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META-ANALYSIS

Safety of fast-track rehabilitation after gastrointestinal surgery: Systematic review and meta-analysis

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Abstract

AIM: To compare the safety of fast-track rehabilitation protocols (FT) and conventional care strategies (CC), or FT and laparoscopic surgery (LFT) and FT and open surgery (OFT) after gastrointestinal surgery.

METHODS: We searched MEDLINE, WHO International Trial Register, Embase and The Cochrane Central Register of Controlled Trials up to 2014 for randomized controlled trials (RCTs) comparing FT and CC or comparing LFT and OFT, with 10 or more randomized participants and about 30 d follow-up. Two reviewers independently extracted data on complications, anastomotic leak, obstruction, wound infection, re-admission between FT and CC or LFT and OFT after gastrointestinal surgery.

RESULTS: Twenty-four RCTs of FT *vs* CC or LFT *vs* OFT were included. Compared with CC, FT reduced overall complications and wound infection. However, anastomotic leak, obstruction and re-admission were not significantly reduced. The pooled risk ratio (RR) of 0.69 (95%CI: 0.60-0.78; $P < 0.001$), pooled RR of 0.71 (95%CI: 0.57-0.88; $P < 0.001$), pooled RR of 0.93 (95%CI: 0.68-1.25; $P > 0.05$), a pooled RR of 0.87 (95%CI: 0.67-1.15; $P > 0.05$) and pooled RR of 0.94 (95%CI: 0.73-1.22; $P > 0.05$) respectively. Compared with OFT, LFT reduced complications, with a pooled RR of 0.66 (95%CI: 0.54-0.81; $P < 0.001$).

CONCLUSION: FTs are safe after gastrointestinal surgery. Additional large, prospective RCTs should be conducted to establish further the safety of this approach.

Key words: Fast-track rehabilitation protocols; Laparoscopic surgery; Open surgery; Enhanced recovery; Gastrointestinal surgery; Complications; Readmission; Anastomotic leak; Wound infection; Obstruction

Core tip: Fast-track rehabilitation protocols (FT) after gastrointestinal surgery have become the most fashionable method of treatment for gastrointestinal malignancy. Complications after FT for gastrointestinal resection have been discussed in China as well as other countries. This study clarified that compared with conventional care strategies, FT has a low level of complications and similar incidence of re-admission of about 1 mo.

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INTRODUCTION

In recent years, fast-track rehabilitation protocols (FT) have frequently appeared in the literature. The concept of FT was first proposed by a Danish surgeon, Kehlet, with the intent to reduce stress, complications, and hospital stay after gastrointestinal surgery[1,2].

FT was investigated initially in the setting of elective gastrointestinal surgery, where it was shown that, by optimizing and standardizing perioperative care, median length of hospital stay could be reduced from 8-12 d to 2-4 d[3-5]. For the surgical treatment of gastrointestinal malignant disease, conventional elective gastrointestinal resection is associated with a complication rate of 10%-45% and a postoperative hospital stay of 8-13 d[7-10]. It has been established that a higher rate of serious postoperative complications is associated with an excessive response to surgical tress[11-13] and that C-reactive protein (CRP), interleukin (IL)-6, tumor necrosis factor (TNF)-α and resting energy expenditure (REE) may act as markers for the severity of the surgical stress response[14-19]. To improve this problem, FT has been developed[20-22]. FT is based on the reduction of surgical stress by various surgical and anesthetic approaches to enhance recovery.

In a prospective study investigating the value of an accelerated recovery program in elective gastrointestinal resection, Grantcharov and Kehlet[23] demonstrated that a number of the principles of FT, such as avoidance of prophylactic nasogastric tubes and abdominal drains, early postoperative feeding, and use of multimodal analgesia, could be applied successfully in this clinical setting without increasing postoperative morbidity[23]. The safety of FT has been fiercely disputed. Therefore, the primary aim of this meta-analysis was to evaluate the safety of FT *vs* conventional care strategies (CC) or FT and laparoscopic surgery (LFT) *vs* FT and open surgery (OFT), as measured by the rate of complications, specifically anastomotic leaks, wound infection, obstruction and re-admission. The secondary aim was to understand the difficulties, limitations, or advantages of FT for gastrointestinal surgery.

MATERIALS AND METHODS

Publication search

Relevant studies were identified by searching the following data: MEDLINE (1985 until present), WHO International Trial Register (1985 until present), Embase (1985 until present) and The Cochrane Central Register of Controlled Trials (1985 until present). The medical subject headings (MeSH) and keywords searched for individually and in combination were as follows: "fast track" or "enhanced recovery" and "colorectal and surgery" or "gastric and surgery". The last search was done on March 1, 2014. The search was limited to randomized controlled trials (RCTs) with about 30-d follow-up, but without age, sex and weight. Reference lists from identified trials and review articles were manually scanned to identify any other relevant studies. Internet search engines were also used to perform a manual search for abstracts from international meetings, which were then downloaded and studied.

Inclusion and exclusion criteria

The inclusion criteria for the study were: (1) RCTs; (2) detailed patient information provided; and (3) to be considered FT, a rehabilitation protocol had to include at least seven of the 20 FT items in the FT group (preoperative counseling, preoperative feeding, no premedication, no bowel preparation, fluid restriction, symbiotics administered before surgery, no preoperative fasting but provision of clear carbohydrate-enriched liquids until 2 h before surgery, multi-way anesthetic techniques, high inspired oxygen concentrations, avoidance of perioperative fluid overload, short/transverse incisions, maintenance of body temperature, no routine use of drains, non-opioid analgesia and nasogastric decompression tubes, standard laxatives, early removal of bladder catheters and prokinetics, and early postoperative mobilization and feeding[6]) to achieve early recovery after gastrointestinal surgery, with no more than two CCs. When a study reporting the same patient cohort was included in several publications, only the most recent or complete study was selected.

The exclusion criteria were: (1) case reports; (2) articles that were not full text or were non-comparative studies; (3) more than two CCs were included; and (4) the FT included no more than seven of the 20 FT items.

Study selection

RCTs met the inclusion criteria if they involved the FT for gastrointestinal malignant disease in adult patients and used CCs for control. Both full-length publications and abstracts were selected. Letters, reviews without original data and animal studies were excluded. If any doubt about suitability remained after the abstract was examined, the full manuscript was obtained.

Data extraction

All included studies were assessed for the quality of their methodology and relevance to the objective of our meta-analysis. Conduct and reporting were in accordance with the QUOROM statement. Data on complications (anastomotic leak, wound infection, obstruction) and re-admission from each trial were extracted and compared independently by the two investigators.

Assessment of risk of bias

To identify potential sources of bias in the reported events, we followed the Cochrane Collaboration's risk of bias framework[24] and considered for each trial the following risk domains: (1) selection bias (random sequence generation and allocation concealment); (2) performance bias (blinding of participants and study investigators for the outcomes of interest); (3) detection bias (blinding of outcome assessors); (4) attrition bias (incomplete out-

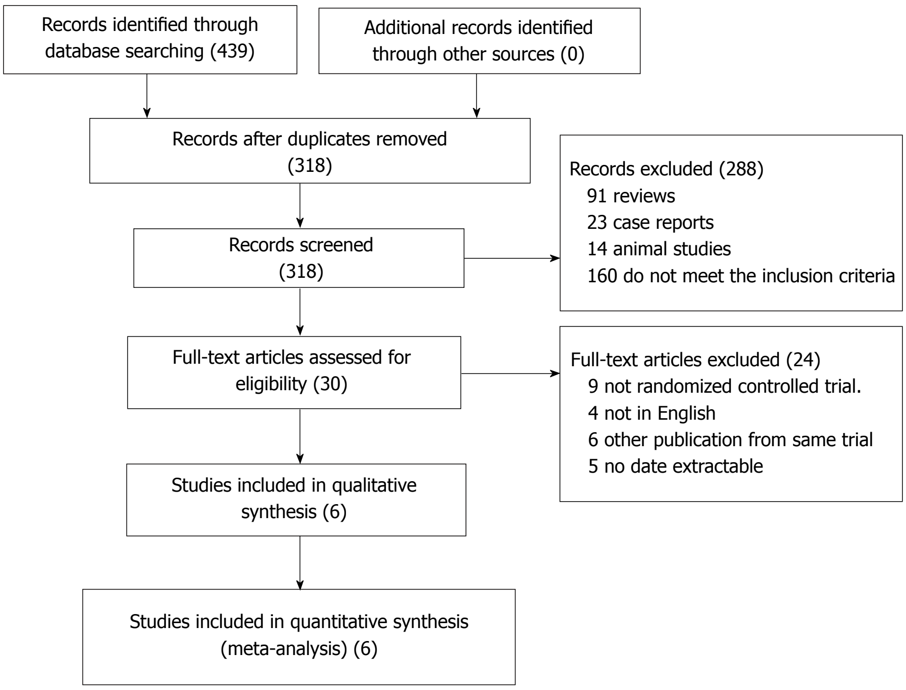

Figure 1 Selection of studies.

come data); and (5) reporting bias (selective outcome reporting). Risk of bias for each domain was categorized as low, unclear, or high. This information was used to make judgments about the overall risk of bias for each trial. We followed the Cochrane Collaboration's recommendation to make judgments on the basis of whether the ranking of the level of bias across domains could have led to any material bias on the outcomes of interests and, where applicable, what the direction of the bias would likely be[24].

Statistical analysis

Statistical analysis was conducted using Review Manager version 5.0.0 (Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). Pooled risk ratios (RRs) with 95% confidence intervals (CIs) were used to assess complications (anastomotic leaks, wound infection, and obstruction) and re-admission. Statistical heterogeneity was assessed with a χ^2 test, for which $P < 0.1$ was considered statistically significant. The I^2 statistic was used to assess the impact of heterogeneity on the meta-analysis. If the test of heterogeneity was statistically significant, then the random-effects model was used; otherwise, a fixed-effects model was used. Two-sided P values < 0.05 were considered statistically significant. Funnel plots and Egger's test were used to evaluate publication bias.

RESULTS

Search results

Five hundred and ninety-six references were identified from the medical journal databases. On examination of the abstracts, 485 articles were rejected based on the criteria outlined in Figure 1. Assessment of the complete text of the 87 remaining articles led to the elimination of 25 papers that contained no data pertaining to the outcome of LFT for colorectal resection, and 24 that were not RCTs. Nine had fewer than seven items of FT, 12 papers were of animal studies, and 17 papers explained the effect of analgesia. The remaining 24 nonduplicated RCTs that compared FT with CC were included in the meta-analysis.

Characteristics of the selected RCTs

Characteristics of the 24 RCTs[2,25-47] included in the meta-analysis are summarized in Table 1. The bias of included studies was low (Table 2). These studies were published between 1985 and 2013 and investigated a total of 3365 patients, 2093 of whom received an FT and 1272 of whom received a CC. Nineteen of the studies compared FT and CC for colorectal resection (2538 patients), 15 of the studies compared OFT and OCC for colorectal resection (1690 patients), eight of the studies compared LFT and LCC for colorectal resection (774 patients), and nine of the studies compared LFT and OFT for colorectal resection (827 patients). Two studies[38,48] published by the same team from the same institute within the same study interval were regarded as one trial, but both studies were included and shared the same study number because some separately published data were complementary.

Meta-analysis results

Complications: Compared with CC, FT reduced complications. The pooled RR was 0.69 (95%CI: 0.60-0.78; $P < 0.001$), $\chi^2 = 95.37$ ($P < 0.001$) and $I^2 = 57\%$ (Figure 2A, Table 3).

Nineteen studies (2538 patients) provided data on complications for FT *vs* CC; 26.7% (338/1266 patients) had complications in the FT group and 36.4% (463/1272)

Table 1 Main characteristics of the 24 included studies

Ref.	Way	Year	No.		Age (yr)		Sex (M:F)	
			FT	CC	FT	CC	FT	CC
Ionescu *et al*[25]	Open	2009	48	48	60.94 ± 9.9	63.1 ± 12.19	30:18	31:17
Ren *et al*[26]	Open	2012	299	298	59	61	178:121	190:108
Yang *et al*[27]	Open	2012	32	30	57.2 ± 11.70	59.5 ± 12.10	20:12	22:8
Hübner *et al*[28]	Open	2010	36	31	60	61	18:18	17:14
Wang *et al*[29]	Open	2012	41	42	57.2 ± 18.1	55.4 ± 16.8	24:17	25:17
Vlug *et al*[30]	Open	2011	93	98	66 ± 10.3	66 ± 7.1	54:39	59:39
van Bree *et al*[31]	Lap	2011	18	18	64 ± 10.1	66 ± 6.9	11:7	11:7
Veenhof *et al*[32]	Lap	2012	17	20	65	68	9:8	14:6
Serclová *et al*[33]	Lap/open	2009	51	52	35.1 ± 11.0	37.6 ± 12.5	20:31	32:20
Muller *et al*[34]	Lap/open	2009	76	75	62	59	37:39	40:35
Wang *et al*[35]	Lap/open	2011	40	38	71	72	22:18	20:18
Wang *et al*[36]	Lap/open	2011	106	104	57	55	65:41	60:44
King *et al*[38]	Lap/open	2008	41	19	72.3	70.4	23:18	8:11
Faiz *et al*[37]	Lap/open	2008	191	50	67.9 ± 14.1	66.3 ± 13.7	20:30	98:93
Srinivasa *et al*[39]	Lap/open	2013	37	37	69 ± 16	72 ± 12	19:18	22:15
Basse *et al*[40]	Lap/open	2005	30	30	75.5	75	14:16	14:16
MacKay *et al*[41]	Lap/open	2006	22	58	72	73.2	12:10	25:33
García-Botello *et al*[42]	Lap/open	2011	61	58	62	60	40:21	32:26
Anderson *et al*[43]	Open	2003	14	11	64	68	6:86	5:6
Gatt *et al*[44]	Open	2005	19	20	67	67	14:6	9:109
Khooet *al*[2]	Open	2007	35	35	69.3	73	12:23	15:20
Wang *et al*[45]	Open	2010	47	45	58.76 ± 9.66	56.87 ± 9.16	32:133	29:18
Chen Hu *et al*[46]	Lap/open	2012	40	42	59/64	62.5/64.5	19:21	22:20
Lemanu *et al*[47]	Lap	2012	40	38	43.5	43.9	13:27	10:28

Lap: Laparoscopy.

Table 2 Risk-of-bias assessment of the randomized controlled trials

Ref.	Selection bias	Performance bias	Detection bias	Attrition bias	Reporting	Overall risk of bias
Ionescu *et al*[25]	Low	Low	Low	Low	Low	Low
Ren et *et al*[26]	Low	Unclear	Low	Low	Low	Low
Yang *et al*[27]	Low	Low	Low	Unclear	Low	Low
Hübner *et al*[28]	Low	Low	Low	Low	Low	Low
Wang *et al*[29]	Low	Low	Low	Low	Unclear	Low
Vlug *et al*[30]	Unclear	Low	Low	Low	Low	Low
van *et al*[31]	Low	Low	Low	Low	Unclear	Low
Veenhof *et al*[32]	Low	Low	Unclear	Low	Low	Low
Serclová *et al*[33]	Low	Low	Low	Low	Unclear	Low
Muller *et al*[34]	Low	Low	Low	Low	Unclear	Low
Wang *et al*[35]	Unclear	Low	Low	Low	Low	Low
Wang *et al*[36]	Unclear	Low	Low	Low	Low	Low
King *et al*[38]	Low	Low	Unclear	Low	Low	Low
Faiz *et al*[37]	Low	Low	Low	Low	Unclear	Low
Srinivasa *et al*[39]	Low	Unclear	Low	Low	Low	Low
Basse *et al*[40]	Unclear	Low	Low	Low	Low	Low
MacKay *et al*[41]	Low	Low	Low	Low	Low	Low
García-Botello *et al*[42]	Low	Low	Low	Low	Unclear	Low
Anderson *et al*[43]	Low	Low	Low	Low	Low	Low
Gatt *et al*[44]	Low	Unclear	Low	Low	Low	Low
Khoo *et al*[2]	Low	Low	Low	Low	Low	Low
Wang *et al*[45]	Low	Low	Low	Low	Low	Low
Chen Hu *et al*[46]	Low	Low	Low	Low	Low	Low
Lemanu *et al*[47]	Low	Low	Low	Low	Unclear	Low

Selection bias is based on random sequence generation and allocation concealment; performance bias includes blinding of participants and study investigators for the outcomes of interest; detection bias includes blinding of outcome assessors; attrition bias indicates systematic loss of participants in one arm, which could lead to missing outcome data for that trial arm over the other trial arm; and reporting bias includes the possibility of selective outcome reporting. Selection bias is a feature of the trial design. Performance and detection bias are overall low given that most data were collected without any prior knowledge of the investigators of the tested hypothesis in this study at the time of event collection. All analyses in this report are based on intention-to-treat and we further mitigated the possible effect of any attrition bias and reporting bias at individual trial level by collection of additional unpublished data.

Table 3 Risk ratio and 95%CI of complications for FT *vs* CC during colorectal surgery in all of the patients

Outcome or subgroup	Studies (*n*)	Participants (*n*)	Effect estimate RR (95%CI)	heterogeneity	
				I^2	*P* value
1.1 Complication					
1.1.1 FT *vs* CC	19	2538	0.67 (0.56, 0.82)	58%	0.0009
1.1.2 OFT *vs* OCC	15	1690	0.73 (0.58, 0.93)	57%	0.003
1.1.3 LFT *vs* LCC	8	774	0.58 (0.38, 0.88)	62%	0.01
1.1.4 LFT *vs* OFT	8	586	0.72 (0.56, 0.92)	24%	0.24
1.2 Anastomotic leak					
1.2.1 FT *vs* CC	11	1939	0.92 (0.60, 1.43)	0%	0.96
1.2.2 OFT *vs* OCC	9	1364	0.90 (0.53, 1.53)	0%	0.90
1.2.3 LFT *vs* LCC	5	575	0.98 (0.48, 2.01)	0%	0.60
1.2.4 LFT *vs* OFT	6	626	0.83 (0.40, 1.73)	0%	0.78
1.3 obstruction					
1.3.1 FT *vs* CC	9	1698	0.87 (0.59, 1.29)	0%	0.96
1.3.2 OFT *vs* OCC	7	1160	0.97 (0.62, 1.52)	0%	1.00
1.3.3 LFT *vs* LCC	4	539	0.67 (0.32, 1.42)	0%	0.62
1.3.4 LFT *vs* OFT	3	295	1.23 (0.51, 3.00)	0%	0.40
1.4 Wound infection					
1.4.1 FT *vs* CC	14	2133	0.72 (0.52, 0.97)	10%	0.34
1.4.2 OFT *vs* OCC	12	1461	0.72 (0.51, 1.02)	28%	0.18
1.4.3 LFT *vs* LCC	5	539	0.64 (0.32, 1.26)	0%	0.91
1.4.4 LFT *vs* OFT	4	329	0.51 (0.26, 1.01)	35%	0.20
1.5 re-admission					
1.5.1 FT *vs* CC	11	1468	0.99 (0.71, 1.39)	0%	0.80
1.5.2 OFT *vs* OCC	8	781	1.07 (0.60, 1.91)	0%	0.85
1.5.3 LFT *vs* LCC	5	613	0.74 (0.43, 1.28)	0%	0.82
1.5.4 LFT *vs* OFT	6	671	0.45 (0.29, 0.71)	14%	0.32

in the CC group. Pooling the results indicated that FT significantly reduced complications compared with CC. The weighted mean difference (WMD) was 0.67 (95%CI: 0.56-0.82, $P < 0.001$), $\chi^2 = 42.76$ ($P = 0.0009$) and $I^2 = 58\%$, indicating heterogeneity among the studies.

Fifteen studies (1690 patients) provided data on complications for OFT *vs* OCC; 25% (211/847 patients) had complications in the OFT group and 32.6% (275/843) in the OCC group. Pooling the results indicated that OFT significantly reduce complications compared with OCC. The WMD was 0.73 (95%CI: 0.58-0.93; $P < 0.05$), $\chi^2 = 32.76$ ($P = 0.003$) and $I^2 = 57\%$, indicating heterogeneity among the studies.

Eight studies (774 patients) provided data on complications for LFT *vs* LCC; 26.5% (101/382 patients) had complications in the LFT group and 34% (133/392) in the LCC group. Pooling the results indicated that LFT significantly reduce complications compared with LCC. The WMD was 0.58 (95%CI: 0.38-0.88; $P < 0.05$), $\chi^2 = 18.33$ ($P = 0.01$) and $I^2 = 62\%$, indicating heterogeneity among the studies.

Eight studies (586 patients) provided data on complications for LFT *vs* OFT; 23.9% (69/289 patients) had complications in the LFT group and 33% (98/297) in the OFT group. Pooling the results indicated that LFT significantly reduce complications compared with OFT. The WMD was 0.72 (95%CI: 0.56-0.92; $P < 0.05$), $\chi^2 = 9.16$ ($P = 0.01$) and $I^2 = 24\%$, which excludes heterogeneity among the studies.

Anastomotic leak: Compared with CC, FT reduced anastomotic leaks. The pooled RR was 0.93 (95%CI: 0.68-1.25; $P > 0.05$), $\chi^2 = 9.95$ ($P = 0.99$) and $I^2 = 0\%$ (Figure 2B, Table 3).

Eleven studies (1939 patients) provided data on anastomotic leaks for FT *vs* CC; 3.7% (36/966 patients) had anastomotic leaks in the FT group and 4.1% (40/973) in the CC group. Pooling the results indicated that FT did not significantly reduce anastomotic leaks compared with CC. The WMD was 0.92 (95%CI: 0.60-1.43, $P > 0.05$), $\chi^2 = 3.68$ ($P = 0.96$) and $I^2 = 0\%$, which excludes heterogeneity among the studies.

Nine studies (1364 patients) provided data on anastomotic leaks for OFT *vs* OCC; 3.4% (23/683 patients) had complications in the OFT group and 3.8% (26/681) in the OCC group. Pooling the results indicated that OFT did not significantly reduce anastomotic leaks compared with OCC. The WMD was 0.90 (95%CI: 0.53-1.53, $P > 0.05$), $\chi^2 = 3.44$ ($P = 0.90$) and $I^2 = 0\%$, which excludes heterogeneity among the studies.

Five studies (575 patients) provided data on anastomotic leaks for LFT *vs* LCC; 4.6% (13/283 patients) had anastomotic leaks in the LFT group and 4.8% (14/292) in the LCC group. Pooling the results indicated that LFT did not significantly reduce anastomotic leaks compared with LCC. The WMD was 0.98 (95%CI: 0.48-2.01, $P > 0.05$), $\chi^2 = 2.73$ ($P = 0.60$) and $I^2 = 0\%$, which excludes heterogeneity among the studies.

Six studies (626 patients) provided data on anastomotic leaks for LFT *vs* OFT; 3.8% (15/399 patients) had anastomotic leaks in the LFT group and 5.3% (12/227) in the OFT group. Pooling the results indicated that LFT significantly reduce anastomotic leaks compared with OFT. The WMD was 0.83 (95%CI: 0.40-1.73, $P > 0.05$),

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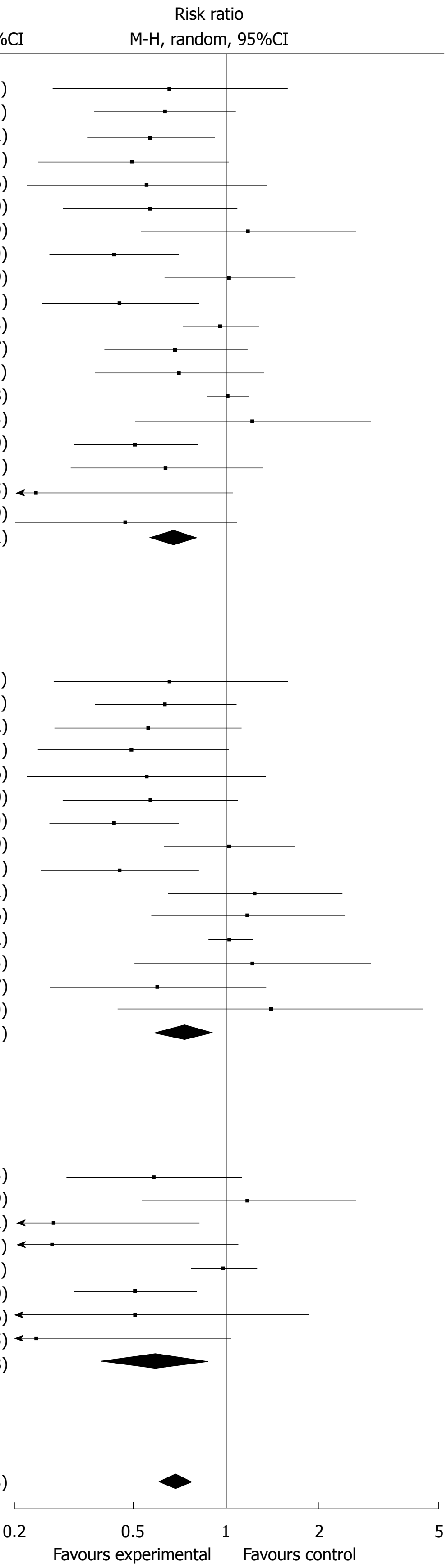
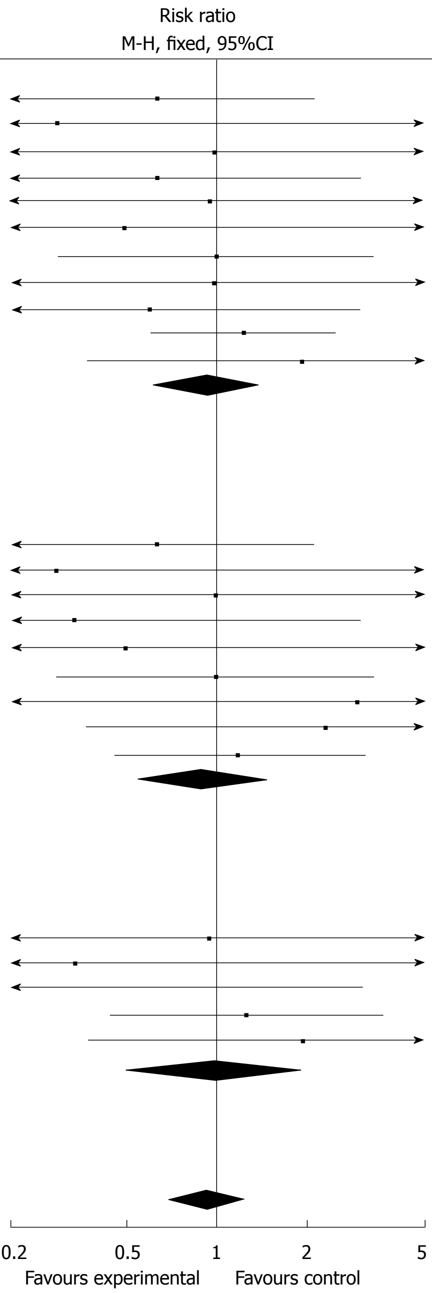
Study or subgroup	FT Events	FT Total	CC Events	CC Total	Weight	Risk ratio M-H, random, 95%CI
1.1.1 FT *vs* CC						
Anderson 2003	5	14	6	11	1.6%	0.65 (0.27, 1.59)
Gatt 2005	9	19	15	20	2.9%	0.63 (0.37, 1.08)
Chen Hu 2012	14	40	26	42	3.2%	0.57 (0.35, 0.92)
Hübner 2010	8	36	14	31	2.1%	0.49 (0.24, 1.01)
Lonescu 2009	6	48	11	48	1.5%	0.55 (0.22, 1.36)
Khoo 2007	9	35	16	35	2.3%	0.56 (0.29, 1.10)
Lemanu 2012	10	40	8	38	1.8%	1.19 (0.52, 2.69)
Muller 2009	16	76	37	75	3.2%	0.43 (0.26, 0.70)
Ren 2012	29	299	28	298	3.2%	1.03 (0.63, 1.69)
Serclova 2009	11	51	25	52	2.6%	0.45 (0.25, 0.81)
Srinivasa 2013	26	37	27	37	4.5%	0.96 (0.72, 1.28)
van Bree 2011	13	36	19	36	2.9%	0.68 (0.40, 1.17)
Veenhof 2012	10	36	17	43	2.4%	0.70 (0.37, 1.34)
Vlug 2011	125	193	132	207	5.3%	1.02 (0.88, 1.18)
Wang 2010	9	47	7	45	1.6%	1.23 (0.50, 3.03)
Wang 2011	20	106	39	104	3.3%	0.50 (0.32, 0.80)
Wang 2012	10	81	16	82	2.1%	0.63 (0.31, 1.31)
Wang 2011	2	40	8	38	0.7%	0.24 (0.05, 1.05)
Yang 2012	6	32	12	30	1.7%	0.47 (0.20, 1.09)
Subtotal (95%CI)		1266		1272	48.9%	0.67 (0.56, 0.82)
Total events	338		463			
Heterogeneity: $Tau^2 = 0.08, \chi^2 = 42.76, df = 18 (P = 0.0009); I^2 = 58\%$						
Test for overall effect: $Z = 4.05 (P < 0.0001)$						
1.1.2 OFT *vs* OCC						
Anderson 2003	5	14	6	11	1.6%	0.65 (0.27, 1.59)
Gatt 2005	9	19	15	20	2.9%	0.63 (0.37, 1.08)
Chen Hu 2012	7	21	12	20	2.2%	0.56 (0.28, 1.12)
Hübner 2010	8	36	14	31	2.1%	0.49 (0.24, 1.01)
Lonescu 2009	6	48	11	48	1.5%	0.55 (0.22, 1.36)
Khoo 2007	9	35	16	35	2.3%	0.56 (0.29, 1.10)
Muller 2009	16	76	37	75	3.2%	0.43 (0.26, 0.70)
Ren 2012	29	299	28	298	3.2%	1.03 (0.63, 1.69)
Serclova 2009	11	51	25	52	2.6%	0.45 (0.25, 0.81)
van Bree 2011	10	18	8	18	2.3%	1.25 (0.65, 2.42)
Veenhof 2012	8	17	8	20	2.1%	1.18 (0.56, 2.46)
Vlug 2011	71	93	72	98	5.2%	1.04 (0.88, 1.22)
Wang 2010	9	47	7	45	1.6%	1.23 (0.50, 3.03)
Wang 2012	7	41	12	42	1.8%	0.60 (0.26, 1.37)
Yang 2012	6	32	4	30	1.1%	1.41 (0.44, 4.50)
Subtotal (95%CI)		847		843	35.5%	0.73 (0.58, 0.93)
Total events	211		275			
Heterogeneity: $Tau^2 = 0.11, \chi^2 = 32.76, df = 14 (P = 0.003); I^2 = 57\%$						
Test for overall effect: $Z = 2.56 (P = 0.01)$						
1.1.3 LFT *vs* LCC						
Chen Hu 2012	7	19	14	22	2.3%	0.58 (0.30, 1.13)
Lemanu 2012	10	40	8	38	1.8%	1.19 (0.52, 2.69)
van Bree 2011	3	18	11	18	1.2%	0.27 (0.09, 0.82)
Veenhof 2012	2	19	9	23	0.8%	0.27 (0.07, 1.10)
Vlug 2011	54	100	60	109	4.7%	0.98 (0.77, 1.26)
Wang 2011	20	106	39	104	3.3%	0.50 (0.32, 0.80)
Wang 2012	3	40	6	40	0.9%	0.50 (0.13, 1.86)
Wang 2011	2	40	8	38	0.7%	0.24 (0.05, 1.05)
Subtotal (95%CI)		382		392	15.6%	0.58 (0.38, 0.88)
Total events	101		155			
Heterogeneity: $Tau^2 = 0.18, \chi^2 = 18.33, df = 7 (P = 0.01); I^2 = 62\%$						
Test for overall effect: $Z = 2.53 (P = 0.01)$						
Total (95%CI)		2495		2507	100.0%	0.69 (0.60, 0.78)
Total events	650		893			
Heterogeneity: $Tau^2 = 0.08, \chi^2 = 95.37, df = 41 (P < 0.00001); I^2 = 57\%$						
Test for overall effect: $Z = 5.57 (P < 0.00001)$						



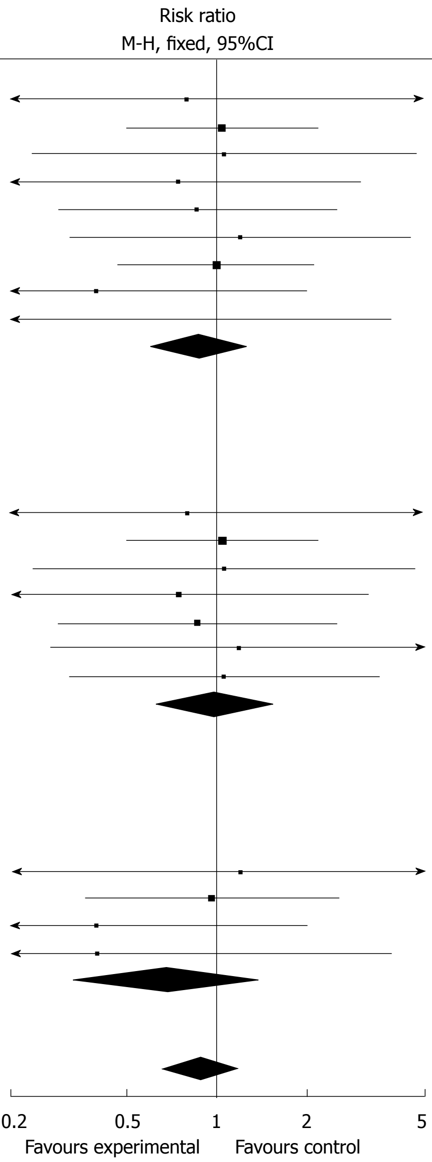
B

Study or subgroup	FT Events	FT Total	CC Events	CC Total	Weight	Risk ratio M-H, fixed, 95%CI
1.2.1 FT *vs* CC						
García-Botello 2011	4	61	6	58	7.5%	0.63 (0.19, 2.13)
Hübner 2010	0	36	1	31	2.0%	0.29 (0.01, 6.83)
Lonescu 2009	1	48	1	48	1.2%	1.00 (0.06, 15.53)
Khoo 2007	1	35	3	35	3.7%	0.33 (0.04, 3.05)
Lemanu 2012	2	40	2	38	2.5%	0.95 (0.14, 6.41)
Muller 2009	1	76	2	75	2.5%	0.49 (0.05, 5.33)
Ren 2012	5	299	5	298	6.1%	1.00 (0.29, 3.41)
van Bree 2011	1	36	1	36	1.2%	1.00 (0.07, 15.38)
Veenhof 2012	2	36	4	43	4.5%	0.60 (0.12, 3.07)
Vlug 2011	15	193	13	207	15.4%	1.24 (0.60, 2.53)
Wang 2011	4	106	2	104	2.5%	1.96 (0.37, 10.48)
Subtotal (95%CI)		966		973	49.1%	0.92 (0.60, 1.43)
Total events	36		40			
Heterogeneity: χ^2 = 3.68, df = 10 (P = 0.96); I^2 = 0%						
Test for overall effect: Z = 0.36 (P = 0.72)						
1.2.2 OFT *vs* OCC						
García-Botello 2011	4	61	6	58	7.5%	0.63 (0.19, 2.13)
Hübner 2010	0	36	1	31	2.0%	0.29 (0.01, 6.83)
Lonescu 2009	1	48	1	48	1.2%	1.00 (0.06, 15.53)
Khoo 2007	1	35	3	35	3.7%	0.33 (0.04, 3.05)
Muller 2009	1	76	2	75	2.5%	0.49 (0.05, 5.33)
Ren 2012	5	299	5	298	6.1%	1.00 (0.29, 3.41)
van Bree 2011	1	18	0	18	0.6%	3.00 (0.13, 69.09)
Veenhof 2012	2	17	1	20	1.1%	2.35 (0.23, 23.75)
Vlug 2011	8	93	7	98	8.4%	1.20 (0.45, 3.19)
Subtotal (95%CI)		683		681	33.1%	0.90 (0.53, 1.53)
Total events	23		26			
Heterogeneity: χ^2 = 3.44, df = 8 (P = 0.90); I^2 = 0%						
Test for overall effect: Z = 0.40 (P = 0.69)						
1.2.3 LFT *vs* LCC						
Lemanu 2012	2	40	2	38	2.5%	0.95 (0.14, 6.41)
van Bree 2011	0	18	1	18	1.8%	0.33 (0.01, 7.68)
Veenhof 2012	0	19	3	23	3.9%	0.17 (0.01, 3.13)
Vlug 2011	7	100	6	109	7.0%	1.27 (0.44, 3.66)
Wang 2011	4	106	2	104	2.5%	1.96 (0.37, 10.48)
Subtotal (95%CI)		283		292	17.8%	0.98 (0.48, 2.01)
Total events	13		14			
Heterogeneity: χ^2 = 2.73, df = 4 (P = 0.60); I^2 = 0%						
Test for overall effect: Z = 0.05 (P = 0.96)						
Total (95%CI)		1932		1946	100.0%	0.93 (0.68, 1.25)
Total events	72		80			
Heterogeneity: χ^2 = 9.95, df = 24 (P = 0.99); I^2 = 0%						
Test for overall effect: Z = 0.50 (P = 0.62)						



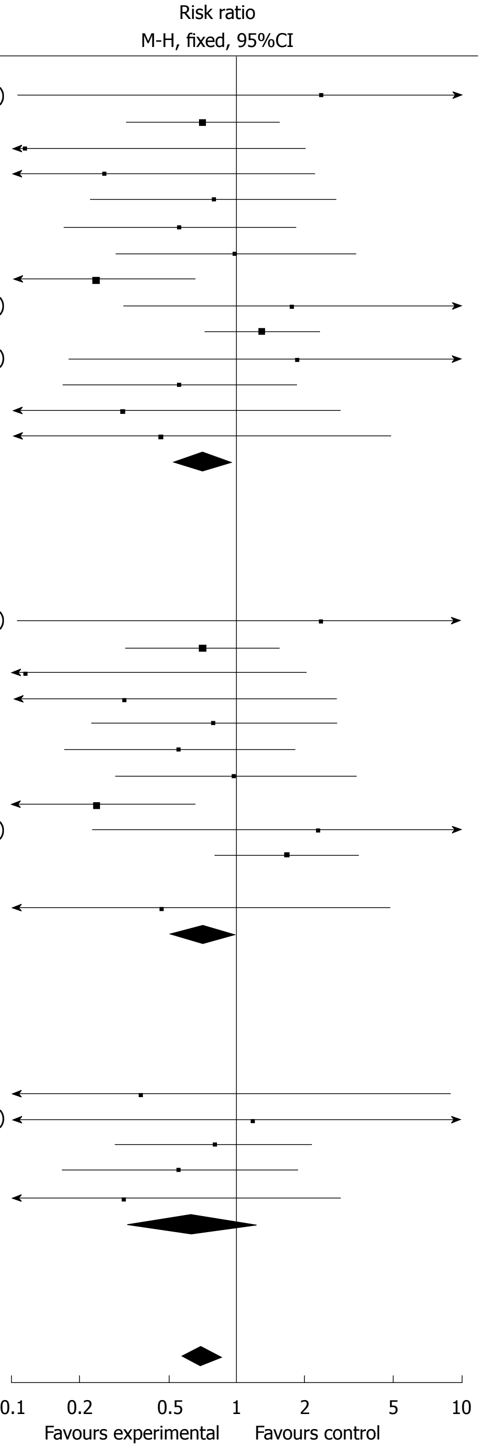
C

Study or subgroup	FT Events	FT Total	CC Events	CC Total	Weight	Risk ratio M-H, fixed, 95%CI
1.3.1 FT *vs* CC						
Anderson 2003	1	14	1	11	1.1%	0.79 (0.06, 11.20)
García-Botello 2011	12	61	11	58	11.2%	1.04 (0.50, 2.16)
Gatt 2005	3	19	3	20	2.9%	1.05 (0.24, 4.59)
Muller 2009	3	76	4	75	4.0%	0.74 (0.17, 3.20)
Ren 2012	6	299	7	298	7.0%	0.85 (0.29, 2.51)
Veenhof 2012	4	36	4	43	3.6%	1.19 (0.32, 4.44)
Vlug 2011	12	193	13	207	12.5%	0.99 (0.46, 2.12)
Wang 2011	2	106	5	104	5.0%	0.39 (0.08, 1.98)
Wang 2011	0	40	2	38	2.6%	0.19 (0.01, 3.84)
Subtotal (95%CI)		844		854	50.0%	0.87 (0.59, 1.29)
Total events	43		50			
Heterogeneity: χ^2 = 2.58, df = 8 (*P* = 0.96); I^2 = 0%						
Test for overall effect: *Z* = 0.68 (*P* = 0.50)						
1.3.2 OFT *vs* OCC						
Anderson 2003	1	14	1	11	1.1%	0.79 (0.06, 11.20)
García-Botello 2011	12	61	11	58	11.2%	1.04 (0.50, 2.16)
Gatt 2005	3	19	3	20	2.9%	1.05 (0.24, 4.59)
Muller 2009	3	76	4	75	4.0%	0.74 (0.17, 3.20)
Ren 2012	6	299	7	299	7.0%	0.86 (0.29, 2.52)
Veenhof 2012	3	17	3	20	2.7%	1.18 (0.27, 5.09)
Vlug 2011	5	93	5	98	4.9%	1.05 (0.32, 3.52)
Subtotal (95%CI)		579		581	33.9%	0.97 (0.62, 1.52)
Total events	33		34			
Heterogeneity: χ^2 = 0.33, df = 6 (*P* = 1.00); I^2 = 0%						
Test for overall effect: *Z* = 0.13 (*P* = 0.90)						
1.3.3 LFT *vs* LCC						
Veenhof 2012	1	19	1	23	0.9%	1.21 (0.08, 18.09)
Vlug 2011	7	100	8	109	7.6%	0.95 (0.36, 2.53)
Wang 2011	2	106	5	104	5.0%	0.39 (0.08, 1.98)
Wang 2011	0	40	2	38	2.6%	0.19 (0.01, 3.84)
Subtotal (95%CI)		265		274	16.1%	0.67 (0.32, 1.42)
Total events	10		16			
Heterogeneity: χ^2 = 1.78, df = 3 (*P* = 0.62); I^2 = 0%						
Test for overall effect: *Z* = 1.04 (*P* = 0.30)						
Total (95%CI)		1688		1709	100.0%	0.87 (0.67, 1.15)
Total events	86		100			
Heterogeneity: χ^2 = 5.17, df = 19 (*P* = 1.00); I^2 = 0%						
Test for overall effect: *Z* = 0.96 (*P* = 0.34)						



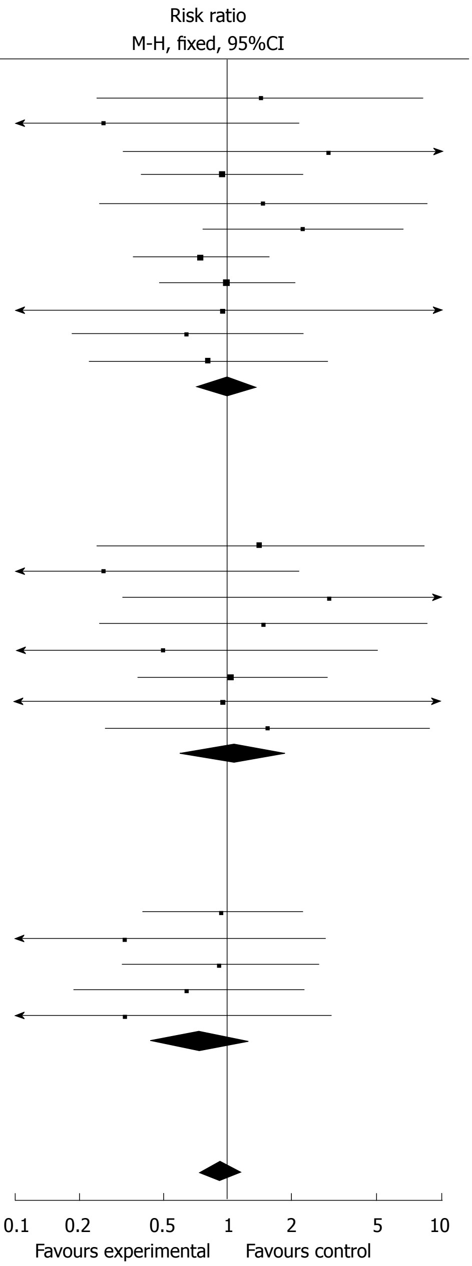
D

Study or subgroup	FT Events	FT Total	CC Events	CC Total	Weight	Risk ratio M-H, fixed, 95%CI
1.4.1 FT *vs* CC						
Anderson 2003	1	14	0	11	0.3%	2.40 (0.11, 53.77)
García-Botello 2011	9	61	12	58	7.1%	0.71 (0.32, 1.56)
Gatt 2005	0	19	4	20	2.5%	0.12 (0.01, 2.03)
Hu 2012	1	40	4	42	2.2%	0.26 (0.03, 2.25)
Lonescu 2009	4	48	5	48	2.9%	0.80 (0.23, 2.80)
Muller 2009	4	76	7	75	4.0%	0.56 (0.17, 1.85)
Ren 2012	5	299	5	298	2.9%	1.00 (0.29, 3.41)
Serclova 2009	4	51	17	52	9.6%	0.24 (0.09, 0.66)
Veenhof 2012	3	36	2	43	1.0%	1.79 (0.32, 10.14)
Vlug 2011	22	193	18	207	10.0%	1.31 (0.73, 2.37)
Wang 2010	2	47	1	45	0.6%	1.91 (0.18, 20.39)
Wang 2011	4	106	7	104	4.0%	0.56 (0.17, 1.86)
Wang 2011	1	40	3	38	1.8%	0.32 (0.03, 2.91)
Yang 2012	1	32	2	30	1.2%	0.47 (0.04, 4.91)
Subtotal (95%CI)		1062		1071	50.1%	0.72 (0.52, 0.97)
Total events	61		87			
Heterogeneity: χ^2 = 14.43, df = 13 (*P* = 0.34); I^2 = 10%						
Test for overall effect: *Z* = 2.13 (*P* = 0.03)						
1.4.2 OFT *vs* OCC						
Anderson 2003	1	14	0	11	0.3%	2.40 (0.11, 53.77)
García-Botello 2011	9	61	12	58	7.1%	0.71 (0.32, 1.56)
Gatt 2005	0	19	4	20	2.5%	0.12 (0.01, 2.03)
Hu 2012	1	21	3	20	1.8%	0.32 (0.04, 2.80)
Lonescu 2009	4	48	5	48	2.9%	0.80 (0.23, 2.80)
Muller 2009	4	76	7	75	4.0%	0.56 (0.17, 1.85)
Ren 2012	5	299	5	298	2.9%	1.00 (0.29, 3.41)
Serclova 2009	4	51	17	52	9.6%	0.24 (0.09, 0.66)
Veenhof 2012	2	17	1	20	0.5%	2.35 (0.23, 23.75)
Vlug 2011	16	93	10	98	5.6%	1.69 (0.81, 3.52)
Wang 2010	0	0	0	0		Not estimable
Yang 2012	1	32	2	30	1.2%	0.47 (0.04, 4.91)
Subtotal (95%CI)		731		730	38.4%	0.72 (0.51, 1.02)
Total events	47		66			
Heterogeneity: χ^2 = 13.87, df = 10 (*P* = 0.18); I^2 = 28%						
Test for overall effect: *Z* = 1.85 (*P* = 0.06)						
1.4.3 LFT *vs* LCC						
Chen Hu 2012	0	19	1	22	0.8%	0.38 (0.02, 8.89)
Veenhof 2012	1	19	1	23	0.5%	1.21 (0.08, 18.09)
Vlug 2011	6	100	8	109	4.4%	0.82 (0.29, 2.27)
Wang 2011	4	106	7	104	4.0%	0.56 (0.17, 1.86)
Wang 2011	1	40	3	38	1.8%	0.32 (0.03, 2.91)
Subtotal (95%CI)		284		296	11.5%	0.64 (0.32, 1.26)
Total events	12		20			
Heterogeneity: χ^2 = 0.97, df = 4 (*P* = 0.91); I^2 = 0%						
Test for overall effect: *Z* = 1.29 (*P* = 0.20)						
Total (95%CI)		2077		2097	100.0%	0.71 (0.57, 0.88)
Total events	120		173			
Heterogeneity: χ^2 = 29.43, df = 29 (*P* = 0.44); I^2 = 1%						
Test for overall effect: *Z* = 3.09 (*P* = 0.002)						



E

Study or subgroup	FT Events	FT Total	CC Events	CC Total	Weight	Risk ratio M-H, fixed, 95%CI
1.5.1 FT *vs* CC						
García-Botello 2011	3	61	2	58	1.9%	1.43 (0.25, 8.23)
Gatt 2005	1	19	4	20	3.7%	0.26 (0.03, 2.15)
Khoo 2007	3	35	1	35	0.9%	3.00 (0.33, 27.46)
Lemanu 2012	8	40	8	38	7.7%	0.95 (0.40, 2.28)
Muller 2009	3	76	2	75	1.9%	1.48 (0.25, 8.61)
Srinivasa 2013	9	37	4	37	3.8%	2.25 (0.76, 6.67)
van Bree 2011	9	36	12	36	11.3%	0.75 (0.36, 1.56)
Vlug 2011	13	193	14	207	12.7%	1.00 (0.48, 2.06)
Wang 2010	1	47	1	45	1.0%	0.96 (0.06, 14.85)
Wang 2011	4	106	6	104	5.7%	0.65 (0.19, 2.25)
Yang 2012	4	81	5	82	4.7%	0.81 (0.23, 2.91)
Subtotal (95%CI)		731		737	55.2%	0.99 (0.71, 1.39)
Total events	58		59			
Heterogeneity: χ^2 = 6.15, df = 10 (P = 0.08); I^2 = 10%						
Test for overall effect: Z = 0.06 (P = 0.95)						
1.5.2 OFT *vs* OCC						
García-Botello 2011	3	61	2	58	1.9%	1.43 (0.25, 8.23)
Gatt 2005	1	19	4	20	3.7%	0.26 (0.03, 2.15)
Khoo 2007	3	35	1	35	0.9%	3.00 (0.33, 27.46)
Muller 2009	3	76	2	75	1.9%	1.48 (0.25, 8.61)
van Bree 2011	1	18	2	18	1.9%	0.50 (0.05, 5.04)
Vlug 2011	7	93	7	98	6.4%	1.05 (0.38, 2.89)
Wang 2010	1	47	1	45	1.0%	0.96 (0.06, 14.85)
Wang 2012	3	41	2	42	1.9%	1.54 (0.27, 8.73)
Subtotal (95%CI)		390		391	19.5%	1.07 (0.60, 1.91)
Total events	22		21			
Heterogeneity: χ^2 = 3.37, df = 7 (P = 0.85); I^2 = 0%						
Test for overall effect: Z = 0.21 (P = 0.83)						
1.5.3 LFT *vs* LCC						
Lemanu 2012	8	40	8	38	7.7%	0.95 (0.40, 2.28)
van Bree 2011	1	18	3	18	2.8%	0.33 (0.04, 2.91)
Vlug 2011	6	100	7	109	6.3%	0.93 (0.32, 2.69)
Wang 2011	4	106	6	104	5.7%	0.65 (0.19, 2.25)
Wang 2012	1	40	3	40	2.8%	0.33 (0.04, 3.07)
Subtotal (95%CI)		304		309	25.3%	0.74 (0.43, 1.28)
Total events	20		27			
Heterogeneity: χ^2 = 1.55, df = 4 (P = 0.82); I^2 = 0%						
Test for overall effect: Z = 1.07 (P = 0.29)						
Total (95%CI)		1425		1437	100.0%	0.94 (0.73, 1.22)
Total events	100		107			
Heterogeneity: χ^2 = 11.83, df = 23 (P = 0.97); I^2 = 0%						
Test for overall effect: Z = 0.45 (P = 0.65)						



F

Study or subgroup	FT Events	FT Total	CC Events	CC Total	Weight	Risk ratio M-H, fixed, 95%CI
4.1.1 complications						
Basse 2005	9	30	8	30	4.3%	1.13 (0.50, 2.52)
Chen Hu 2012	7	19	7	21	3.6%	1.11 (0.48, 2.57)
King 2008	6	41	5	19	3.7%	0.56 (0.19, 1.60)
Mackay 2006	6	22	13	58	3.9%	1.22 (0.53, 2.80)
van Bree 2011	3	18	10	18	5.4%	0.30 (0.10, 0.91)
Veenhof 2012	2	19	8	17	4.6%	0.22 (0.05, 0.91)
Vlug 2011	34	100	43	93	24.1%	0.74 (0.52, 1.04)
Wang 2012	2	40	4	41	2.1%	0.51 (0.10, 2.64)
Subtotal (95%CI)		289		297	51.7%	0.72 (0.56, 0.92)
Total events	69		98			
Heterogeneity: χ^2 = 9.16, df = 7 (*P* = 0.24); I^2 = 24%						
Test for overall effect: *Z* = 2.57 (*P* = 0.01)						
4.1.2 anastomotic leak						
Basse 2005	1	30	0	30	0.3%	3.00 (0.13, 70.83)
Faiz 2008	6	191	1	50	0.9%	1.57 (0.19, 12.75)
King 2008	1	41	0	19	0.4%	1.43 (0.06, 33.54)
van Bree 2011	0	18	1	18	0.8%	0.33 (0.01, 7.68)
Veenhof 2012	0	19	2	17	1.4%	0.18 (0.01, 3.50)
Vlug 2011	7	100	8	93	4.5%	0.81 (0.31, 2.16)
Subtotal (95%CI)		399		227	8.2%	0.83 (0.40, 1.73)
Total events	15		12			
Heterogeneity: χ^2 = 2.45, df = 5 (*P* = 0.78); I^2 = 0%						
Test for overall effect: *Z* = 0.48 (*P* = 0.63)						
4.1.3 wound infection						
Basse 2005	4	30	1	30	0.5%	4.00 (0.47, 33.73)
Chen Hu 2012	0	19	2	21	1.3%	0.22 (0.01, 4.31)
Veenhof 2012	1	19	2	17	1.1%	0.45 (0.04, 4.50)
Vlug 2011	6	100	16	93	9.0%	0.35 (0.14, 0.85)
Subtotal (95%CI)		168		161	11.9%	0.51 (0.26, 1.01)
Total events	11		21			
Heterogeneity: χ^2 = 4.60, df = 3 (*P* = 0.20); I^2 = 35%						
Test for overall effect: *Z* = 1.93 (*P* = 0.05)						
4.1.4 obstruction						
Basse 2005	2	30	0	30	0.3%	5.00 (0.25, 99.95)
Veenhof 2012	1	19	3	23	1.5%	0.40 (0.05, 3.57)
Vlug 2011	7	100	5	93	2.8%	1.30 (0.43, 3.96)
Subtotal (95%CI)		149		146	4.5%	1.23 (0.51, 3.00)
Total events	10		8			
Heterogeneity: χ^2 = 1.86, df = 2 (*P* = 0.40); I^2 = 0%						
Test for overall effect: *Z* = 0.46 (*P* = 0.65)						
4.1.5 re-admission						
Basse 2005	6	30	8	30	4.3%	0.75 (0.30, 1.90)
Faiz 2008	11	191	11	50	9.4%	0.26 (0.12, 0.57)
King 2008	2	41	5	19	3.7%	0.19 (0.04, 0.87)
van Bree 2011	1	18	1	18	0.5%	1.00 (0.07, 14.79)
Vlug 2011	6	100	7	93	3.9%	0.80 (0.28, 2.29)
Wang 2012	1	40	3	41	1.6%	0.34 (0.04, 3.15)
Subtotal (95%CI)		420		251	23.5%	0.45 (0.29, 0.71)
Total events	27		35			
Heterogeneity: χ^2 = 5.83, df = 5 (*P* = 0.32); I^2 = 14%						
Test for overall effect: *Z* = 3.41 (*P* = 0.0007)						
Total (95%CI)		1425		1082	100.0%	0.66 (0.54, 0.81)
Total events	132		174			
Heterogeneity: χ^2 = 30.19, df = 26 (*P* = 0.26); I^2 = 14%						
Test for overall effect: *Z* = 4.07 (*P* < 0.0001)						

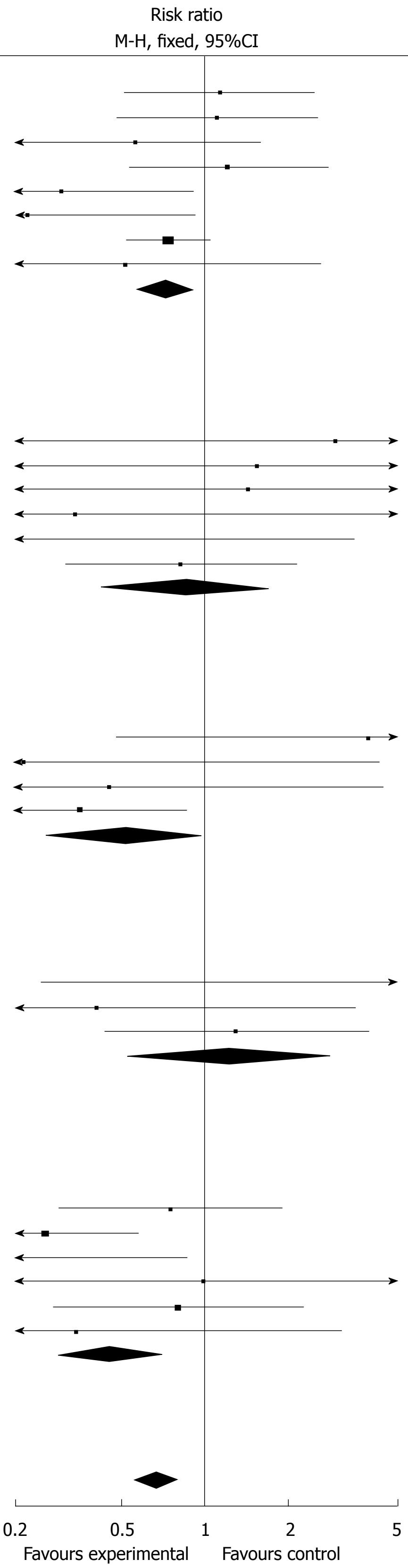


Figure 2 Forest plot of comparison. A: Complications; B: Anastomotic leak; C: Obstruction; D: Wound infection; E: Re-admission; F: LFT *vs* OFT. RRs are shown with 95% CIs.

χ^2 = 2.45 (P = 0.78) and I^2 =0%, which excludes heterogeneity among the studies.

Wound infection: Compared with CC, FT reduced wound infection. The pooled RR was 0.71 (95%CI: 0.57-0.88, P < 0.001), χ^2 = 29.43 (P = 0.44) and I^2 = 1% (Figure 2C, Table 3).

Fourteen studies (2133 patients) provided data on wound infection for FT *vs* CC; 5.7% (61/1062 patients) had wound infection in the FT group and 8.1% (87/1071) in the CC group. Pooling the results indicated that FT did not significantly reduce wound infection compared with CC. The WMD was 0.72 (95%CI: 0.52-0.97, P < 0.05), χ^2 = 14.43 (P = 0.34) and I^2 =10%, which excludes heterogeneity among the studies.

Twelve studies (1461 patients) provided data on wound infection for OFT *vs* OCC; 6.5% (47/731 patients) had wound infection in the OFT group and 9.0% (66/730) in the OCC group. Pooling the results indicated that OFT did not significantly reduce wound infection compared with OCC. The WMD was 0.72 (95%CI: 0.51-1.02, P > 0.05), χ^2 = 13.87 (P = 0.18) and I^2 = 28%, which excludes heterogeneity among the studies.

Five studies (580 patients) provided data on wound infection for LFT *vs* LCC; 4.2% (12/284 patients) had wound infection in the LFT group and 6.8% (20/296) in the LCC group. Pooling the results indicated that LFT did not significantly reduce wound infection compared with LCC. The WMD was 0.64 (95%CI: 0.32-1.26, P > 0.05), χ^2 = 0.97 (P = 0.91) and I^2 = 0%, which excludes heterogeneity among the studies.

Four studies (329 patients) provided data on wound infection for LFT *vs* OFT; 6.5% (11/168 patients) had wound infection in the LFT group and 13% (21/161) in the OFT group. Pooling the results indicated that LFT significantly reduce wound infection compared with OFT. The WMD was 0.51 (95%CI: 0.26-1.01, P = 0.05), χ^2 = 4.6 (P = 0.20) and I^2 =35%, which excludes heterogeneity among the studies.

Obstruction: Compared with CC, FT reduced obstruction. The pooled RR was 0.87 (95%CI: 0.67-1.15, P > 0.05), χ^2 = 5.17 (P = 1.00) and I^2 = 0% (Figure 2D, Table 3).

Nine studies (1698 patients) provided data on obstruction for FT *vs* CC; 5.1% (43/844 patients) had obstruction in the FT group and 5.9% (50/854) in the CC group. Pooling the results indicated that FT did not significantly reduce obstruction compared with CC. The WMD was 0.87 (95%CI: 0.59-1.29, P = 0.05), χ^2 = 2.58 (P = 0.96) and I^2 = 0%, which excludes heterogeneity among the studies.

Seven studies (1160 patients) provided data on obstruction for OFT *vs* OCC; 5.7% (33/579 patients) had obstruction in the OFT group and 5.9% (34/581) in the OCC group. Pooling the results indicated that OFT did not significantly reduce obstruction compared with OCC. The WMD was 0.97 (95%CI: 0.62-1.52; P > 0.05), χ^2 = 0.33 (P = 1.00) and I^2 = 0%, which excludes heterogeneity among the studies.

Four studies (539 patients) provided data on obstruction for LFT *vs* LCC; 3.8% (10/265 patients) had obstruction in the LFT group and 5.8% (16/274) in the LCC group. Pooling the results indicated that LFT did not significantly reduce obstruction compared with LCC. The WMD was 0.67 (95%CI: 0.32-1.42; P > 0.05), χ^2 = 1.78 (P = 0.62) and I^2 = 0%, which excludes heterogeneity among the studies.

Three studies (295 patients) provided data on obstruction for LFT *vs* OFT; 6.7% (10/149 patients) had obstruction in the LFT group and 5.5% (8/146) in the OFT group. Pooling the results indicated that LFT significantly reduce obstruction compared with OFT. The WMD was 1.23 (95%CI: 0.51-3.00; P > 0.05), χ^2 = 1.86(P = 0.40) and I^2 = 0%, which excludes heterogeneity among the studies.

Re-admission: Compared with CC, FT reduced re-admission The pooled RR was 0.94 (95%CI: 0.73-1.22, P > 0.05), χ^2 = 11.83 (P = 0.97) and I^2 = 0% (Figure 2E, Table 3).

Eleven studies (1468 patients) provided data on readmission for FT *vs* CC; 7.9% (58/731 patients) had readmission in the FT group and 8% (59/737) in the CC group. Pooling the results indicated that FT did not significantly reduce re-admission compared with CC. The WMD was 0.99 (95%CI: 0.71-1.39, P = 0.05), χ^2 = 6.15 (P = 0.80) and I^2 = 0%, which excludes heterogeneity among the studies.

Eight studies (781 patients) provided data on readmission for OFT *vs* OCC; 5.6% (22/390 patients) had obstruction in the OFT group and 5.4% (21/391) in the OCC group. Pooling the results indicated that OFT did not significantly reduce re-admission compared with OCC. The WMD was 1.07 (95%CI: 0.60-1.91, P > 0.05), χ^2 = 3.37 (P = 0.85) and I^2 = 0%, which excludes heterogeneity among the studies.

Five studies (613 patients) provided data on re-admission for LFT *vs* LCC; 6.6% (20/304 patients) had re-admission in the LFT group and 8.7% (27/309) in the LCC group. Pooling the results indicated that LFT did not significantly reduce re-admission compared with LCC. The WMD was 0.74 (95%CI: 0.43-1.28, P > 0.05), χ^2 = 1.5 5 (P = 0.82) and I^2 = 0%, which excludes heterogeneity among the studies.

Six studies (671 patients) provided data on re-admission for LFT *vs* OFT; 6.7% (27/420 patients) had re-admission in the LFT group and 5.5% (35/251) in the OFT group. Pooling the results indicated that LFT significantly reduced re-admission compared with OFT. The WMD was 0.45 (95%CI: 0.29-0.71; P < 0.001), χ^2 = 5.83 (P = 0.32) and I^2 =14%, which excludes heterogeneity among the studies.

Publication bias

A funnel plot was created to access the publication bias of the literature. The shapes of the funnel plots did not reveal any evidence of obvious asymmetry (Figures 2F and 3).

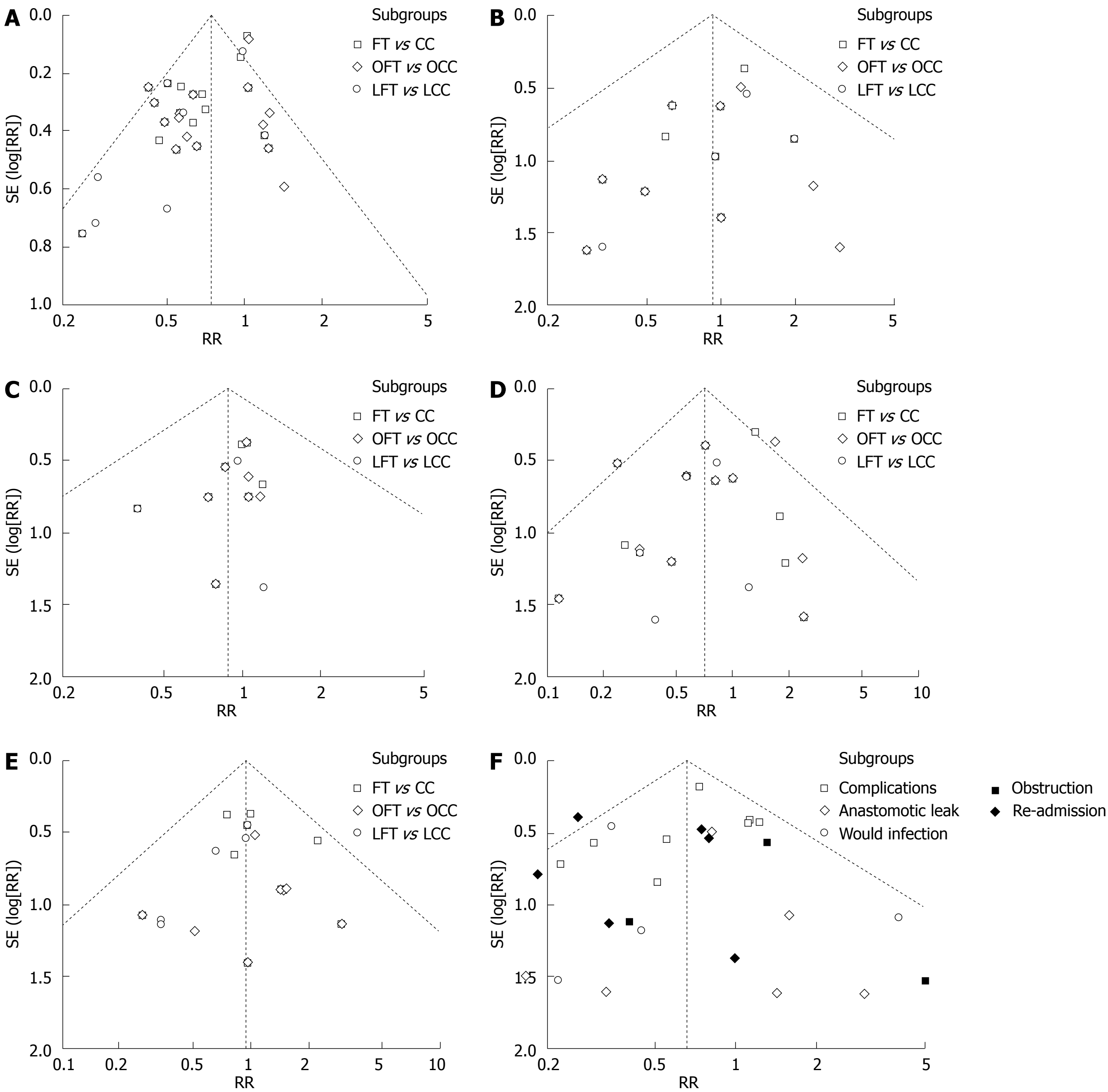


Figure 3 Funnel plot of comparison. A: Complications; B: Anastomotic leak; C: Obstruction; D: Wound infection; E: Re-admission; F: LFT *vs* OFT.

DISCUSSION

The present meta-analysis showed that compared with CC, FT reduced complications and re-admission, and had a similar probability of anastomotic leaks, wound infection and obstruction. Compared with OFT, LFT reduced complications and re-admission, the probability of anastomotic leaks, wound infection and obstruction are similar.

The safety of FT after gastrointestinal surgery has been discussed in worldwide. A recent multivariate analysis demonstrated that male sex[49], preoperative education, psychological counseling, anesthesia[50], early postoperative oral nutrition[51] and quality of care were potential risk factors for complications after gastrointestinal surgery. In addition, some studies have found an increased risk of anastomotic leaks in men and 10.1% of the men required reoperation for anastomotic leak *vs* 3.3% of women[52-55].

Preoperative education and psychological counseling are crucial factors for FT. It is necessary to introduce the detailed treatment program, different steps of FT, and relevant measures, and ease the psychological pressure in order to help patients better understand and coordinate the FT.

Better cooperation of patients can bring better outcomes of FT. Generally, the gastric emptying time of solid meal and fluid is 6 h and 2 h, respectively[56]. Moderate activity after surgery may enhance recover and reduce complications. The patients should be encouraged to have a liquid meal 2 h before the operation instead of fasting. It has been shown that preoperative oral carbohydrate is safe and can efficiently reduce complications[57-59].

The role of epidural or regional anesthesia in FT should be stressed. Postoperative epidural analgesia can avoid stress-induced neurological, endocrinological and homeostatic changes or the blocking of sympathetic nerve-related surgical stress response, reduce postoperative complications such as nausea, vomiting and enteroparalysis, increase early ambulation, improve intestinal function, and shorten hospital stay after resection of gastrointestinal cancer[49,60-65].

Early postoperative oral nutrition is regarded as an essential part of FT. Food intake can stimulate gastrointestinal peristalsis, and early feeding during the first 24 h after surgery promotes recovery of obstruction. It has been illustrated that early postoperative oral nutrition attenuates catabolism and potentially decreases infectious complications[50,66].

FT can improve the rehabilitation of patients after resection of gastrointestinal cancer better than CC can, thus benefiting surgery, anesthesia, pain management, physical therapy, and social work. The primary work of FT is the preoperative education of patients to make them understand the whole plan and the aim of each stage. Therefore, it is necessary to obtain cooperation from nurses.

The pathophysiological mechanisms involved in postoperative obstruction are still not completely understood, but recent studies have stressed the importance of inflammation of the intestinal muscularis resulting from handling during surgery[67-70]. The faster clinical recovery observed after laparoscopic surgery compared with open surgery could be explained by decreased tissue trauma with concomitantly decreased mast cell activation, leading to attenuated intestinal inflammation and thus quicker gastrointestinal recovery[67,68,70]. The mechanisms behind the beneficial effect of FT remain unclear.

Several cytokines, such as IL-6, TNF-α and CRP, are involved in the response to surgical stress and are therefore useful serum markers for evaluating the severity of surgery-induced stress[14-17].

CRP is a nonspecific acute phase protein produced by the liver following trauma or inflammation. Serum CRP level is closely associated with trauma and stress[71]; therefore, measurement of postoperative CRP may reflect the degree of trauma caused by a surgical procedure. The CRP level after colon surgery with LFT was significantly lower than that after other strategies[29], demonstrating that LFT is less traumatic for patients and reduces stress in the perioperative period, protecting the postoperative immune system. IL-6 is produced and activated by monocytes, macrophages and endothelial cells under conditions of surgical trauma and stress. IL-6 levels are positively correlated with the severity of surgical trauma[15]. The increase in serum IL-6 was less after colon surgery with LFT29, suggesting that a suitable surgical mode combined with better perioperative care can lead to less surgical trauma and better prognosis. Surgical trauma causes marked metabolic changes, and REE also acts as the marker for surgical stress[18,19]. The REE rate of patients from the FT group was lower than that in the conventional surgery group, particularly on postoperative days 1 and 3.

Postsurgical complications in patients who underwent FT for colorectal diseases were treated without specific side effects or complications. Compared with CC, FT greatly reduced complications, and no other side effects were found. FT is safe and feasible. Compared with OFT, LTF significantly reduced complications, in addition to reducing hospitalization time and improving quality of life. LFT is not yet practiced widely, but we believe that it will become increasingly popular. Further large studies with more stringent quality criteria may improve the statistical power and confirm that LFT programs reduce morbidity and promote recovery. We believe that FT is significantly advantageous over other procedures for patients after resection of gastrointestinal malignant disease.

There have been eight previous systematic reviews, including meta-analyses on this topic[72-79]. These included three reviews of controlled clinical trials and RCTs[72,74,75], and five reviews of RCTs only[73,76-79]. The present study is the first meta-analysis to have compared FT *vs* CC or OFT *vs* OCC or LFT *vs* LCC or LFT *vs* OFT in resection for gastrointestinal malignancy, and the first meta-analysis of patients undergoing elective gastrointestinal surgery to demonstrate that FT is associated with a significant reduction in postoperative complications but not re-admission rates. The quality of evidence from the present study was supported by the increased number of included studies. In our study, reports from all trials had previously been subject to external peer review, and the risk of bias in these trials for the outcomes of interest was judged to be low in our assessments (Table 2).

There were several limitations to the present meta-analysis. First, the sample size of some of the studies was low, as was the number of studies included in our meta-analysis. Data extraction and analyses were not blinded to the authors, journals or institutions of the publications; however, the literature screening and data extraction were conducted independently by two investigators, and thus, the selection bias was unlikely. Second, the funnel plots were asymmetrical for some outcomes, which indicated the existence of publication bias. However, other factors such as study size and clinical and statistical heterogeneity may also cause an asymmetric funnel in the present meta-analysis. Finally, the included studies did not adequately evaluate hospital costs and quality of life after surgery, which are important outcomes for patients undergoing elective colorectal surgery.

In conclusion, this study provides a more detailed assessment of the potential effects of FT than has previously been possible. We were unable to confirm the large proportional reduction in risk suggested by some previous studies. However, more modest but perhaps clinically worthwhile reduction of complications in some or all types of patient cannot be ruled out. Implementation of FT and the maintenance of compliance may require collaboration and communication between dietitians, nurses, surgeons, anesthesiologists, and patients. Additional RCTs of FT with long-term follow-up are necessary to assess hospital costs and quality of life after surgery. Future studies may assess the benefits of FT in elderly patients and patients having other gastrointestinal surgery.

COMMENTS

Background

Fast-track rehabilitation protocols (FP) have become the most fashionable method of treatment for gastrointestinal malignancy. Complications of FP after gastrointestinal resection have been discussed in China as well as other countries.

Research frontiers

Over the past three decades, many studies have assessed the performance of FT. However, comparisons of FT and conventional care strategies (CC) or FT and laparoscopic surgery and FT and open surgery after gastrointestinal surgery have not been published.

Innovations and breakthroughs

Based on this meta-analysis, FT for gastrointestinal malignancy is safe and efficacious. Similar associations were indicated in subgroup analyses of East Asian, Western, cohort, and high-quality studies. These findings were not presented clearly in previous systematic reviews.

Applications

FT appears to be neither directly nor indirectly associated with the risk. Further studies should seek to clarify this conclusion.

Peer review

FT is rapidly becoming the focal point of attraction for specialists worldwide. This article shows the advantages of the procedure. This analysis has great practical value for clinicians

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