carbohydrate + protein- enriched solutions are safe, reduce insulin resistance, and do not increase the
Basant Narayan Singh ¹	2015 120	(40)	No-diabetes	~	~ 2	12.5% Carbohydrate	400	Placebo/blank	risk of profictioaspirauon. Carbohydrate-rich drinks can minimize postoperative nausea, vomiting and pain without additional
Zelic M ¹⁹	2013	2013 70 (35)	No-diabetes 1–2	12	5	12.5% Carbohydrate	400	Blank	complications. Preoperative feeding can reduce discomfort and decrease the perioperative
Huseyin Yildiz ¹⁷	2013	2013 60 (30)	No-diabetes I–2	12	23	12.5% Carbohydrate	400	Blank	stress response. Preoperative CHO reduces perioperative discomfort and improves periopera- rive well-heing
Diana Borges Dock-nascimento ²⁰	2012 36		(11;12) No-diabetes 1–2	1-2	7	12.5% Carbohydrate; 12.5% Carbohydrate + free alutamine	200	Blank	Preoperative feeding improves insulin sensitivity.
Sherif Awad ²¹	2012 30	(15)	N/A	~.	8- 4-	Carbohydrate + (50 g Carbohydrate + 15 g glutamine + antioxidants	300	Placebo	Carbohydrates prevent excessive/incomplete mitochondrial β-oxidation.
									(continued)

26

Author	Year	No. of patients Year (Exp)	Inclusion	ASA	Fasting Nutrient ASA time (h) type	ent	Intake volume (ml)	Intake volume Control (ml) type	Conclusion
Diana Borges Dock-nascimento ²²	2011	2011 48 (12)	No-diabetes I-2 2	1-2	2	Maltodextrin + glutamine; 200 Maltodextrin	200	Placebo	Carbohydrates improve insu- lin resistance and antioxi- dant defenses and decrease the inflammatory response.
D. Borges Dock-nascimento ³	2011		56 (12;14) No-diabetes 1–2 2	1-2	2	12.5% Carbohydrate; 12.5% Carbohydrate + 10 g L-glutamine	200	Placebo/blank	Carbohydrate + L-glutamine is safe and does not increase the RGV during induction of anesthesia.
Faria MS ²³	2009	2009 25 (12)	No-diabetes I–2 2	1-2	5	12.5% Maltodextrin	200	Blank	Carbohydrates diminish insu- lin resistance and the organic response to trauma.
J. Hausel ²⁴	2005	172 (55)	No-diabetes 1–2	1-2	7	12.5% Carbohydrate	400	Placebo/blank	CHO may have a beneficial effect on postoperative nausea and vomiting 12–24 h after laparoscopic cholecystectomy.
ASA, American Society of Anesthesiologists: CHO, Carbohydrate: RGV	Anesth	iesiologists; Cl	HO, Carbohydra	ate; RC	, , ,				

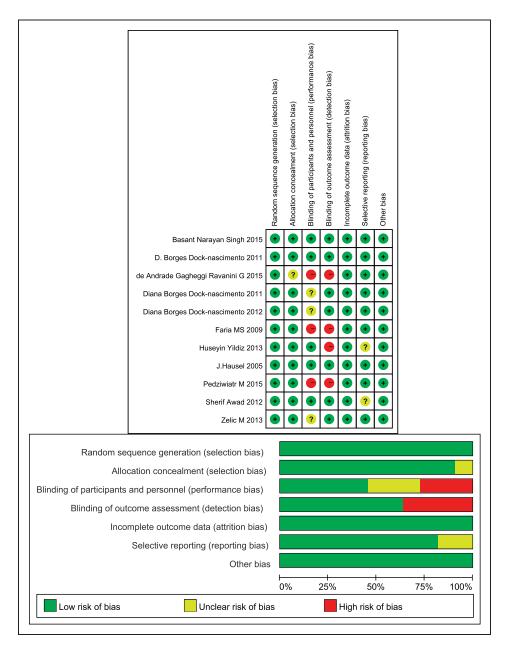


Figure 2. Methodological quality of trials included in the meta-analysis. Risk-of-bias graph and summary.

For the glucose metabolism index, a shortened fasting time significantly reduced abnormalities in the ratio of insulin sensitivity (lg(OR), -0.66; 95% CI, -1.31 to -0.01; P = 0.046). A shortened fasting time

also significantly reduced the postsurgical glucose concentration (SMD, -0.84; 95% CI, -1.67 to -0.00; P = 0.049). There were no significant differences in either the insulin or homeostatic model assessment–insulin

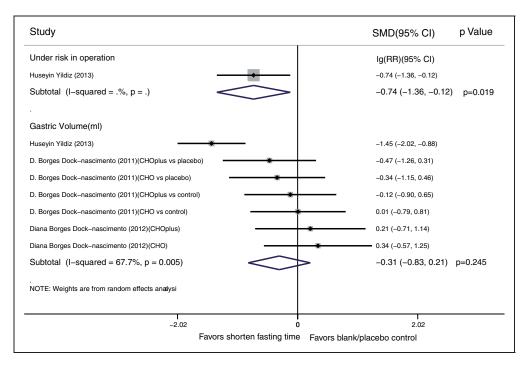


Figure 3. Results of operative risk and gastric volume index in assessment of shortened fasting time. Forest plot showing that a shortened fasting time significantly reduced the operative risk (lg(risk ratio), -0.74; 95% confidence interval, -1.36 to -0.12; P = 0.019), but had no significant effect on gastric volume (standardized mean difference, -0.31; 95% confidence interval, -0.83 to 0.21).

resistance (HOMA-IR) results between the shortened fasting and control groups (insulin: SMD, -0.09; 95% CI, -0.94 to 0.75 and HOMA-IR: SMD, -1.25; 95% CI, -2.62 to 0.12) (Figure 5).

For the stress response index, there was no significant difference in the cortisol results between the shortened fasting and control groups (SMD, -0.61; 95% CI, -1.24 to 0.03). The results also indicated that a shortened fasting time reduced the concentrations of CRP (SMD, -1.42; 95% CI, -2.33 to -0.51; P = 0.002) and carnitine (SMD, -0.99; 95% CI, -1.75 to -0.23; P = 0.011) (Figure 6).

Subgroup analysis

We used subgroup analysis to reduce significant heterogeneity among the results. Measurement of the intake volume before surgery reduced the heterogeneity among the gastric volume results, and adjusting for the control type reduced the heterogeneity of the nausea results (Table 2).

Publication bias

The Begg and Egger tests provided no evidence of significant publication bias in most outcome assessments except the gastric volume (Egger test, P=0.000; Begg test, N.S.), glucose (Egger test, P=0.001; Begg test, P=0.004) and HOMA-IR (Egger test, P=0.035; Begg test, N.S.) (Figure 7). The nonparametric "trim-and-fill" method was used to determine the reliability of our results; it showed no qualitative alterations except that a shortened fasting time reduced the gastric volume (random-effects model:

Study	lg(OR)(95% CI)	p Value
Pain(Visual analog scale)	SMD (95% CI)	
I.Hausel (2005)(vs control)	-1.50 (-1.92, -1.08)	
I.Hausel (2005)(vs placebo)	-1.00 (-1.39, -0.61)	
Basant Narayan Singh (2015)(vs placebo)	-0.89 (-1.35, -0.43)	
Basant Narayan Singh (2015)(vs control)	-0.79 (-1.25, -0.34)	
le Andrade Gagheggi Ravanini G (2015)	-0.07 (-0.71, 0.57)	
Subtotal (I-squared = 72.7%, p = 0.006)	-0.89 (-1.29, -0.50)	p=0.000
PONV(Preoperative nausea and vomiting)		
Pedziwiatr M (2015)	-0.32 (-1.40, 0.75)	
I.Hausel (2005)(vs control)	-0.24 (-0.59, 0.10)	
I.Hausel (2005)(vs placebo)	-0.23 (-0.57, 0.11)	
Subtotal (I-squared = 0.0%, p = 0.987)	-0.24 (-0.48, -0.00)	p=0.046
Nausea		
Basant Narayan Singh (2015)(vs placebo)	-0.76 (-1.25, -0.27)	
Basant Narayan Singh (2015)(vs control)	-0.51 (-0.95, -0.08)	
luseyin Yildiz (2013)	- 0.00 (-0.44, 0.44)	
le Andrade Gagheggi Ravanini G (2015)	0.11 (-0.65, 0.87)	
Subtotal (I-squared = 57.4%, p = 0.071)	-0.33 (-0.72, 0.06)	p=0.099
/omiting		
le Andrade Gagheggi Ravanini G (2015)(vs con trol)	-0.65 (-2.00, 0.70)	
Basant Narayan Singh (2015)	-0.63 (-1.08, -0.18)	
Faria MS (2009)	-0.59 (-1.45, 0.27)	
Basant Narayan Singh (2015)(vs placebo)	-0.54 (-0.99, -0.10)	
I.Hausel (2005)(vs placebo)	-0.21 (-0.85, 0.44)	
I.Hausel (2005)(vs control)	-0.11 (-0.78, 0.56)	
Subtotal (I-squared = 0.0%, p = 0.775)	-0.47 (-0.71, -0.22)	p=0.000
NOTE: Weights are from random effects analysis		
-2 0	1	
Favors shorten fasting time Fav	ors blank/placebo control	

Figure 4. Results of subjective sensation index in assessment of shortened fasting time. Forest plot showing that a shortened fasting time significantly reduced postoperative pain (standardized mean difference, -0.89; 95% confidence interval [CI], -1.29 to -0.50; P = 0.000), postoperative nausea and vomiting (lg(odds ratio [OR]), -0.24; 95% CI, -0.48 to -0.00; P = 0.046) and intraoperative vomiting (lg(OR), -0.47; 95% CI, -0.71 to -0.22; P = 0.000), but had no significant effect on intraoperative nausea (lg(OR), -0.33; 95% CI, -0.72 to 0.06).

SMD, -0.697; 95% CI, -1.207 to -0.187; asymptotic *P* = 0.007).

Discussion

In total, 11 articles and 701 patients were included in this systematic review of a variety of outcome measures. The data demonstrate that there is an overall benefit associated with a shortened preoperative fasting time, especially in terms of the subjective sensation index. In 2009, Brady et al.⁶ published a study on the effect of preoperative fasting on perioperative complications in children. Their study showed that 120 minutes of preoperative fasting did not lead to a higher gastric volume and lower gastric pH, but reduced perioperative discomfort. In 2015, Pinto Ados et al.⁷ published a meta-analysis of the impact of a shortened fasting time on perioperative complications in patients undergoing elective cancer surgery. The effects of preoperative carbohydrates on

Study	Low	High	SMD (95% CI)	p Value
Insulin sensitivity abnormal(Quicki test)		1	lg(OR)(95%CI)	
Diana Borges Dock-nascimento (2012)(CHOplus)			-1.00 (-2.07, 0.07)	
Diana Borges Dock-nascimento (2012)(CHO)		-	-0.46 (-1.28, 0.35)	
Subtotal (I-squared = 0.0%, p = 0.436)	0	1	-0.66 (-1.31, -0.01)	p=0.046
Glucose				
Diana Borges Dock-nascimento (2012)(CHOplus)			-3.98 (-5.64, -2.32)	
Diana Borges Dock-nascimento (2012)(CHO)			-1.90 (-3.01, -0.80)	
Diana Borges Dock-nascimento (2011)(CHOplus vs control)			-1.60 (-2.53, -0.67)	
Diana Borges Dock-nascimento (2011)(CHO vs control)	-+	4	-0.72 (-1.55, 0.10)	
Diana Borges Dock-nascimento (2011)(CHOplus vs placebo)		÷	-0.44 (-1.25, 0.37)	
Faria MS (2009)		+	-0.31 (-1.18, 0.55)	
Diana Borges Dock-nascimento (2011)(CHO vs placebo)		•	0.39 (-0.42, 1.20)	
Pedziwiatr M (2015)		+	0.79 (0.15, 1.44)	
Subtotal (I-squared = 85.7%, p = 0.000)	0		-0.84 (-1.67, -0.00)	p=0.049
Insulin				
Diana Borges Dock-nascimento (2012)(CHOplus)			-2.51 (-3.77, -1.24)	
Diana Borges Dock-nascimento (2012)(CHO)			-1.65 (-2.70, -0.59)	
Faria MS (2009)	•	1	-1.00 (-1.92, -0.09)	
Diana Borges Dock-nascimento (2011)(CHO vs control)		t	-0.63 (-1.45, 0.19)	
Pedziwiatr M (2015)	+	-	-0.23 (-0.85, 0.39)	
Diana Borges Dock-nascimento (2011)(CHOplus vs control)	-	÷	0.09 (-0.71, 0.89)	
de Andrade Gagheggi Ravanini G (2015)		•	0.54 (-0.11, 1.19)	
Diana Borges Dock-nascimento (2011)(CHO vs placebo)			1.98 (0.99, 2.97)	
Diana Borges Dock-nascimento (2011)(CHOplus vs placebo)		L —	2.35 (1.29, 3.41)	
Subtotal (I-squared = 88.4%, p = 0.000)	<	P	-0.09 (-0.94, 0.75)	p=0.826
HOMA-IR			,	
Faria MS (2009)			-9.88 (-13.14, -6.63)	
Diana Borges Dock-nascimento (2011)(CHOplus vs control)			-3.04 (-4.24, -1.83)	
Diana Borges Dock-nascimento (2011)(CHO vs control) Diana Borges Dock-nascimento (2011)(CHOplus vs placebo)		L	-2.03 (-3.03, -1.03)	
Pedziwiatr M (2015)			-0.45 (-1.26, 0.36) 0.34 (-0.28, 0.97)	
de Andrade Gagheggi Ravanini G (2015)			0.60 (-0.06, 1.25)	
Diana Borges Dock-nascimento (2011)(CHO vs placebo)			1.70 (0.75, 2.64)	
Subtotal (I-squared = 93.5% , p = 0.000)	\diamond		-1.25 (-2.62, 0.12)	p=0.074
NOTE: Weights are from random effects analysis				
I			l	
-13.1		0	13.1	

Figure 5. Results of glucose metabolism index in assessment of shortened fasting time. Forest plot showing that a shortened fasting time significantly reduced abnormalities in the ratio of insulin sensitivity (lg(odds ratio), -0.66; 95% confidence interval [CI], -1.31 to -0.01; P = 0.046) and reduced the postoperative glucose concentration (standardized mean difference [SMD], -0.84; 95% CI, -1.67 to -0.00; P = 0.049), but had no significant effects on the insulin concentration or homeostatic model assessment–insulin resistance (HOMA-IR) (insulin: SMD, -0.09; 95% CI, -0.94 to 0.75 and HOMA-IR: SMD, -1.25; 95% CI, -2.62 to 0.12).

glycaemic parameters, inflammatory markers, indicators of malnutrition and the hospital stay were evaluated in patients who underwent surgery for colorectal cancer and gastric cancer. However, because their analysis included only a small number of clinical studies, the evidence was unreliable. A meta-analysis of shortened preoperative fasting times published in 2014 included elective abdominal surgery, orthopaedic surgery, cardiac surgery and thyroidectomy and assessed the length of hospital stay, passage of flatus, glucose metabolism and postoperative complications. However, the design risk of the included studies was relatively high and included variety.⁸ Studies of laparoscopic cholecystectomy were included in this study. This procedure is

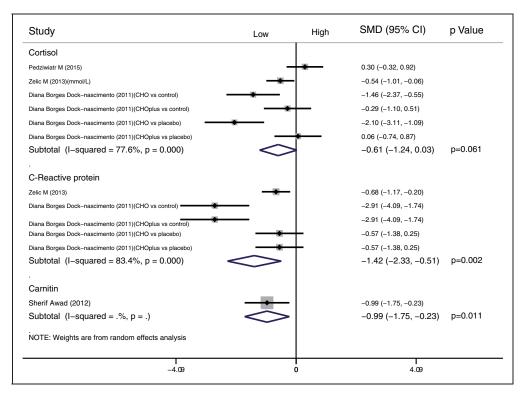


Figure 6. Results of stress response index in assessment of shortened fasting time. Forest plot showing significant differences in the C-reactive protein and carnitine concentrations between the shortened fasting and control groups (standardized mean difference [SMD], -1.42; 95% confidence interval [CI], -2.33 to -0.51; P = 0.002 and SMD, -0.99; 95% CI, -1.75 to -0.23; P = 0.011, respectively).

associated with low levels of trauma and is very common in general surgery. This type of surgical research could lead to promotion of a shortened fasting time in the clinical setting.

The present meta-analysis indicates that oral carbohydrates taken 2 hours before surgery do not affect the gastric volume. One report even concluded that carbohydrates can reduce the gastric volume to a greater extent than can routine fasting. Okabe et al.²¹ indicated that clear fluids, orange juice, and non-human milk had no significant effect on gastric emptying, although the total calories were the main influencing factor.¹³ Oral carbohydrates significantly reduced postoperative pain,

nausea and vomiting; one clinical trial of adenotonsillectomy had similar findings, although the results were not statistically significant.¹⁴ Postoperative insulin resistance refers to the reduction in tissue sensitivity and reactivity after surgery. HOMA-IR, calculated according to the formula blood glucose concentration (mg/dl) × blood insulin concentration $(\mu U/ml)/405$, can be used to evaluate the level of insulin resistance. Abnormal glucose tolerance and insulin resistance lead to poor recovery after surgery. Our analysis showed that oral carbohydrates reduce insulin resistance and enhance sensitivity. One study showed that carbohydrates also reduce insulin resistance in patients undergoing maxillofacial surgery.¹⁵ A certain

Outcome	Subgroup	lg(OR)/SMD (95% CI)	P-value	Heterogeneity	P for heterogeneity
Pain	Overall	-0.892 (-1.287 to -0.497)			
	Nutritional types	(
	Carbohydrate	-1.055 (-1.365 to -0.745)	0.000	52.00%	0.100
	Carbohydrate plus	-0.066 (-0.706 to 0.574)	0.840	.%	
	Control types				
	Blank control	-0.817 (-1.587 to -0.047)	0.038	86.20%	0.001
	Placebo control	-0.956 (-1.254 to -0.658)	0.000	0.00%	0.709
	Intake volume		0.000	0.00/0	007
	200 ml liquid	-0.066 (-0.706 to 0.574)	0.840	.%	
	400 ml liquid	-1.055 (-1.365 to -0.745)	0.000	52.00%	0.100
Nausea	Overall	-0.329 (-0.720 to 0.061)	0.099	57.40%	0.089
1 ausea	Nutritional types	0.527 (0.720 to 0.001)	0.077	37.10/0	0.007
	Carbohydrate	-0.417 (-0.850 to 0.016)	0.059	63.30%	0.065
	Carbohydrate plus	0.109 (-0.649 to 0.867)	0.778	.%	
	Control types	0.107 (-0.047 10 0.007)	0.770	.76	•
	Blank control	-0.187 (-0.580 to 0.207)	0.352	42.20%	0.177
	Placebo control	-0.758 (-1.247 to -0.269)	0.002	.%	0.177
	Intake volume	-0.756 (-1.247 to -0.207)	0.002	.76	
	200 ml liquid	0.109 (-0.649 to 0.867)	0.778	.%	
	400 ml liquid	-0.417 (-0.850 to 0.016)	0.059	. <i>7</i> % 63.30%	0.065
Glucose	Overall	-0.836 (-1.668 to -0.003)	0.037	85.70%	0.000
Glucose		-0.858 (-1.888 to -0.885)	0.077	05.70%	0.000
	Nutritional types	-0.292 (-1.150 to 0.567)	0.505	81.30%	0.000
	Carbohydrate		0.030	86.40%	0.000
	Carbohydrate plus Control types	-1.859 (-3.533 to -0.185)	0.050	00.10%	0.001
	Blank control	-1.541 (-2.518 to -0.564)	0.002	78.20%	0.001
	Placebo control	0.277 (-0.441 to 0.995)	0.002	63.40%	0.065
	Intake volume	0.277 (-0.441 to 0.775)	0.777	03.10%	0.005
	200 ml liquid	-1.073 (-1.888 to -0.259)	0.010	80.70%	0.000
			0.010	.%	
المعيدانية	400 ml liquid	0.791 (0.146 to 1.436)			
Insulin	Overall	-0.095 (-0.939 to 0.749)	0.826	88.40%	0.000
	Nutritional types	0.20((1.249 to 0.727)	0.565	96 40%	0.000
	Carbohydrate	-0.306 (-1.349 to 0.737)		86.40%	0.000
	Carbohydrate plus	0.160(-1.357 to 1.677)	0.836	91.20%	0.000
	Control types	0.774(-1.017)	0.070	01 70%	0.000
	Blank control	-0.774 (-1.617 to 0.069)	0.072	81.70%	0.000
	Placebo control	1.328 (-0.441 to 3.097)	0.141	91.80%	0.000
	Intake volume	0.001 (1.004 += 0.022)	0.075	00 70%	0.000
	200 ml liquid	-0.081 (-1.084 to 0.923)	0.875	89.70%	0.000
	400 ml liquid	-0.231 (-0.853 to 0.391)	0.466	.%	
HOMA-IR	Overall	-1.249 (-2.621 to 0.123)	0.074	93.50%	0.000
	Nutritional types		0.120	05 40%	0.000
	Carbohydrate	-1.839 (-4.272 to 0.594)	0.138	95.40%	0.000
	Carbohydrate plus	-0.898 (-2.729 to 0.932)	0.336	92.70%	0.000

 Table 2. Subgroup analysis of the effect of a shortened fasting time in patients undergoing laparoscopic cholecystectomy.

(continued)

Outcome	Subgroup	lg(OR)/SMD (95% CI)	P-value	Heterogeneity	P for heterogeneity
	Control types				
	Blank control	-3.126 (-5.811 to -0.440)	0.023	95.50%	0.000
	Placebo control	0.502 (-0.585 to 1.589)	0.366	82.60%	0.003
	Intake volume				
	200 ml liquid	-1.666 (-3.403 to 0.072)	0.060	94.40%	0.000
	400 ml liquid	0.341 (-0.284 to 0.965)	0.285	.%	
Cortisol	Overall	-0.607 (-1.241 to 0.027)	0.061	77.60%	0.000
	Nutritional types				
	Carbohydrate	-0.876~(-1.795 to 0.044)	0.062	85.00%	0.000
	Carbohydrate plus	-0.112 (-0.680 to 0.455)	0.698	0.00%	0.538
	Control types				
	Blank control	-0.699 (-1.282 to -0.115)	0.019	50.40%	0.133
	Placebo control	-0.528 (-1.849 to 0.794)	0.434	87.80%	0.000
	Intake volume				
	200 ml liquid	-0.911 (-1.869 to 0.048)	0.063	79.10%	0.002
	400 ml liquid	-0.143 (-0.961 to 0.676)	0.732	77.10%	0.037
CRP	Overall	-1.420 (-2.334 to -0.505)	0.002	83.40%	0.000
	Nutritional types				
	Carbohydrate	-1.279 (-2.431 to -0.127)	0.030	84.20%	0.002
	Carbohydrate plus	-1.699 (-3.996 to 0.598)	0.147	90.30%	0.001
	Control types				
	Blank control	-2.102 (-3.825 to -0.379)	0.017	90.30%	0.000
	Placebo control	-0.566 (-1.144 to 0.012)	0.055	0.00%	1.000
	Intake volume				
	200 ml liquid	-1.331 (-1.805 to -0.856)	0.000	85.50%	0.000
	400 ml liquid	-0.683 (-1.165 to -0.200)	0.006	.%	

Table 2. Continued.

OR, odds ratio; SMD, standardized mean difference; CI, confidence interval; HOMA-IR, homeostatic model assessmentinsulin resistance

stress response occurs after any type of surgery. Cortisol, which is regulated by adrenocorticotrophic hormone and increases after surgery, plays an important role in the immune system. CRP is another inflammatory indicator that significantly increases in the first 24 to 48 hours after surgery. The results of the present study indicate that oral carbohydrates lower cortisol concentrations, although the effect is not statistically significant. Furthermore, oral carbohydrates significantly reduce the CRP concentration. A study involving gastrointestinal surgery showed that oral carbohydrates taken 2 hours before surgery significantly reduced the postoperative inflammatory response and CRP/albumin ratio and shortened the hospital stay.¹⁶ Volume intake was a source of heterogeneity. There were no significant differences between the 200-ml carbohydrate intake group and the control group, while the gastric volume was reduced in the 400-ml intake group. After the publication bias was eliminated using the "trim-and-fill" method, a shortened fasting time and carbohydrate intake were found to reduce the gastric volume, which is consistent with the findings of another clinical trial.¹⁷ The control type may be a source of heterogeneity in postoperative nausea. A shortened fasting

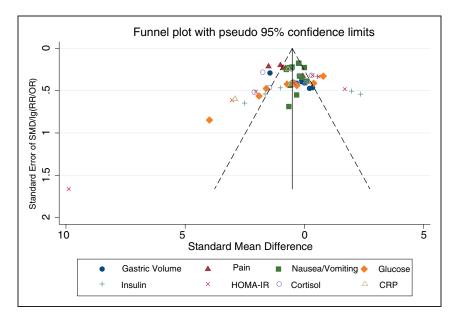


Figure 7. Funnel plots of publication bias. Begg and Egger tests provided no evidence of significant publication bias in most outcome assessments except gastric volume (Egger test, P = 0.000; Begg test, P = N.S.), glucose (Egger test, P = 0.001; Begg test, P = 0.004) and homeostatic model assessment-insulin resistance (Egger test, P = 0.035; Begg test, P = N.S.).

time and carbohydrate intake significantly reduced nausea when the control type was placebo (water).

Although the outcome measures of a shortened preoperative fasting time for laparoscopic cholecystectomy were comprehensively evaluated, this study had several limitations. First, we did not have specific individual data for all of the trials; thus, our statistical analysis could only be performed at the study level. Second, although subgroup analysis was performed, there was heterogeneity in several outcomes. This indicates that there are still unknown factors that cause heterogeneity. Third, the gastric volume, glucose concentration, and HOMA-IR were likely sources of publication bias.

Conclusions

The findings of our study suggest that the preoperative fasting time is associated with

increased postoperative comfort, improved insulin resistance, and a reduced stress response in patients undergoing laparoscopic cholecystectomy. This evidence supports the clinical application of a shortened fasting time in patients undergoing laparoscopic cholecystectomy.

Declaration of conflicting interests

The authors declare that there are no conflicts of interest.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Ethics

Not applicable. The study was a systematic review and meta-analysis of published data.

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