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Impact of visceral obesity on postoperative outcomes in colorectal cancer: a systematic review and meta-analysis

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Background: This systematic review and meta-analysis aimed to assess the impact of visceral obesity (VO) on postoperative outcomes in colorectal cancer (CRC) patients.

Methods: Primary studies were obtained from sources like Embase, PubMed, and Web of Science during the search, which ran until October 2024. Patients with colorectal cancer who had visceral obesity (VO) and those who did not were compared in terms of intraoperative conditions, postoperative outcomes, postoperative complications, and long-term prognoses, including overall survival (OS) and disease-free survival (DFS).

Results: 5,756 individuals with VO and 5,373 patients without VO were among the 11,129 patients who had colorectal cancer resected. Patients with VO had higher conversion rates (p = 0.03), fewer lymph nodes removed (p = 0.05), and longer recovery times for bowel movements (p = 0.009). Furthermore, patients with VO had a considerably greater overall incidence of sequelae than those without (p = 0.0003), including anastomotic leaks (p = 0.001), intestinal obstruction (p = 0.0003), intra-abdominal abscesses (p = 0.004), wound infections (p < 0.00001), and pulmonary problems (p = 0.003). OS and DFS, however, did not differ between the two groups (p > 0.05).

Conclusions: Colorectal cancer patients with VO who have surgery tend to have fewer lymph nodes taken, more problems after surgery, and a higher rate of switching to open surgery.

KEYWORDS

colorectal cancer, visceral obesity, visceral fat area, surgery, complications

1 Introduction

Colorectal cancer (CRC) is one of the most common gastrointestinal malignancies globally, ranking third in incidence and second in mortality (1). Although curative surgery remains the most effective treatment for colorectal cancer, the incidence of postoperative complications remains high, reaching up to 35% (2). These complications are not only related to the surgery itself but are also influenced by the patient's overall health and other nonsurgical factors.

After potentially curative surgery for colorectal cancer, prognosis and treatment decisions are typically based on tumor pathology. However, an increasing body of research indicates that tumor staging is not the only factor determining patient outcomes. Body composition has increasingly been recognized as playing an important role in prognosis. Body composition parameters, such as obesity, are strongly linked to the prognosis of colorectal cancer. Epidemiological studies have shown that obesity is a significant risk factor for colorectal cancer (3). Furthermore, obesity is considered a risk factor for postoperative complications in various abdominal surgeries (4). However, the impact of obesity on colorectal cancer prognosis remains controversial. Some studies report worse outcomes in both obese (5, 6) and underweight patients (7), while others have not observed such associations (8).

Visceral obesity (VO) refers to the excessive accumulation of intraabdominal adipose tissue and is generally considered a more accurate indicator of obesity than body mass index (BMI) (9, 10). Due to its central role in metabolism and its potential impact on postoperative recovery, accurately measuring visceral fat may have significant clinical value in the preoperative risk assessment of colorectal cancer patients. Compared to traditional BMI, computed tomography (CT) provides a more precise and reproducible method for measuring visceral fat area (VFA) (11). In the preoperative evaluation of colorectal cancer patients, abdominal CT imaging is routinely used not only to screen for metastatic disease but also to assess visceral fat accumulation.

This study aims to conduct a systematic review and meta-analysis to explore the impact of VO, measured exclusively by CT imaging, on the prognosis of colorectal cancer patients. Specifically, the study will evaluate the predictive value of visceral obesity for both short-term outcomes, such as postoperative complications, and long-term outcomes, including overall survival (OS) and disease-free survival (DFS), following elective colorectal cancer surgery.

2 Materials and methods

2.1 Search strategy

The search was conducted until October 2024, and primary studies were retrieved from databases such as Embase, PubMed, and Web of Science. "Colorectal cancer," "visceral obesity," and "visceral fat area" were among the search terms. The comprehensive search approach is available in Supplementary Appendix 1.

2.2 Inclusion and exclusion criteria

The following requirements had to be fulfilled for a study to be included: (1) all patients had been diagnosed with colorectal cancer and treated surgically; (2) patients had a CT scan prior to surgery, and VFA was measured; (3) the article includes intraoperative information or short-term or long-term postoperative outcomes. The study with more recent data collection or more extensive data was preferred among several papers written by the same researcher from a certain university.

Studies that satisfied any of the following requirements were disqualified: (1) did not employ CT scans to evaluate VFA for diagnosing VO; (2) did not compare patients with and without VO; (3) was not published in English; and (4) was a conference abstract, case report, review article, or letter.

2.3 Data extraction

Detailed information, including the names of the authors, study duration, year of publication, type of surgery performed, sample size, mean age of participants, gender distribution, study location, diagnostic criteria, length of hospital stay, operative time, intraoperative blood loss, number of lymph nodes retrieved, conversion rates, reoperation rates, postoperative readmission and mortality rates, overall and severe complication rates, the incidence of specific complications, and OS and DFS outcomes, was included in the compiled data.

2.4 Study quality

Using the Newcastle-Ottawa Scale (NOS), we assessed the calibre of the research that were part of our review. The maximum score on this scale is nine points. Research is considered methodologically sound if it receives a score of six or higher.

2.5 Statistical analysis

RevMan 5.4 and Stata 12.0 software were used for the data analysis. Weighted mean differences (WMD) were applied to continuous variables, odds ratios (OR) to binary variables, and hazard ratios (HR) to survival data. Heterogeneity between studies was evaluated using the I^2 statistic. For I^2 values of 50% or less, a fixed-effects model was used; for I^2 values more than 50%, a random-effects model was used. To evaluate publication bias, funnel plots were employed in conjunction with Begg's and Egger's tests. Statistical significance was defined as a P-value of less than 0.05.

3 Results

3.1 Selected articles

1231 publications were selected during the first search phase. 28 (12–39) researches were eventually included in the meta-analysis after these publications were reviewed (Figure 1).

3.2 Study characteristics and study quality

The characteristics of the studies that were part of the analysis are compiled in Table 1. From 2005 to 2024, these studies were carried out in Japan, Korea, China, the Netherlands, the United Kingdom, the United States, Scotland, Canada, Italy, Chile, and Denmark. 5,756 individuals with VO and 5,373 patients without VO were among the 11,129 patients who had colorectal cancer resected. All of the publications that were part of this investigation had NOS values between 6 and 9, which meant that the study quality was adequate.

3.3 Length of hospital stay

The average length of stay for the VO group ranged from 6 to 15.21 days, whereas for the non-VO group, it ranged from 6 to 13.2 days (Table 2). The length of hospital stay for the VO and non-VO groups did not differ significantly, as seen by Figure 2a (WMD, 0.33 days; 95% confidence interval [CI], -0.25 to 0.91; p = 0.26).

3.4 Operative time

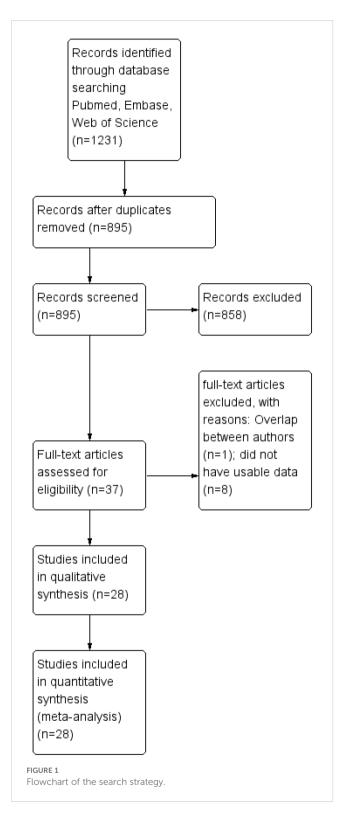
The average operative time for the VO group ranged from 160 to 377 minutes, while for the non-VO group, it spanned from 149 to 337.4 minutes (Table 2). The operative duration for the VO and non-VO groups was not substantially different, as illustrated in Figure 2b (WMD, 0.15 minutes; 95% CI, -3.61 to 23.69; p = 0.15).

3.5 Blood loss

In the VO group, the average intraoperative blood loss was between 20 and 431 ml, whereas in the non-VO group, it was between 10 and 401 ml (Table 2). As Figure 2c illustrates, the difference was not substantial (WMD, 8.37 ml; 95% CI, -0.8 to 17.55; p = 0.07).

3.6 Number of lymph nodes retrieved

Compared to the non-VO group, fewer lymph nodes were recovered from the VO group (WMD, -2.87; 95% CI, -5.53 to -0.04; p = 0.05, Figure 2d).



3.7 Time to first flatus, bowel movement, and intake of food

There was no difference in the time to first flatus between the VO and non-VO groups (WMD, 0.01 days; 95% CI, -0.08 to 0.09; p = 0.87, Figure 2e). Although the time to first bowel movement was

Study	Nation	Year	Time	Definition	Definition of	Disease	Туре	Pati	ents	Fema	ale/Male	Mean age		Ottawa
			period	of VO	non-VO		of surgery	VO	Non- VO	VO	Non-VO	VO	Non-VO	Scores
Ishii	Japan	2005	1993-2002	≥100 cm ²	<100 cm ²	Colorectal cancer	Laparoscopic	9	37	1/8	21/16	N/A	N/A	6
Tsujinaka	Japan	2008	2001-2007	≥130 cm ²	<130 cm ²	Sigmoid colon cancer	Laparoscopic	68	65	19/49	35/30	65.5 (41-88)	64 (31-84)	7
Kang	Korea	2012	2003-2009	\geq 130 cm ²	<130 cm ²	Rectal cancer	Laparoscopic	29	113	13/16	40/73	67.5 ± 9.6	60.9 ± 10.6	6
Yamamoto	Japan	2012	2000-2005	Men: $\geq 130 \text{ cm}^2$ Women: $\geq 90 \text{ cm}^2$	Men: < 130 cm ² Women: <90 cm ²	Colorectal cancer	N/A	102	171	38/64	62/109	66.7 ± 9.6	66.3 ± 10.5	6
Watanabe	Japan	2014	2005-2010	≥100 cm ²	<100 cm ²	Colon cancer	Laparoscopic	144	194	37/ 107	122/72	66.2 (35-90)	64.8 (35–87)	6
Cakir	The Netherlands	2015	2006-2013	>100 cm ²	$\leq 100 \text{ cm}^2$	Colon cancer	Open and laparoscopic	367	197	130/ 237	147/50	71 ± 10	68 ± 12	6
Chen B	China	2016	2011-2014	$\geq 100 \text{ cm}^2$	<100 cm ²	Rectal cancer	Laparoscopic	192	130	N/A	N/A	N/A	N/A	6
Malietzis	UK	2016	2006-2011	Male: ≥163.8 cm^2 Female: ≥80.1 cm^2	Male: <163.8 cm ² Female: <80.1 cm ²	Colorectal cancer	Open and laparoscopic	420	385	N/A	N/A	N/A	N/A	6
Shiomi	Japan	2016	2017-2018	≥130 cm ²	<130 cm ²	Rectal cancer	Robotic and laparoscopic	82	154	65/69	89/65	NA	NA	7
Yu	Korea	2016	2011-2013	Male: >130 cm ² Female: >90 cm ²	Male: ≤130 cm ² Female: ≤90 cm ²	Colorectal cancer	Open and laparoscopic	22	80	12/10	24/56	65.1 ± 2.7	60. ± 1.1	6
Ozoya	USA	2017	2006-2015	>100 cm ²	$\leq 100 \text{ cm}^2$	Colon cancer	Open and laparoscopic	82	28	32/50	18/10	66.2 ± 10.9	64 ± 14.5	6
Chen WZ	China	2018	2014-2017	Male: >130 cm ² Female: >90 cm ²	Male: ≤130 cm ² Female: ≤90 cm ²	Colorectal cancer	Open and laparoscopic	191	185	87/ 104	61/124	N/A	N/A	7
Choi	Korea	2018	2009-2013	>100 cm ²	$\leq 100 \text{ cm}^2$	Rectal cancer	Open and laparoscopic	97	91	30/67	41/50	62.7 ± 11.4	59.9 ± 10.8	8
Almasaudi	Scotland	2019	2008-2016	Male: >160 cm ² Female: >80 cm ²	Male: $\leq 160 \text{ cm}^2$ Female: $\leq 80 \text{ cm}^2$	Colorectal cancer	N/A	543	198	246/ 297	85/113	N/A	N/A	6
Heus	The Netherlands	2019	2006-2013	>100 cm ²	<100 cm ²	Rectal cancer	Open and laparoscopic	272	134	80/ 192	73/61	69 ± 9	65 ± 12	6

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(Continued)

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Study	Nation	Year	Time	Definition	Definition of	Disease	Туре	Pati	ents	Fema	ale/Male	Mean age		Ottawa
			period	of VO	non-VO		of surgery	VO	Non- VO	VO	Non-VO	VO	Non-VO	Scores
Hopkins	Canada	2019	2007-2009	Male: >160 cm ² Female: >80 cm ²	Male: $\leq 160 \text{ cm}^2$ Female: $\leq 80 \text{ cm}^2$	Colorectal cancer	N/A	494	474	142/ 352	237/237	N/A	N/A	6
Morimoto	Japan	2019	2010-2012	≥100 cm ²	<100 cm ²	Colorectal cancer	Open and laparoscopic	156	261	N/A	N/A	N/A	N/A	6
Zhai TS	China	2019	2015-2017	≥100 cm ²	<100 cm ²	Colon cancer	Open and laparoscopic	73	34	32/41	11/23	69.6 ± 9.1	65.8 ± 14.5	6
Han	Korea	2020	2005-2012	≥100 cm ²	<100 cm ²	Rectal cancer	N/A	670	714	173/ 497	323/391	N/A	N/A	6
Pedrazzani	Italy	2020	2012-2019	Male: ≥163.8 cm^2 Female: ≥80.1 cm^2	Male: <163.8 cm ² Female: <80.1 cm ²	Colorectal cancer	Laparoscopic	173	88	76/97	37/51	69.6 ± 11	64.4 ± 12.3	8
Cárcamo	Chile	2021	2010-2015	Male: >160 cm ² Female: >80 cm ²	Male: $\leq 160 \text{ cm}^2$ Female: $\leq 80 \text{ cm}^2$	Colorectal cancer	Open and laparoscopic	263	96	N/A	N/A	N/A	N/A	6
Frostberg	Denmark	2021	2010-2011	≥130 cm ²	<130 cm ²	Colorectal cancer	Open and laparoscopic	130	148	30/ 100	83/65	71.5	70	6
Dong	China	2022	2015-2020	Male: >130 cm ² Female: >90 cm ²	Male: $\leq 130 \text{ cm}^2$ Female: $\leq 90 \text{ cm}^2$	Colorectal cancer	Open and laparoscopic	261	267	123/ 138	87/180	74.0 ± 6.0	74.1 ± 6.4	6
Fujimoto	Japan	2022	2018-2020	≥100 cm ²	<100 cm ²	Colorectal cancer	Laparoscopic	46	78	N/A	N/A	N/A	N/A	6
Gachabayov	USA	2023	N/A	>100 cm ²	≤100 cm ²	Rectal cancer	Robotic	106	394	N/A	N/A	57.9 ± 12	59.3 ± 12.3	6
Zhai W	China	2023	2015-2021	≥100 cm ²	<100 cm ²	Colorectal cancer	Open and laparoscopic	337	183	212/ 125	95/88	N/A	N/A	6
Zhou	China	2023	2013-2019	≥100 cm ²	<100 cm ²	Rectal cancer	N/A	306	318	105/ 201	140/178	N/A	N/A	6
Zhao	China	2024	2019-2023	≥100 cm ²	<100 cm ²	Rectal cancer	Robotic	121	156	54/67	74/82	N/A	N/A	6

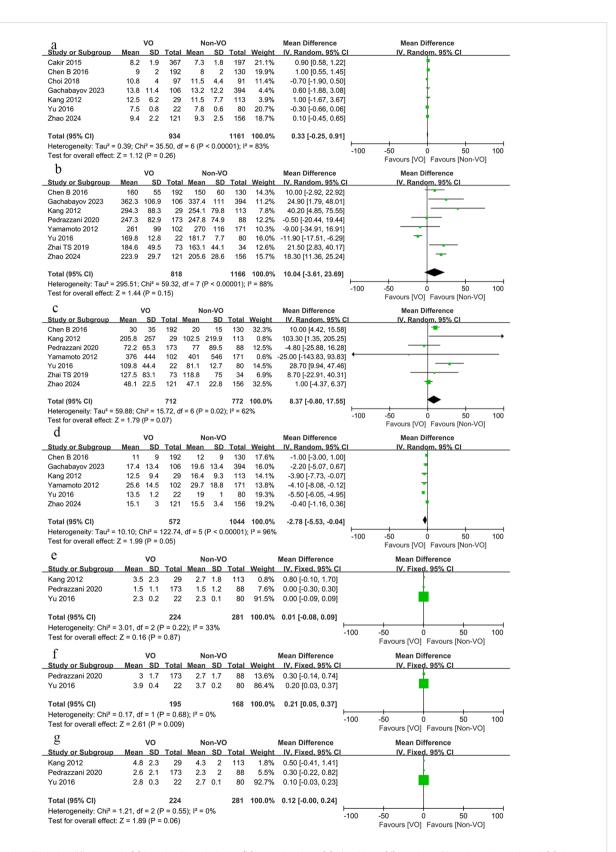
N/A not available, VO visceral obesity, non-VO non- visceral obesity.

Study	Length of hosp	oital stay (days)	Operative tim	ne (min)	Blood loss (m	າໄ)	Conversion r	ate (%)	Lymph nodes	retrieved
	VO	Non-VO	VO	Non-VO	VO	Non-VO	VO	Non-VO	VO	Non-VO
Ishii	15 (6-55)	8 (5-74)	377 (276–550)	305 (184–590)	20 (10-945)	10 (10–965)	N/A	N/A	N/A	N/A
Tsujinaka	10.5 (5–31)	9 (5-29)	220 (125-410)	190 (115–325)	42.5 (10-530)	10 (10-890)	6 (8.8)	3(4.6)	N/A	N/A
Kang	12.5 ± 6.2	11.5 ± 7.7	294.3 ± 88.3	254.1 ± 79.8	205.8 ± 257.0	102.5 ± 219.9	5 (17.2)	6 (5.3)	12.5 ± 9.4	16.4 ± 9.3
Yamamoto	N/A	N/A	261 ± 99	270 ± 116	376 ± 444	401 ± 546	N/A	N/A	25.6 ± 14.5	29.7 ± 18.8
Watanabe	11.2 (6-320)	11.3 (6–53)	197 (86–576)	178 (55–319)	45.1 (0-400)	35.6 (0-1900)	N/A	N/A	23.6 (2-76)	30.8 (9-92)
Cakir	8.2 ± 1.9	7.3 ± 1.8	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Chen B	9 ± 2	8 ± 2	160 ± 55	150± 60	30 ± 35	20 ± 15	N/A	N/A	11 ± 9	12 ± 9
Malietzis	6 (5-10)	7 (5–12)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Yu	7.5 ± 0.8	7.8 ± 0.6	169.8 ± 12.8	181.7 ± 7.7	109.8 ± 44.4	81.1 ± 12.7	0 (0)	2 (2.5)	19.0 ± 1.0	13.5 ± 1.2
Choi	10.8 ± 4.0	11.5 ± 4.4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Heus	11.3	9.4	166	149	431	310	6 (8)	3 (10)	N/A	N/A
Zhai TS	15.21 ± 7.59	12.29 ± 5.40	184.6 ± 49.5	163.1 ± 44.1	127.5 ± 83.1	118.8 ± 75.0	N/A	N/A	N/A	N/A
Pedrazzani	6 (2-68)	6 (3-53)	247.3 ± 82.9	247.8 ± 74.9	72.2 ± 65.3	77 ± 89.5	20 (11.6)	5 (5.7)	N/A	N/A
Dong	13 (7.5)	13 (6)	180 (80)	160 (85)	N/A	N/A	N/A	N/A	25 (6)	31 (5)
Gachabayov	13.8 ± 11.4	13.2 ± 12.2	362.3 ± 106.9	337.4 ± 111	N/A	N/A	N/A	N/A	17.4 ± 13.4	19.6 ± 13.4
Zhai W	13.00 (11.00, 16.00)	13.00 (11.00,15.00)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Zhao	9.4 ± 2.2	9.3 ± 2.5	223.9 ± 29.7	205.6 ± 28.6	48.1 ± 22.5	47.1 ± 22.8	3 (2.5)	3 (1.9)	15.1 ± 3.0	15.5 ± 3.4

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N/A not available, VO visceral obesity, non-VO non- visceral obesity.



Forest plot describing the differences in (a) length of hospital stay, (b) operative time, (c) blood loss, (d) number of lymph nodes retrieved, (e) time to first flatus, (f) time to first bowel movement and (g) time to first food intake between VO and non-VO.

<u>Study or Subgroup</u> Cakir 2015	Events	<u>Tot</u> al	Non-V Events		Weight	Odds Ratio M-H. Fixed, 95% C		Odds M-H, Fixe		
	60	367	20	197	34.1%	1.73 [1.01, 2.96]			-	
Dong 2022	1	261	3	267	4.6%	0.34 [0.03, 3.27]	-	· · · ·		
Gachabayov 2023	4	106	18	394	11.5%	0.82 [0.27, 2.47]				
Heus 2019	52	272	18	134	30.5%	1.52 [0.85, 2.72]		+	•	
Pedrazzani 2020	12	173	9	88	17.4%	0.65 [0.26, 1.62]				
Yu 2016	1	22	3	80	1.9%	1.22 [0.12, 12.36]			•	
					100			l	•	
Total (95% CI)		1201		1160	100.0%	1.30 [0.94, 1.81]		1	•	
Total events	130		71				<u> </u>			
Heterogeneity: Chi ² =				11%			0.01	0.1 1	10	100
Test for overall effect:	∠ = 1.57 (I	- = 0.1	2)						Favours [Non-VO]	
b	1/0		Non-V	0		Odde Batia		Odds		
-	VO Events	Total			Woight	Odds Ratio M-H. Fixed, 95% C				
Study or Subgroup Chen WZ 2018	Events 4	191	Events 1	185	Weight 1.3%	3.94 [0.44, 35.55]		M-H, Fixe		
Dong 2022	4 13	261	12	267	14.6%	1.11 [0.50, 2.49]		_		
Gachabayov 2023	33	106	103	394	38.9%	1.28 [0.80, 2.04]		-	-	
Heus 2019	43	272	28	134	40.8%	0.71 [0.42, 1.21]			-	
Pedrazzani 2020	43	173	20	88	1.6%	3.67 [0.44, 30.30]		_		
Yu 2016	0	22	5	88	2.9%	0.34 [0.02, 6.33]		· · · ·		
	0	22	5	00	2.3/0	0.04 [0.02, 0.00]				
Total (95% CI)		1025		1156	100.0%	1.07 [0.78, 1.46]				
Total events	100		150					Ī		
Heterogeneity: Chi ² =		5 (P = 0		18%			H		+	
Test for overall effect:				/0			0.01	0.1 1		100
ereran ondot.	(1	5.5	·					⊢avours [VO]	Favours [Non-VO]	
с	vo		Non-V	0		Odds Ratio		Odds I	Ratio	
Study or Subgroup		Total	Events		Weight	M-H, Fixed, 95% CI		M-H, Fixed		
Gachabayov 2023	0	106	2	394	9.2%	0.74 [0.04, 15.47]	_	-		
Heus 2019	11	272	3	134	33.3%	1.84 [0.50, 6.71]		-+	-	
Kang 2012	1	29	0	113	1.7%	11.95 [0.47, 301.07]		-+		→
Malietzis 2016	5	420	5	385	44.5%	0.92 [0.26, 3.19]				
Pedrazzani 2020	3	173	1	88	11.3%	1.54 [0.16, 14.98]		+	•	
						-			•	
Total (95% CI)		1000		1114	100.0%	1.47 [0.69, 3.11]		4		
Total events	20		11					[
Heterogeneity: Chi ² =				0%			0.01	0.1 1	10	100
Test for overall effect:	Z = 1.00 (F	P = 0.32	2)						Favours [Non-VO]	
d	140		M *	0		Odda D-ti-				
	VO	Tet-	Non-V		Walet	Odds Ratio		Odds		
Study or Subgroup						M-H, Fixed, 95% C		M-H, Fixe	u, 95% Cl	
Heus 2019	6	272	3	134	21.5%	0.98 [0.24, 4.00]				
Kang 2012 Redrozzoni 2020	5	29	6	113	11.1%	3.72 [1.05, 13.19]		1	-	
Pedrazzani 2020	20	173	5	88	32.1%	2.17 [0.79, 5.99]				
Tsujinaka 2008	6	68	3	65	15.3%	2.00 [0.48, 8.36]	_			
Yu 2016 7bao 2024	0 3	22 121	2 3	80 156	5.9%	0.70 [0.03, 15.07]				
Zhao 2024	3	121	3	156	14.0%	1.30 [0.26, 6.54]				
Total (95% CI)		685		636	100.0%	1.85 [1.05. 3.27]			•	
Total (95% CI) Total events	40	685	22	636	100.0%	1.85 [1.05, 3.27]			•	
Total (95% CI) Total events Heterogeneity: Chi ² =	40 2.62, df = 1		22).76); l² =		100.0%	1.85 [1.05, 3.27]	—		◆ 	
Total events	2.62, df =	5 (P = 0	0.76); l² =		100.0%	1.85 [1.05, 3.27]	0.01	0.1 1		100
Total events Heterogeneity: Chi ² = Test for overall effect:	2.62, df = Z = 2.12 (I	5 (P = 0	0.76); l² = 3)	0%	100.0%		0.01	Favours [VO]	Favours [Non-VO]	100
Total events Heterogeneity: Chi ² =	2.62, df =	5 (P = 0	0.76); l² =	0%	100.0%	1.85 [1.05, 3.27] Odds Ratio	0.01	Favours [VO]		100
Total events Heterogeneity: Chi ² = Test for overall effect: C Study or Subgroup	2.62, df = Z = 2.12 (I VO Events	5 (P = 0 P = 0.03 Total	0.76); l² = 3) Non-V0 Events	0% D Total	Weight	Odds Ratio M-H. Random, 95% (Favours [VO] Odds	Favours [Non-VO]	100
Total events Heterogeneity: Chi ² = Test for overall effect: C Study or Subgroup Almasaudi 2019	2.62, df = 5 Z = 2.12 (I <u>VO</u> <u>Events</u> 138	5 (P = 0 P = 0.03 <u>Total</u> 543	0.76); I ² = 3) Non-V(<u>Events</u> 51	0% D Total 198	<u>Weight</u> 8.2%	Odds Ratio <u>M-H. Random, 95% (</u> 0.98 [0.68, 1.43		Favours [VO] Odds	Favours [Non-VO] Ratio	100
Total events Heterogeneity: Chi ² = Test for overall effect: C Study or Subgroup Almasaudi 2019 Chen B 2016	2.62, df = 5 Z = 2.12 (1 VO Events 138 36	5 (P = 0 P = 0.0 Total 543 192	0.76); I ² = 3) Non-V(<u>Events</u> 51 19	0% D Total 198 130	<u>Weight</u> 8.2% 6.1%	Odds Ratio <u>M-H. Random. 95% (</u> 0.98 [0.68, 1.43 1.35 [0.73, 2.47	<u>; </u> 	Favours [VO] Odds	Favours [Non-VO] Ratio	100
Total events Heterogeneity: Chi ² = Test for overall effect: Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018	2.62, df = 5 Z = 2.12 (l <u>VO</u> <u>Events</u> 138 36 68	5 (P = 0 P = 0.03 Total 543 192 191	0.76); I ² = 3) Non-V(<u>Events</u> 51 19 35	0% D Total 198 130 185	<u>Weight</u> 8.2% 6.1% 7.3%	Odds Ratio <u>M-H. Random. 95% (</u> 0.98 [0.68, 1.43 1.35 [0.73, 2.47 2.37 [1.48, 3.80]	<u> </u> 	Favours [VO] Odds	Favours [Non-VO] Ratio	100
Total events Heterogeneity: Chi ² = Test for overall effect: Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022	2.62, df = 1 Z = 2.12 (1 <u>VO</u> <u>Events</u> 138 36 68 89	5 (P = 0 P = 0.02 Total 543 192 191 261	0.76); I ² = 3) Non-V(Events 51 19 35 48	0% D Total 198 130 185 267	<u>Weight</u> 8.2% 6.1% 7.3% 7.9%	Odds Ratio <u>M-H. Random. 95% (</u> 0.98 [0.68, 1.43 1.35 [0.73, 2.47 2.37 [1.48, 3.80 2.36 [1.58, 3.54	CI 	Favours [VO] Odds	Favours [Non-VO] Ratio	100
Total events Heterogeneity: Chi ² = Test for overall effect: 2 Study or Subgroup Almasaudi 2019 Chen B 2016 Chen B 2016 Chen WZ 2018 Dong 2022 Gachabayov 2023	2.62, df = 5 Z = 2.12 (I <u>VO</u> <u>Events</u> 138 36 68 89 36	5 (P = 0 P = 0.03 Total 543 192 191 261 106	0.76); I ² = 3) Non-VC Events 51 19 35 48 114	0% D Total 198 130 185 267 394	Weight 8.2% 6.1% 7.3% 7.9% 7.4%	Odds Ratio M-H. Random, 95% (0.98 [0.68, 1.43 1.35 [0.73, 2.47 2.37 [1.48, 3.80 2.36 [1.58, 3.54 1.26 [0.80, 2.00	CI 	Favours [VO] Odds	Favours [Non-VO] Ratio	 100
Total events Heterogeneity: Chi ² = Test for overall effect: 2 Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Gachabayov 2023 Heus 2019	2.62, df = 5 Z = 2.12 (I VO Events 138 36 68 89 36 136	5 (P = 0 P = 0.02 543 192 191 261 106 272	0.76); I ² = 3) Non-VC Events 51 19 35 48 114 46	0% Total 198 130 185 267 394 134	Weight 8.2% 6.1% 7.3% 7.9% 7.4% 7.7%	Odds Ratio MH. Random. 95% (0.98 [0.68, 1.43 1.35 [0.73, 2.47 2.37 [1.48, 3.80 2.36 [1.58, 3.54 1.26 [0.80, 2.00 1.91 [1.25, 2.94	CI 	Favours [VO] Odds	Favours [Non-VO] Ratio	 100
Total events Heterogeneity: Chi ² = Test for overall effect: 2 Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Gachabayov 2023 Heus 2019 shii 2005	2.62, df = 5 Z = 2.12 (I VO Events 138 36 68 89 36 136 7	5 (P = 0 P = 0.02 543 192 191 261 106 272 9	0.76); I ² = 3) Non-VC Events 51 19 35 48 114 46 13	0% Total 198 130 185 267 394 134 37	Weight 8.2% 6.1% 7.3% 7.9% 7.4% 7.7% 1.6%	Odds Ratio M-H. Random. 95% (0.98 [0.68, 1.43 1.35 [0.73, 2.47 2.37 [1.48, 3.80 2.36 [1.58, 3.54 1.26 [0.80, 2.00 1.91 [1.25, 2.94 6.46 [1.17, 35.74	21 	Favours [VO] Odds	Favours [Non-VO] Ratio	100
Total events Heterogeneity: Chi ² = Test for overall effect: Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Gachabayov 2023 Heus 2019 Ishii 2005 Kang 2012	2.62, df = 5 Z = 2.12 (I <u>VO</u> <u>Events</u> 138 36 68 89 36 136 7 8	5 (P = 0 P = 0.02 543 192 191 261 106 272 9 29).76); I ² = 3) Non-VC Events 51 19 35 48 114 46 13 25	0% Total 198 130 185 267 394 134 37 113	Weight 8.2% 6.1% 7.3% 7.9% 7.4% 7.7% 1.6% 4.0%	Odds Ratio 0.98 (0.68, 1.95% (0.98 (0.68, 1.95% (0.98 (0.68, 0.54) 1.26 (0.8, 0.54) 1.26 (0.8, 0.200 1.91 (1.25, 2.94) 6.46 (1.17, 35.74) 1.34 (0.53, 3.39	<mark>21</mark> 	Favours [VO] Odds	Favours [Non-VO] Ratio	100
Total events Heterogeneity: Chi ² = Test for overall effect: Contemport Almasaudi 2019 Chen B 2016 Chen W2 2018 Dong 2022 Gachabayov 2023 Heus 2019 Ishii 2005 Kang 2012 Malietzis 2016	2.62, df = 5 Z = 2.12 (1 VO Events 36 68 89 36 136 7 8 51	5 (P = 0 P = 0.03 543 192 191 261 106 272 9 29 420	0.76); I ² = 3) Non-VC Events 51 19 35 48 114 46 13 25 61	0% Total 198 130 185 267 394 134 37 113 385	Weight 8.2% 6.1% 7.3% 7.9% 7.4% 7.7% 1.6% 4.0% 7.9%	Odds Ratio M-H. Random. 95% (0.98 [0.68, 143 1.35 [0.73, 2.47 2.37 [1.48, 3.80 2.36 [1.58, 3.54 1.26 [0.80, 2.00 1.91 [1.25, 2.94 6.46 [1.17, 35.74 1.34 [0.53, 3.39 0.73 [0.49, 1.10	21 	Favours [VO] Odds	Favours [Non-VO] Ratio	 100
Total events Heterogeneity: Chi ² = Test for overall effect: 2 Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Sachabayov 2023 Heus 2019 shii 2005 Kang 2012 Malietzis 2016 Dozoya 2017	2.62, df = 1 Z = 2.12 (I VO Events 138 36 68 89 36 136 136 7 8 51 25	5 (P = 0.02 Total 543 192 191 261 106 272 9 29 420 82).76); I ² = 3) Non-VC <u>Events</u> 51 19 35 48 114 46 13 25 61 3	0% Total 198 130 185 267 394 134 37 113 385 28	Weight 8.2% 6.1% 7.3% 7.9% 7.4% 7.7% 4.0% 7.9% 2.5%	Odds Ratio M-H. Random, 95% 0 0.98 [0.68, 1.35 1.35 [0.73, 2.47 2.37 [1.48, 3.80 2.36 [1.58, 3.54 1.26 [0.80, 2.00 1.91 [1.25, 2.94 6.46 [1.17, 35.74 1.34 [0.53, 3.39 0.73 [0.49, 1.10 3.65 [1.01, 13.23	CI 	Favours [VO] Odds	Favours [Non-VO] Ratio	 100
Total events Heterogeneity: Chi ² = Test for overall effect: Study or Subgroup Almasaudi 2019 Chen B 2016 Chen W2 2018 Dong 2022 Sachabayov 2023 Heus 2019 shii 2005 Kang 2012 Malietzis 2016 Dzoya 2017 Pedrazzani 2020	2.62, df = 1 Z = 2.12 (I VO Events 138 36 68 89 36 136 136 7 8 136 7 8 5 136 5 5 64	5 (P = 0.02 543 192 191 261 106 272 9 29 420 82 173	0.76); I ² = 3) Non-VC <u>Events</u> 51 19 35 48 114 46 13 25 61 3 36	0% Total 198 130 185 267 394 134 37 113 385 28 88	Weight 8.2% 6.1% 7.3% 7.4% 7.4% 7.7% 1.6% 4.0% 2.5% 6.8%	Odds Ratio M-H. Random. 95% (0.98 [0.68, 1.43 1.35 [0.73, 2.47 2.37 [1.48, 3.80 2.36 [1.58, 3.54 1.26 [0.80, 2.00 1.91 [1.25, 2.94 6.46 [1.17, 35.74 1.34 [0.53, 3.39 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.85 [0.50, 1.43]	CI 	Favours [VO] Odds	Favours [Non-VO] Ratio	 100
Total events Heterogeneity: Chiª = Test for overall effect: 2 Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Gachabayov 2023 Heus 2019 Shii 2005 Kang 2012 Malietzis 2016 Dzoya 2017 Pedrazzani 2020 Shiomi 2016	2.62, df = 1 Z = 2.12 (f VO Events 138 36 68 89 36 136 7 7 8 51 25 64 4 14	5 (P = 0 P = 0.03 543 192 191 261 106 272 9 29 420 82 173 82	0.76); I ² = 3) Non-VC Events 51 19 35 48 114 46 13 25 61 3 36 24	0% Total 198 130 185 267 394 134 37 113 385 28 88 154	Weight 8.2% 6.1% 7.3% 7.4% 7.7% 1.6% 4.0% 7.9% 2.5% 6.8% 5.2%	Odds Ratio M.H. Random. 95% d 0.98 (0.68, 1.43 1.35 (0.73, 2.47 2.37 (1.48, 3.60 2.36 (1.58, 3.54 1.26 (0.80, 2.00 1.91 (1.25, 2.94 6.46 (1.17, 35.74 1.34 (0.53, 3.39 0.73 (0.49, 1.10 3.65 (1.01, 13.23 0.05 (0.50, 1.13, 2.29	21 	Favours [VO] Odds	Favours [Non-VO] Ratio	 100
Total events Heterogeneity: Chi ² = Test for overall effect: 2 Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Sachabayov 2023 Heus 2019 Ishii 2005 Sachabayov 2023 Heus 2019 Ishii 2005 Sachabayov 2023 Heus 2019 Shi 2005 Shiomi 2016 Shiomi 2016 Shiomi 2016 Shiomi 2016	2.62, df = 1 Z = 2.12 (f VO Events 138 36 68 89 36 136 7 8 51 25 64 14 22	5 (P = 0 P = 0.07 543 192 191 261 106 272 9 29 420 82 173 82 68	0.76); I ² = 3) Non-VC <u>Events</u> 51 19 35 48 114 46 13 25 61 3 36 24 8	0% Total 198 130 185 267 394 134 37 113 385 28 88 154 65	Weight 8.2% 6.1% 7.3% 7.9% 7.4% 7.7% 4.0% 7.9% 2.5% 6.8% 5.2% 4.1%	Odds Ratio M-H. Random, 95% (0.98 (0.68, 1.247 2.37 [1.48, 3.80 2.36 [1.58, 3.247 1.26 [0.80, 2.00 1.91 [1.25, 2.94 6.46 [1.17, 35.74 1.34 (0.53, 3.39 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.85 [0.50, 1.43 1.12 [0.54, 2.29 3.41 [1.39, 8.36	21 	Favours [VO] Odds	Favours [Non-VO] Ratio	100
Total events Heterogeneity: Chi ² = Test for overall effect: Study or Subgroup Almasaudi 2019 Chen B 2018 Chen W2 2018 Dong 2022 Gachabayov 2023 Heus 2019 shii 2005 Kang 2012 Malietzis 2016 Dzoya 2017 Pedrazzani 2020 Shiomi 2016 Tsujinaka 2008 Watanabe 2014	2.62, df = 1 Z = 2.12 (f VO Events 138 36 68 89 36 136 7 8 51 55 64 14 22 22 37	5 (P = 0 P = 0.03 543 191 261 106 272 9 29 420 82 173 82 68 144	0.76); I ² = 3) Non-VC Events 51 19 35 48 114 46 13 25 61 3 36 24 8 27	0% Total 198 130 185 267 394 134 37 113 385 28 88 154 65 194	Weight 8.2% 6.1% 7.3% 7.9% 7.4% 7.7% 4.0% 4.0% 2.5% 6.8% 5.2% 4.1% 6.6%	Odds Ratio M-H. Random. 95% (0.98 [0.68, 1.43 1.35 [0.73, 2.47 2.37 [1.48, 3.80 2.36 [1.58, 3.54 1.26 [0.80, 2.00 1.91 [1.25, 2.94 6.46 [1.17, 35.74 1.34 [0.53, 3.39 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.85 [0.50, 1.43 1.12 [0.54, 2.29 3.41 [1.39, 8.36 2.14 [1.23, 3.72	21 	Favours [VO] Odds	Favours [Non-VO] Ratio	 100
Total events Heterogeneity: Chi ² = Test for overall effect: Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Gachabayov 2023 Heus 2019 Shii 2005 Kang 2012 Malietzis 2016 Dzoya 2017 Pedrazzani 2020 Shiomi 2016 Tsujinaka 2008 Watanabe 2014 Zhai TS 2019	2.62, df = 1 Z = 2.12 (f VO Events 138 36 68 89 36 136 7 8 51 25 64 14 22	5 (P = 0 P = 0.03 543 192 191 261 106 272 9 29 420 82 173 82 173 82 144 73	0.76); I ² = 3) Non-VC Events 51 19 35 48 114 46 13 25 61 3 36 24 8 27 4	0% Total 198 130 185 267 394 134 37 113 385 28 88 88 85 154 65 194 34	Weight 8.2% 6.1% 7.3% 7.9% 7.7% 1.6% 4.0% 7.9% 2.5% 6.8% 5.2% 4.1% 6.6% 3.0%	Odds Ratio M-H. Random, 95% (0.98 (0.68, 1.48, 3.60 2.36 [1.58, 3.54 1.26 (0.80, 2.00 1.91 [1.25, 2.94 1.34 [0.53, 3.39 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.85 [0.50, 1.43 1.12 [0.54, 2.29 3.41 [1.39, 8.36 2.14 [1.23, 3.72 3.67 [1.16, 11.62]	21 	Favours [VO] Odds	Favours [Non-VO] Ratio	 100
Total events Heterogeneity: Chi ^a = Test for overall effect: Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Gachabayov 2023 Heus 2019 Ishii 2005 Kang 2012 Malietzis 2016 Ozoya 2017 Pedrazzani 2020 Shiomi 2016 Shiomi 2016 Shiomi 2016 Shiomi 2016 Zhaya 2008 Watanabe 2014 Zhai TS 2019 Zhao 2024	2.62, df = 1 Z = 2.12 (f vo Events 138 36 68 89 36 61 136 7 8 8 51 25 64 14 22 37 24 22 37	5 (P = 0) Total 192 191 261 106 272 9 29 420 82 173 82 68 144 73 121	0.76); I ² = 3) Non-VC Events 51 19 35 48 114 46 13 25 61 3 36 61 3 36 24 8 27 4 19	0% Total 198 130 185 267 394 134 37 113 385 28 88 85 154 65 194 34 156	Weight 8.2% 6.1% 7.3% 7.4% 7.7% 1.6% 4.0% 2.5% 6.8% 5.2% 4.1% 6.6% 3.0%	Odds Ratio M-H. Random. 95% (0.98 [0.68, 1.33 1.35 [0.73, 2.47 2.37 [1.48, 3.80 2.36 [1.58, 3.54 1.26 [0.8, 0.200 1.91 [1.25, 2.94 6.46 [1.17, 35.74 1.34 [0.53, 3.39 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.85 [0.50, 1.43 1.12 [0.54, 2.36 2.341 [1.39, 8.36 2.14 [1.23, 3.72 3.67 [1.16, 11.62	21 	Favours [VO] Odds	Favours [Non-VO] Ratio	 100
Total events Heterogeneity: Chi ² = Test for overall effect: Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Gachabayov 2023 Heus 2019 Shii 2005 Kang 2012 Malietzis 2016 Dzoya 2017 Pedrazzani 2020 Shiomi 2016 Tsujinaka 2008 Watanabe 2014 Zhai TS 2019	2.62, df = 1 Z = 2.12 (f VO Events 138 36 68 89 36 136 7 7 8 51 25 56 4 14 22 77 24	5 (P = 0 P = 0.03 543 192 191 261 106 272 9 29 420 82 173 82 173 82 144 73	0.76); I ² = 3) Non-VC Events 51 19 35 48 114 46 13 25 61 3 36 24 8 27 4	0% Total 198 130 185 267 394 134 37 113 385 28 88 88 85 154 65 194 34	Weight 8.2% 6.1% 7.3% 7.9% 7.7% 1.6% 4.0% 7.9% 2.5% 6.8% 5.2% 4.1% 6.6% 3.0%	Odds Ratio M-H. Random, 95% (0.98 (0.68, 1.48, 3.60 2.36 [1.58, 3.54 1.26 (0.80, 2.00 1.91 [1.25, 2.94 1.34 [0.53, 3.39 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.85 [0.50, 1.43 1.12 [0.54, 2.29 3.41 [1.39, 8.36 2.14 [1.23, 3.72 3.67 [1.16, 11.62]	21 	Favours [VO] Odds	Favours [Non-VO] Ratio	 100
Total events Heterogeneity: Chi ^a = Test for overall effect: Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Gachabayov 2023 Heus 2019 Ishii 2005 Kang 2012 Malietzis 2016 Ozoya 2017 Pedrazzani 2020 Shiomi 2016 Shiomi 2016 Shiomi 2016 Shiomi 2016 Zhaya 2008 Watanabe 2014 Zhai TS 2019 Zhao 2024	2.62, df = 1 Z = 2.12 (J VO Events 138 36 68 89 36 136 7 8 51 125 64 14 22 37 24 422 37 24 22 76	5 (P = 0) Total 192 191 261 106 272 9 29 420 82 173 82 68 144 73 121	0.76); I ² = 3) Non-VC Events 51 19 35 48 114 46 13 25 61 3 36 24 8 27 4 19 69	0% Total 198 130 185 267 394 134 37 113 385 28 88 154 65 194 34 154 318	Weight 8.2% 6.1% 7.3% 7.4% 7.7% 1.6% 4.0% 2.5% 6.8% 5.2% 4.1% 6.6% 3.0%	Odds Ratio M-H. Random. 95% (0.98 [0.68, 1.33 1.35 [0.73, 2.47 2.37 [1.48, 3.80 2.36 [1.58, 3.54 1.26 [0.8, 0.200 1.91 [1.25, 2.94 6.46 [1.17, 35.74 1.34 [0.53, 3.39 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.85 [0.50, 1.43 1.12 [0.54, 2.36 2.341 [1.39, 8.36 2.14 [1.23, 3.72 3.67 [1.16, 11.62	51 	Favours [VO] Odds	Favours [Non-VO] Ratio	
Total events Heterogeneity: Ch ² = Test for overall effect: 2 Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Sachabayov 2023 Heus 2019 shii 2005 Kang 2012 Malietzis 2016 Dzoya 2017 Pedrazzani 2020 Shiomi 2016 Tsujinaka 2008 Watanabe 2014 Zhai TS 2019 Zhao 2024 Zhou 2023	2.62, df = 1 Z = 2.12 (J VO Events 138 36 68 89 36 136 7 8 51 125 64 14 22 37 24 422 37 24 22 76	5 (P = 0) Total 543 192 191 106 272 9 29 420 82 68 144 73 306	0.76); I ² = 3) Non-VC Events 51 19 35 48 114 46 13 25 61 3 36 24 8 27 4 19 69	0% Total 198 130 185 267 394 134 37 113 385 28 88 154 65 194 34 154 318	Weight 8.2% 6.1% 7.3% 7.4% 7.7% 1.6% 4.0% 7.9% 2.5% 6.8% 6.8% 5.2% 4.1% 6.6% 8.2%	Odds Ratio M-H. Random, 95% (0.98 (0.68, 1.48, 3.80 2.36 (1.58, 3.54 1.26 (0.80, 2.00 1.91 (1.25, 2.94 6.46 (1.17, 35.74 1.34 (0.53, 3.39 0.73 (0.49, 1.10 3.65 [1.01, 1.3.23 0.85 (0.50, 1.43 1.12 (0.54, 2.29 3.41 [1.39, 8.36 2.14 [1.23, 3.72 3.67 [1.16, 11.62 1.60 (0.82, 3.12 1.19 (0.82, 1.73	51 	Favours [VO] Odds	Favours [Non-VO] Ratio	100
Total events Heterogeneity: Chi ^a = Test for overall effect: Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Gachabayov 2023 Heus 2019 Ishii 2005 Kang 2012 Malietzis 2016 Ozoya 2017 Pedrazzani 2020 Shiomi 2016 Tsujinaka 2008 Watanabe 2014 Zhai TS 2019 Zhao 2024 Zhou 2023 Total (95% CI) Total events Heterogeneity: Tau ² =	2.62, df = : Z = 2.12 (J VO Events 138 36 68 89 36 6136 7 8 51 25 64 14 22 23 7 6 8 51 25 64 14 22 23 7 6 8 53 0.14; ChF = :	5 (P = 0.0) Total 543 192 191 261 106 272 9 29 420 82 68 144 73 306 3072 = 45.52	0.76); I ² = 3) Non-VC Events 51 19 35 48 114 46 13 25 61 3 66 24 8 27 4 19 69 	0% Total 198 130 185 267 394 134 37 113 385 28 88 154 65 194 34 156 318 22880	Weight 8.2% 6.1% 7.3% 7.4% 7.4% 7.9% 2.5% 4.0% 5.2% 4.1% 6.8% 3.0% 5.6% 3.0% 5.6% 3.2% 100.0%	Odds Ratio M-H. Random, 95% (0.98 (0.68, 1.48, 3.64 1.35 (0.73, 2.47 2.37 [1.48, 3.60 2.36 [1.58, 3.54 1.26 (0.80, 2.00 1.91 [1.25, 2.94 1.34 [0.53, 3.39 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.65 [0.50, 1.43, 2.29 3.41 [1.39, 8.36 2.14 [1.23, 3.72 3.67 [1.16, 11.62 1.60 [0.82, 3.12 1.19 [0.82, 1.73] 1.55 [1.22, 1.96]		Favours [VO] Odds <u>M-H, Rand</u>	Favours [Non-VO] Ratio Join 95% Cl	
Total events Heterogeneity: Ch ² = Test for overall effect: 2 Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Gachabayov 2023 Heus 2019 Shii 2005 Kang 2012 Malietzis 2016 Dzoya 2017 Pedrazzani 2020 Shiomi 2016 Tsujinaka 2008 Matanabe 2014 Zhao 2024 Zhou 2023 Total (95% CI) Total events	2.62, df = : Z = 2.12 (J VO Events 138 36 68 89 36 6136 7 8 51 25 64 14 22 23 77 8 37 24 22 76 853 0.14; Chi ² :	5 (P = 0.0) Total 543 192 191 261 106 272 9 29 420 82 68 144 73 306 3072 = 45.52	0.76); I ² = 3) Non-VC Events 51 19 35 48 114 46 13 25 61 3 66 24 8 27 4 19 69 	0% Total 198 130 185 267 394 134 37 113 385 28 88 154 65 194 34 156 318 22880	Weight 8.2% 6.1% 7.3% 7.4% 7.4% 7.9% 2.5% 4.0% 5.2% 4.1% 6.8% 3.0% 5.6% 3.0% 5.6% 3.2% 100.0%	Odds Ratio M-H. Random, 95% (0.98 (0.68, 1.48, 3.64 1.35 (0.73, 2.47 2.37 [1.48, 3.60 2.36 [1.58, 3.54 1.26 (0.80, 2.00 1.91 [1.25, 2.94 1.34 [0.53, 3.39 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.65 [0.50, 1.43, 2.29 3.41 [1.39, 8.36 2.14 [1.23, 3.72 3.67 [1.16, 11.62 1.60 [0.82, 3.12 1.19 [0.82, 1.73] 1.55 [1.22, 1.96]	51 	Favours [VO] Odds M-H. Rand	Favours [Non-VO] Ratio Join 95% Cl	1 100
Total events Heterogeneity: Chi ² = Test for overall effect: 2 Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Gachabayov 2023 Heus 2019 Ishii 2005 Kang 2012 Malietzis 2016 Ozoya 2017 Pedrazzani 2020 Shiomi 2016 Tsujinaka 2008 Watanabe 2014 Zhai TS 2019 Zhao 2024 Zhou 2023 Total (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect:	2.62, df = : Z = 2.12 (J VO Events 138 36 68 89 36 61 36 136 7 8 51 25 56 44 14 22 76 853 0.14; Chi ² (Z Z = 3.65 (F	5 (P = 0.0) Total 543 192 191 261 106 272 9 29 420 82 68 144 73 306 3072 = 45.52	0.76); I ² = 3) Non-VC Events 51 19 35 48 114 46 13 25 61 3 36 24 8 27 4 19 60 24 60 2 4 6 10 3 3 6 24 6 1 3 3 6 24 6 1 3 3 6 24 8 27 7 8 7 7 8 7 7 8 7 8 7 8 7 7 7 8 7 7 8 7 7 7 7 7 7 7 7 7 7 7 7 7	0% Total 198 130 135 267 394 134 37 113 385 28 88 154 65 318 28 34 156 318 2880 P = 0.0	Weight 8.2% 6.1% 7.3% 7.4% 7.4% 7.9% 2.5% 4.0% 5.2% 4.1% 6.8% 3.0% 5.6% 3.0% 5.6% 3.2% 100.0%	Odds Ratio M-H. Random, 95% (0.98 [0.68, 1.247 2.37 [1.48, 3.80 2.36 [1.58, 3.54 1.26 [0.80, 2.00 1.91 [1.25, 2.94 6.46 [1.17, 35.74 1.34 [0.53, 3.39 0.73 [0.49, 1.10] 3.65 [1.01, 13.23 0.85 [0.50, 1.43 1.12 [0.54, 2.29 3.41 [1.39, 8.36 2.14 [1.23, 3.72 3.67 [1.16, 11.62 1.60 [0.82, 3.12 1.19 [0.82, 1.73 1.55 [1.22, 1.96] 65%		Favours [VO] Odds M-H. Rand	Favours [Non-VO] Ratio Join 95% Cl	
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Total events Heterogeneity: Chi ² = Test for overall effect: 2 Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Sachabayov 2023 Heus 2019 Ishii 2005 Sachabayov 2023 Heus 2019 Shioi 2005 Shiomi 2016 Socya 2017 Pedrazzani 2020 Shiomi 2016 Touga 2024 Zhao 2024 Zhao 2024 Zhao 2024 Zhao 2024 Choil 95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: f Study or Subgroup	2.62, df = : Z = 2.12 (J VO Events 138 36 68 89 36 61 36 61 36 63 36 63 36 63 36 64 136 7 8 51 25 56 44 14 22 76 853 0.14; Chi ² : Z = 3.65 (F VO Events 4 22 76	5 (P = 0.0) Total 543 192 191 261 106 272 9 420 82 68 82 68 144 73 121 306 3072 = 45.522 = 0.00 Total	0.76); I ^a = Non-VC Events : 51 19 35 48 114 46 13 35 48 14 46 13 35 61 35 61 35 61 35 61 36 61 36 61 30 Non-VC 80 80 80 80 80 80 80 80 80 80	0% Total 198 130 185 267 394 134 37 154 65 194 154 65 194 2880 P = 0.0 70 Total 1 134	Weight 8.2% 6.1% 7.3% 7.3% 7.3% 1.6% 4.0% 7.3% 6.8% 5.2% 4.1% 6.6% 5.2% 4.1% 6.8% 5.2% 100.0%	Odds Ratio M-H. Random, 95% (0.98 [0.68, 1.247 2.37 [1.48, 3.80 2.36 [1.58, 3.54 1.26 [0.80, 2.00 1.91 [1.25, 2.94 6.46 [1.17, 35.74 1.34 [0.53, 3.39 0.73 [0.49, 1.10 3.65 [1.01, 1.3.23 0.85 [0.50, 1.43 1.12 [0.54, 2.29 3.41 [1.39, 8.36 2.14 [1.23, 3.72 3.67 [1.16, 11.62 1.60 [0.82, 3.12 1.19 [0.82, 1.73 1.55 [1.22, 1.96] 65% Odds Ratio M-H. Fixed, 95% C 1.31 [0.73, 2.36]	2	Favours [VO] Odds <u>M-H, Rand</u> 	Favours [Non-VO] Ratio	
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Total events Heterogeneity: Chi ² = Test for overall effect: 2 Study or Subgroup Almasaudi 2019 Chen B 2016 Chen WZ 2018 Dong 2022 Sachabayov 2023 Heus 2019 Shii 2005 Kang 2012 Malietzis 2016 Zozoya 2017 Pedrazzani 2020 Shiomi 2016 Toujal exerts Heterogeneity: Tau ² = Test for overall effect: f Study or Subgroup Heus 2019 Dicaya 2017 Pedrazzani 2020 Shiomi 2016 Study or Subgroup Heus 2019 Dicaya 2017 Pedrazzani 2020 Shiomi 2016 Study or Subgroup Heus 2019 Dicaya 2017 Pedrazzani 2020 Shiomi 2016 Zhai TS 2019 Zhou 2023 Total (95% CI) Total events	2.62, df = : Z = 2.12 (I VO Events 138 36 68 89 36 68 89 36 61 136 7 8 51 25 64 14 22 76 853 0.14; Chi ² : Z = 3.65 (F Events 46 4 18 4 4 18 8 4 4 18 4 18 4 18 18 18 18 18 18 18 18 18 18	5 (P = () 7 (P = 0) 102 192 191 201 106 272 9 9 29 420 82 173 82 68 121 306 3072 = 45.52 = 0.00 Total 272 82 73 306 988	0.76); ² = Non-V/V <u>51</u> 19 35 48 114 46 13 35 48 114 46 13 36 24 48 27 4 19 69 :: 60 : 03) Non-V/V <u>51</u> 114 46 13 36 24 48 27 49 69 : 10 114 114 114 114 114 114 114	0% Total 198 130 185 267 394 133 385 28 394 134 37 385 28 88 154 318 70 Total 134 2880 70 Total 134 318 52 70 Total 134 318 52 70 70 Total 134 318 52 70 70 70 70 70 70 70 70 70 70	Weight 8.2% 6.1% 7.3% 7.4% 7.7% 2.6% 4.0% 2.5% 3.0% 5.2% 4.1% 5.6% 3.0% 3.0% 3.0% 4.1% 3.0% 3.0% 4.1% 3.0% 4.1% 3.0% 4.1% 5.2% 4.2% 5.2% 4.1% 5.2% 4.2% 5.2% 4.2% 5.2% 4.2% 5.2% 4.2% 5.2% 4.2% 5.2% 4.2% 5.2% 4.2% 5.2% 4.2% 5.2% 5.2% 4.2% 5.2% 5.2% 5.2% 5.2% 5.2% 5.2% 5.2% 5	Odds Ratio M.H. Random. 95% C 0.98 [0.68, 1.43 1.35 [0.73, 2.47 2.37 [1.48, 3.60 2.36 [1.58, 3.54 1.26 [0.80, 2.00 1.91 [1.25, 2.94 6.46 [[1.17, 35.74 1.34 [0.53, 3.39 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.73 [0.49, 1.10 3.65 [1.12, 1.39, 3.36 1.19 [0.82, 1.73 1.55 [1.22, 1.96] 65% Odds Ratio M.H. Fixed. 95% C 1.31 [0.73, 2.36] 1.38 [0.15, 12.94] 0.81 [0.37, 1.81] 1.06 [0.31, 3.79] 1.91 [0.21, 17.80] 1.14 [0.49, 2.62]	2	Favours [VO] Odds <u>M-H, Rand</u> 	Favours [Non-VO] Ratio om. 95% Cl	
Total events Heterogeneity: Chi ² = Test for overall effect: 2 Study or Subgroup Almasaudi 2019 Chen B 2016 Chen VZ 2018 Dong 2022 Gachabayov 2023 Heus 2019 Shii 2005 Kang 2012 Malietzis 2016 Dozoya 2017 Pedrazzani 2020 Shiomi 2016 Tsujinaka 2008 Matanabe 2014 Zhao 2024 Zhou 2023 Total (95% CI) Total events Heterogeneity: Tau ² = Test for overall effect: f Study or Subgroup Heus 2019 Dzoya 2017 Pedrazzani 2020 Shiomi 2016 Pedrazzani 2020 Shiomi 2017 Pedrazzani 2020 Shiomi 2016 Zhai TS 2019 Zhou 2023 Total 2017 Pedrazzani 2020 Shiomi 2016 Zhai TS 2019 Zhou 2023 Total 95% CI)	2.62, df = : Z = 2.12 (J VO Events: 138 36 68 89 36 136 68 89 36 136 7 8 51 25 64 14 22 27 6 853 0.14; Chi ² : 76 853 0.14; Chi ² : 76 VO Events: 46 4 4 18 37 24 22 76 853 0.14; Chi ² : 76 853 0.14; Chi ² : 853 0.14; Chi ² : 853 0.14; Chi ² : 853 0.14; Chi ² : 86 86 86 87 86 85 85 85 85 85 85 85 85 85 85	5 (P = 0) Total 543 192 191 261 106 272 9 9 29 420 82 68 114 306 3072 = 45.52 = 0.000 Total 272 82 73 306 3072 82 73 306 3072 82 73 306 3072 82 73 306 3072 82 73 306 3072 82 73 306 3072 82 73 306 3072 82 73 306 3072 82 73 306 3072 82 73 306 3072 73 82 73 306 3072 82 73 306 3072 82 73 306 3072 82 73 306 306 55 (P = 0) (P =	0.76); ² = Non-VC 51 19 55 48 114 46 13 35 48 113 35 48 114 46 13 36 61 36 24 48 27 4 19 69 50 27 49 69 50 10 10 10 10 10 10 10 10 10 1	0% Total 198 130 185 267 394 133 385 28 394 134 37 385 28 88 154 318 70 Total 134 2880 70 Total 134 318 52 70 Total 134 318 52 70 70 Total 134 318 52 70 70 70 70 70 70 70 70 70 70	Weight 8.2% 6.1% 7.3% 7.4% 7.7% 2.6% 4.0% 2.5% 3.0% 5.2% 4.1% 5.6% 3.0% 3.0% 3.0% 4.1% 3.0% 3.0% 4.1% 3.0% 4.1% 3.0% 4.1% 5.2% 4.2% 5.2% 4.1% 5.2% 4.2% 5.2% 4.2% 5.2% 4.2% 5.2% 4.2% 5.2% 4.2% 5.2% 4.2% 5.2% 4.2% 5.2% 4.2% 5.2% 5.2% 4.2% 5.2% 5.2% 5.2% 5.2% 5.2% 5.2% 5.2% 5	Odds Ratio M.H. Random. 95% C 0.98 [0.68, 1.43 1.35 [0.73, 2.47 2.37 [1.48, 3.60 2.36 [1.58, 3.54 1.26 [0.80, 2.00 1.91 [1.25, 2.94 6.46 [[1.17, 35.74 1.34 [0.53, 3.39 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.73 [0.49, 1.10 3.65 [1.01, 13.23 0.73 [0.49, 1.10 3.65 [1.12, 1.39, 3.36 1.19 [0.82, 1.73 1.55 [1.22, 1.96] 65% Odds Ratio M.H. Fixed. 95% C 1.31 [0.73, 2.36] 1.38 [0.15, 12.94] 0.81 [0.37, 1.81] 1.06 [0.31, 3.79] 1.91 [0.21, 17.80] 1.14 [0.49, 2.62]	2	Favours [VO] Odds <u>M-H, Rand</u> 	Favours [Non-VO] Ratio	

Forest plot describing the differences in (a) reoperation rate, (b) readmission rate, (c) mortality, (d) conversion rate, (e) total complications and (f) severe complications between VO and non-VO.

significantly shorter in the non-VO group compared to the VO group (WMD, 0.21 days; 95% CI, 0.05 to 0.37; p = 0.009, Figure 2f), the difference in the time to first food intake was not significant (WMD, 0.12 days; 95% CI, -0.00 to 0.24; p = 0.06, Figure 2g).

3.8 Conversion, reoperation, postoperative readmission and mortality rates

Reoperation (OR, 1.3; 95% CI, 0.94 to 1.81; p = 0.12; Figure 3a), postoperative readmission (OR, 1.07 95% CI, 0.78 to 1.46; p = 0.67; Figure 3b), and mortality rates (OR, 1.47; 95% CI, 0.16 to 2.53; p = 0.32; Figure 3c) did not significantly differ between the two groups, however the conversion rate in the VO group was significantly higher than that in the non-VO group (OR, 1.85; 95% CI, 1.05 to 3.27; p = 0.03; Figure 3d) (Table 3).

3.9 Complications

The total complication rate in the VO group exceeded that of the non-VO group (OR, 1.55; 95% CI, 1.22 to 1.96; p = 0.0003; Figure 3e), although there was no significant difference in the occurrence of severe complications between the two groups (OR, 1.14; 95% CI, 0.78 to 1.67; p = 0.49; Figure 3f) (Table 3).

We subsequently compared complications associated with surgery, including anastomotic leak, hemorrhage, intestinal obstruction, intra-abdominal abscess, wound infection, and gastrointestinal dysfunction, alongside other complications such as pulmonary issues, cardiac complications, urinary tract infections, and urinary retention. The findings indicated that the occurrence of anastomotic leak (OR, 1.38; 95% CI, 1.07 to 1.78; p = 0.01; Figure 4a), intestinal obstruction (OR, 1.56; 95% CI, 1.16 to 2.11; p = 0.0003; Figure 4b), intra-abdominal abscess (OR, 2.08; 95% CI, 1.26 to 3.44; p = 0.004, Figure 4c), and wound infection (OR, 2.57; 95% CI, 1.92 to 3.47; p < 0.00001; Figure 4d) was markedly elevated in the VO group relative to the non-VO group, whereas no statistically significant difference was observed between the two groups regarding bleeding (p = 0.74; Figure 4e)and gastrointestinal dysfunction (p = 0.74; Figure 4f). The occurrence of pulmonary problems (OR, 1.79; 95% CI, 1.31 to 2.45; p = 0.0003; Figure 5a) was elevated in the VO group, although no significant disparity was observed in the frequencies of cardiac issues (p = 0.25; Figure 5b), urinary tract infections (p = 0.69; Figure 5c), and urine retention (p = 0.53; Figure 5d) between the two groups.

TABLE 3 Postoperative conditions and complications in each group.

Study	Postope mortality		Reoper	ation	Readm	ission	Overall Complica	ations	Severe complica	ations
	VO	Non-VO	VO	Non-VO	VO	Non-VO	VO	Non-VO	VO	Non-VO
Ishii	N/A	N/A	N/A	N/A	N/A	N/A	7 (77.7)	13 (35.1)	N/A	N/A
Tsujinaka	N/A	N/A	N/A	N/A	N/A	N/A	22 (32.4)	8 (12)	N/A	N/A
Kang	1 (1)	0 (0)	N/A	N/A	N/A	N/A	8 (27.6)	25 (22.1)	N/A	N/A
Cakir	N/A	N/A	60 (16.3)	20 (10.2)	N/A	N/A	N/A	N/A	N/A	N/A
Chen B	N/A	N/A	N/A	N/A	N/A	N/A	36 (18.8)	19 (14.6)	N/A	N/A
Malietzis	5 (1.2)	5 (1.3)	N/A	N/A	N/A	N/A	51 (12.1)	61 (15.8)	N/A	N/A
Shiomi	N/A	N/A	N/A	N/A	N/A	N/A	14 (17.1)	24 (15.6)	4 (4.6)	7 (4.5)
Yu	N/A	N/A	1 (4.5)	3 (3.8)	0 (0)	5 (6.3)	N/A	N/A	N/A	N/A
Ozoya	N/A	N/A	N/A	N/A	N/A	N/A	25 (30.5)	3 (10.7)	4 (4.9)	1 (3.6)
Chen WZ	N/A	N/A	N/A	N/A	4 (2.1)	1 (0.5)	68 (35.6)	35 (18.9)	N/A	N/A
Almasaudi	N/A	N/A	N/A	N/A	N/A	N/A	138 (47)	51 (45)	N/A	N/A
Heus	11	3	52 (19)	18 (14)	43 (16)	28 (21)	136 (50)	46 (34)	46 (17)	18 (13)
Zhai TS	N/A	N/A	N/A	N/A	N/A	N/A	24 (32.9)	4 (11.8)	4 (5.5)	1 (2.9)
Pedrazzani	3 (1.7)	1 (1.1)	12 (6.9)	9 (10.2)	7 (4)	1 (1.1)	64 (37)	36 (40.9)	18 (10.4)	11 (12.5)
Dong	N/A	N/A	1 (0.4)	3 (1.1)	13 (5.0)	12 (4.5)	89 (34.1)	48 (18)	N/A	N/A
Gachabayov	0 (0)	2 (0.5)	4 (3.8)	18 (4.6)	33 (31.1)	103 (26.1)	36 (33.9)	114 (28.9)	N/A	N/A
Zhou	N/A	N/A	N/A	N/A	N/A	N/A	76 (24.8)	69 (21.7)	12 (3.9)	11 (3.5)
Zhao	N/A	N/A	N/A	N/A	N/A	N/A	22 (18.2)	19 (11.5)	N/A	N/A

N/A not available, VO visceral obesity, non-VO non- visceral obesity.

d Study or Subgroup	VO Events	Total	Non-\ Events		Weight	Odds Ratio M-H. Fixed, 95% C		s Ratio ed. 95% Cl
Almasaudi 2019	18	543	3	198	4.1%	2.23 [0.65, 7.65]		
Cakir 2015	29	367	7	197	8.1%	2.33 [1.00, 5.42]		
Chen B 2016	3	192	1	130	1.1%	2.05 [0.21, 19.90]		
Chen WZ 2018 Choi 2018	12	191	4	185	3.7% 10.4%	3.03 [0.96, 9.58] 0.40 [0.13, 1.19]		
Dong 2022	5 16	97 261	11 9	91 267	8.1%	1.87 [0.81, 4.32]		
Heus 2019	13	272	3	134	3.7%	2.19 [0.61, 7.83]	_	
shii 2005	0	9	6	37	2.5%	0.26 [0.01, 4.95]		
Kang 2012	4	29	8	113	2.7%	2.10 [0.59, 7.53]		
Malietzis 2016	24	420	26	385	24.7%	0.84 [0.47, 1.48]		<u> </u>
Pedrazzani 2020 Shiomi 2016	11 3	173 82	7 3	88 154	8.4% 1.9%	0.79 [0.29, 2.10] 1.91 [0.38, 9.69]		
Watanabe 2014	9	144	2	194	1.5%	6.40 [1.36, 30.09]		
Yu 2016	1	22	3	80	1.2%	1.22 [0.12, 12.36]		
Zhai W 2023	11	337	9	183	10.9%	0.65 [0.27, 1.60]		+
Zhao 2024	6	121	5	156	4.0%	1.58 [0.47, 5.29]		
Zhou 2023	7	306	3	318	2.8%	2.46 [0.63, 9.59]		
Total (95% CI)		3566		2910	100.0%	1.38 [1.07, 1.78]		◆
Total events	172		110					
Heterogeneity: Chi ² =				= 31%	,		0.01 0.1	1 10 100
Test for overall effect:	: Z = 2.48 (F	$P = 0.0^{\circ}$	1)					Favours [Non-VO]
b	vo		Non-V			Odds Ratio		Ratio
Study or Subgroup		Total			Weight	M-H. Fixed, 95% C		ed. 95% Cl
Chen WZ 2018	4	191	3	185	4.2%	1.30 [0.29, 5.88]		
Dong 2022	6	261	5	267	6.9%	1.23 [0.37, 4.09]		
Fujimoto 2022	6	46	6	78	5.5%	1.80 [0.54, 5.95]		
Heus 2019	82	272	28	134	37.2%	1.63 [1.00, 2.67]		
Hopkins 2019	13	494	5	474	7.1%	2.54 [0.90, 7.17]		
shii 2005	1	9	2	37	1.0%	2.19 [0.18, 27.20]		
Kang 2012 Pedrazzani 2020	0 20	29 173	5 5	113 88	3.2% 8.3%	0.33 [0.02, 6.22]		—
Pedrazzani 2020 Shiomi 2016	20 3	173	5	88 154	8.3% 5.7%	2.17 [0.79, 5.99] 0.94 [0.23, 3.85]		
Tsujinaka 2008	3	62 68	4	65	5.6%	0.94 [0.23, 3.85]		<u>+</u>
Watanabe 2014	5	144	2	194	2.3%	3.45 [0.66, 18.06]	-	+
Yu 2016	3	22	7	80	3.7%	1.65 [0.39, 6.98]		<u>├</u>
Zhao 2024	3	121	2	156	2.4%	1.96 [0.32, 11.90]		+ • • • • • • • • • • • • • • • • • • •
Zhou 2023	3	306	5	318	6.9%	0.62 [0.15, 2.62]		<u> </u>
Total (95% CI)		2218		2242	100.0%	1.56 [1.16, 2.11]		•
Total events	152	2210	85	2343	100.0%	1.50 [1.10, 2.11]		•
Heterogeneity: Chi ² =		13 (P =	0.92): 12	= 0%			II	l
Test for overall effect:	: Z = 2.93 (F	P = 0.00	03)				0.01 0.1 Eavours N(O)	1 10 100 Favours [Non-VO]
с	vo		Non-V			Odds Ratio		Ratio
Study or Subgroup						M-H. Fixed, 95% C		ed. 95% Cl
Dong 2022	19	261	8	267	33.0%	2.54 [1.09, 5.91]		-
shii 2005 Kana 2012	2	9	2	37	2.7%	5.00 [0.60, 41.71]		
Kang 2012	1	29	2	113	3.6%	1.98 [0.17, 22.65]		<u> </u>
Kang 2012 Shiomi 2016			2 5	113 154	3.6% 15.5%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20]		
Kang 2012	1 1	29 82	2	113	3.6%	1.98 [0.17, 22.65]		
Kang 2012 Shiomi 2016 Zhai W 2023	1 1 21	29 82 337	2 5 2	113 154 183	3.6% 15.5% 11.0%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95]		
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023	1 1 21 1	29 82 337 121 306	2 5 2 1	113 154 183 156 318	3.6% 15.5% 11.0% 3.9% 30.3%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67]		
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI)	1 21 1 6	29 82 337 121	2 5 2 1 7	113 154 183 156 318	3.6% 15.5% 11.0% 3.9%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86]		
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhao 2023 Total (95% CI) Total events	1 21 1 6 51	29 82 337 121 306 1145	2 5 2 1 7 27	113 154 183 156 318 1228	3.6% 15.5% 11.0% 3.9% 30.3%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67]		
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total events Heterogeneity: Chi ² =	1 21 1 6 7.77, df = 6	29 82 337 121 306 1145 6 (P = 0	2 5 2 1 7 27 0.26); ² =	113 154 183 156 318 1228	3.6% 15.5% 11.0% 3.9% 30.3%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67]	0.01 0.1	
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect:	1 21 1 6 7.77, df = 6	29 82 337 121 306 1145 6 (P = 0	2 5 2 1 7 27 0.26); ² =	113 154 183 156 318 1228	3.6% 15.5% 11.0% 3.9% 30.3%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67]	0.01 0.1	+ 1 10 100 Favours (Non-VO)
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% Cl) Total events Heterogeneity: Chi ² = Fest for overail effect: d	1 21 1 6 7.77, df = 6 : Z = 2.87 (f	29 82 337 121 306 1145 6 (P = 0 P = 0.00	2 5 2 1 7 27 0.26); l ² = 04) Non-VO	113 154 183 156 318 1228 23%	3.6% 15.5% 11.0% 3.9% 30.3%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: d Study or Subgroup	1 21 1 6 : 7.77, df = 6 : Z = 2.87 (f VO Events 1	29 82 337 121 306 1145 6 (P = 0) P = 0.00 Total E	2 5 2 1 7 27 0.26); I ² = 04) Non-VO Events T	113 154 183 156 318 1228 23%	3.6% 15.5% 11.0% 3.9% 30.3% 100.0%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] Odds Ratio 4.H. Fixed, 95% Cl	0.01 0.1 Favours [VO]	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Cl Study or Subgroup Almasaudi 2019	1 21 1 6 7.77, df = 6 : Z = 2.87 (f <u>VO</u> <u>Events 1</u> 48	29 82 337 121 306 1145 6 (P = 0 P = 0.00) P = 0.000 Total E 543	2 5 2 1 7 0.26); l ² = 04) Non-VO Events T 7	113 154 183 156 318 1228 23% otal V 198	3.6% 15.5% 11.0% 3.9% 30.3% 100.0%	1.98 [0.17, 22.65] 0.37 (0.04, 3.20) 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.88 [0.30, 2.67] 2.08 [1.26, 3.44] Odds Ratio 0H_Fixed, 95% Cl 2.65 [1.18, 5.95]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Total (95% CI) Total (95% CI) Total events Heterogeneity: Chi ^a = Budy or Subgroup Study or Subgroup Almassudi 2019 Jakir 2015	1 21 1 6 51 7.77, df = e : Z = 2.87 (f <u>VO</u> <u>Events T</u> 48 31	29 82 337 121 306 1145 6 (P = 0 P = 0.00 Fotal E 543 367	2 5 2 1 7 0.26); l ² = 04) Non-VO <u>Events</u> 7 7	113 154 183 156 318 1228 23% otal V 198 197	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% /eight // 14.8% 13.2%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] Odds Ratio dH, Fixed, 95% Cl 2.65 [1.18, 5.66] 2.50 [1.08, 5.60]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhao 2024 Zhou 2023 Total (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: d Study or Subgroup Almasaud 2019 Zakir 2015 Zhen B 2016	1 1 21 1 6 7.77, df = 6 : Z = 2.87 (f Events T 48 31 7	29 82 337 121 306 1145 6 (P = 0 P = 0.00 Fotal E 543 367 192	2 5 2 1 7 0.26); l ² = 04) Non-VO Events T 7 3	113 154 183 156 318 1228 23% otal V 198 197 130	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% //////////////////////////////////	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0dds Ratio 0dds Ratio 0dd Ratio 6.41, 6.56] 2.50 [1.08, 5.69] 2.50 [1.08, 5.80]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Total (95% CI) Total events Heterogeneity: Chi ^a = Budy or Subgroup Mimssaudi 2019 Zakir 2015 Chen W2 2018	1 21 1 6 51 7.77, df = 6 : Z = 2.87 (f <u>VO</u> <u>Events 1</u> 48 31 7 26	29 82 337 121 306 1145 6 ($P = 0$ P = 0.00 Total E 543 367 192 191	2 5 2 1 7 0.26); $I^2 =$ 04) Non-VO Events T 7 7 3 5	113 154 183 156 318 1228 23% 0tal V 198 197 130 185	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% 100.0% 14.8% 13.2% 5.5% 7.0%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 2.08 [1.26, 3.44] 2.65 [1.18, 5.95] 2.65 [1.18, 5.96] 1.60 [0.41, 6.31] 1.60 [0.41, 6.31]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhao 2024 Zhou 2023 Total (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: d Btudy or Subgroup Aimasaud 2019 Zakir 2015 Zhen B 2016 Zhen B 2016	1 1 21 1 6 7.77, df = 6 : Z = 2.87 (f VO Events 1 48 31 7 26 20	29 82 337 121 306 1145 6 (P = 0 P = 0.00 P = 0.00 Fotal E 543 367 192 191 261	2 5 2 1 7 2 2 7 0.26); l ² = 04) Non-VO Events T 7 7 3 5 9	113 154 183 156 318 1228 23% 0tal V 198 197 130 185 267	3.6% 15.5% 11.0% 3.9% 30.3% 100.0%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0dds Ratio 14H Fixed, 95% Cl 2.65 [1.18, 5.65] 2.50 [1.08, 5.80] 1.60 [0.41, 6.31] 5.67 [2.13, 15.12] 2.38 [1.06, 5.33]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhao 2024 Zhou 2023 Total (95% CI) Total events Test for overall effect: d Study or Subgroup Amasaud 2019 Zakir 2015 Zhen B 2016 Zhen B 2016 Zhen W 22018 Zong 2022 Heus 2019 Shi 2005	1 1 21 1 6 7.77, df = (2 = 2.87 (f Events 1 48 31 7 26 20 39 2	29 82 337 121 306 1145 6 (P = 0 P = 0.00 Fotal E 543 367 192 191 261 272 9	2 5 2 1 7 0.26); I ² = 0.4) Non-VO <u>Events T</u> 7 7 7 3 5 9 10 2	113 154 183 156 318 1228 23% 0tal V 198 197 130 185 267 134 37	3.6% 15.5% 11.0% 3.9% 30.3% 100.0%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0dds Ratio dH, Eixed, 95% Cl 2.65 [1.18, 5.65] 2.50 [1.08, 5.80] 1.60 [0.41, 6.31] 5.67 [2.13, 15.12] 2.08 [1.06, 5.33] 2.08 [1.00, 4.30] 5.00 [0.60, 4.71]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total events Heterogeneity: Chi² = Study or Subgroup Almassuell 2019 Shem V2 2018 Dong 2022 Heus 2019 Shiomi 2016	1 1 21 3 1 6 51 7.77, df = (2 2.87 (f VO Events 1 48 31 7 26 20 20 39 2 0	$\begin{array}{c} 29\\ 82\\ 337\\ 121\\ 306\\ \textbf{1145}\\ 6\ (P=0)\\ P=0.00\\ \hline \textbf{543}\\ 367\\ 192\\ 191\\ 261\\ 272\\ 9\\ 82\\ \end{array}$	2 5 2 1 7 0.26); ² = 04) Non-VO <u>Events T</u> 7 7 3 5 9 10 2 1	113 154 183 156 318 1228 23% 0tal V 198 197 130 185 267 134 37 154	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% (eight 1 14.8% 5.5% 7.0% 18.2% 1.0%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 2.68 [1.48, 5.45] 2.50 [1.48, 5.45] 2.50 [1.08, 5.45] 5.2 [1.08, 5.45] 5.00 [0.60, 4.17] 5.00 [0.60, 4.17]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total events Test for overall effect: Cl Study or Subgroup Amasaud 2019 Cakir 2015 Chen B 2016 Chen VZ 2018 Orag 2022 Heus 2019 Shiomi 2016 Shiomi 2016 Shiomi 2016 Shiomi 2016	1 1 21 1 6 51 52 = 2.87 (f vo Events 1 7 26 20 39 20 39 2 0 14	29 82 337 121 306 1145 6 (P = 0 P = 0.00 Fotal E 543 367 192 191 261 272 9 82 68	2 5 2 1 7 0.26); I ² = 04) Non-VO Events T 7 7 3 5 9 10 2 1 10 2 3	113 154 183 156 318 1228 23% 0tal V 198 197 130 185 267 134 37 154 65	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% 144.8% 13.2% 13.0% 13.0% 1.0% 1.6% 3.9%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0dds Ratio 14H. Fixed, 95% Cl 2.65 [1.18, 5.65] 2.50 [1.08, 5.80] 1.60 [0.41, 6.31] 5.67 [2.13, 15.12] 2.08 [1.06, 5.33] 2.08 [1.06, 5.33] 2.08 [1.06, 5.33] 2.08 [1.00, 4.30] 5.00 [0.60, 41.71] 0.62 [0.02, 15.40] 5.35 [1.46, 19.64]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Total (95% CI) Total events Heterogeneity: Ch² = Test for overall effect: d Study or Subaroup Amasaud 2019 Zakir 2015 Dong 2021 House 2019 Shiomi 2016 Shiomi 2016 Faujinaka 2008 Yu 2016	1 1 21 1 6 51 7.77, df = (: Z = 2.87 (f VO Events 1 48 31 7 7 26 20 39 39 2 0 0 14 0	$\begin{array}{c} 29\\ 82\\ 337\\ 121\\ 306\\ \textbf{1145}\\ 6 \ (P=0)\\ P=0.00\\ \hline \textbf{543}\\ 367\\ 192\\ 191\\ 261\\ 272\\ 9\\ 82\\ 68\\ 22\\ \end{array}$	2 5 2 1 7 0.26); ² = 04) Non-VO <u>Events T</u> 7 7 3 5 9 10 2 1 3 2	113 154 183 156 318 1228 23% 0tal V 198 197 130 185 267 134 37 154 65 80	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% 100.0% 14.8% 13.2% 5.5% 7.0% 13.0% 18.2% 1.0% 1.0% 1.6% 3.9%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0.44 [1.86, 5.45] 2.50 [1.08, 5.45] 2.50 [1.08, 5.45] 5.45 [1.48, 5.45] 5.45 [1.46, 5.45] 5.45 [1.46, 5.45] 5.45 [1.46, 5.45] 5.45 [1.46, 5.45] 5.45 [1.46, 5.45] 5.45 [1.46, 1.45] 5.45 [1.46, 1.45] 5.45 [1.46, 1.45] 5.45 [1.46, 1.57]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total events Test for overall effect: Almasaud 2019 Takir 2015 Chen B 2016 Chen B 2016 Chen B 2016 Shiomi 2016 Shiomi 2016 Shiomi 2016 Zhai W 2023	1 1 21 21 51 7.77, df = (: Z = 2.87 (f VO Events 1 7 26 20 39 2 0 14 0 1 48 31 7 26 20 39 2 2 0 14 2	29 82 337 121 306 1145 6 (P = 0 P = 0.00 Fotal E 543 367 192 191 261 272 9 82 68 222 337	2 5 2 1 7 0.26); I ² = 04) Non-VO <u>Events T</u> 7 7 5 9 10 2 1 3 2 5	113 154 183 156 318 1228 23% 0tal V 198 197 130 185 267 134 37 154 65 80 183	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% (eight 1 14.8% 13.2% 5.5% 7.0% 13.0% 13.0% 13.0% 13.0% 1.6% 3.9% 1.7%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0dds Ratio dH, Fixed, 95% C1 2.65 [1.18, 5.95] 2.50 [1.08, 5.80] 1.60 [0.41, 6.31] 5.67 [2.13, 15.12] 2.38 [1.06, 5.33] 2.08 [1.00, 4.30] 5.00 [0.60, 41.71] 0.62 [0.02, 15.40] 5.35 [1.46, 19.64] 0.70 [0.03, 15.07] 2.61 [0.97, 6.89]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Total (95% CI) Total events Heterogeneity: Ch² = Test for overall effect: d Study or Subaroup Amasaud 2019 Zakir 2015 Dong 2021 House 2019 Shiomi 2016 Shiomi 2016 Faujinaka 2008 Yu 2016	1 1 21 21 51 7.77, df = (: Z = 2.87 (f VO Events 1 7 26 20 39 2 0 14 0 1 48 31 7 26 20 39 2 2 0 14 2	$\begin{array}{c} 29\\ 82\\ 337\\ 121\\ 306\\ \textbf{1145}\\ 6 \ (P=0)\\ P=0.00\\ \hline \textbf{543}\\ 367\\ 192\\ 191\\ 261\\ 272\\ 9\\ 82\\ 68\\ 22\\ \end{array}$	2 5 2 1 7 0.26); I ² = 04) Non-VO <u>Events T</u> 7 7 5 9 10 2 1 3 2 5	113 154 183 156 318 1228 23% 0tal V 198 197 130 185 267 134 37 154 65 80 183	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% 100.0% 14.8% 13.2% 5.5% 7.0% 13.0% 18.2% 1.0% 1.0% 1.6% 3.9%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0.44 [1.86, 5.45] 2.50 [1.08, 5.45] 2.50 [1.08, 5.45] 5.45 [1.48, 5.45] 5.45 [1.46, 5.45] 5.45 [1.46, 5.45] 5.45 [1.46, 5.45] 5.45 [1.46, 5.45] 5.45 [1.46, 5.45] 5.45 [1.46, 1.45] 5.45 [1.46, 1.45] 5.45 [1.46, 1.45] 5.45 [1.46, 1.57]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total events Test for overall effect: d Study or Subgroup Amasaud 2019 Jakir 2015 Dhen B 2016 Dhen B 2016 Dhen B 2016 Dhen 2006 Shiomi 2016 Fsujinaka 2008 Shiomi 2016 Tsujinaka 2008 Zhai W 2023 Zhou 2023 Total (95% CI)	$\begin{array}{c} 1 \\ 1 \\ 21 \\ 1 \\ 6 \\ 51 \\ 7.77, df = 6 \\ 22 \\ 2.87 \\ 6 \\ 10 \\ 20 \\ 39 \\ 2 \\ 0 \\ 20 \\ 39 \\ 2 \\ 0 \\ 14 \\ 0 \\ 23 \\ 10 \\ 23 \\ 10 \\ 2 \\ 2 \\ 0 \\ 2 \\ 2 \\ 0 \\ 2 \\ 2 \\ 0 \\ 2 \\ 2$	29 82 337 121 306 1145 6 (P = 0 P = 0.00 Fotal E 543 367 192 191 261 272 9 82 68 222 337	2 5 2 1 7 0.26); ² = 0.4) Non-VO <u>Events T</u> 7 7 3 5 5 9 10 2 1 3 2 5 7 7	113 154 183 156 318 1228 23% 0tal V 198 197 130 185 267 134 37 154 65 80 183	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% 100.0% 14.8% 13.2% 5.5% 7.0% 13.2% 1.0% 18.2% 1.6% 3.9% 1.6% 3.9% 9.6% 10.5%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0dds Ratio dH, Fixed, 95% C1 2.65 [1.18, 5.95] 2.50 [1.08, 5.80] 1.60 [0.41, 6.31] 5.67 [2.13, 15.12] 2.38 [1.06, 5.33] 2.08 [1.00, 4.30] 5.00 [0.60, 41.71] 0.62 [0.02, 15.40] 5.35 [1.46, 19.64] 0.70 [0.03, 15.07] 2.61 [0.97, 6.89]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Xang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Total (95% CI) Total events d Mmssaud 2019 Cakir 2015 Chen B 2016 Chen B 2016 Chen B 2016 Shiomi 2016 Faujinzaka 2008 Yu 2018 Zhai W 2023 Zhai W 2023 Zhai W 2023 Total 95% CI) Total 95% CI)	1 1 21 3 7.77, df = (2 = 2.87 (f VO Events 1 7 4 8 31 7 26 20 0 14 0 23 9 2 0 14 10 23 10 2220	29 82 337 121 306 1145 6 (P = C P = 0.00 Fotal E 543 367 192 261 272 9 82 68 22 337 306 2650	2 5 2 1 7 0.26); ² = 04) Non-VO 5vents T 7 7 7 3 5 9 10 2 1 3 2 1 3 2 5 7 7 1 1 3 1 1 3 2 5 7 7	113 154 183 156 318 23% 1228 23% 0tal V 198 197 130 185 267 134 37 154 65 80 183 318 948 1	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% 100.0% 14.8% 13.2% 5.5% 7.0% 13.2% 1.0% 18.2% 1.6% 3.9% 1.6% 3.9% 9.6% 10.5%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] Odds Ratio CH. Fixed, 95% C1 2.65 [1.18, 5.95] 2.65 [1.18, 5.95] 2.65 [1.6, 5.80] 1.60 [0.41, 6.31] 5.67 [2.13, 15.12] 2.38 [1.06, 5.33] 2.08 [1.00, 4.30] 5.00 [0.60, 41.71] 0.62 [0.02, 15.40] 5.36 [1.46, 19.64] 0.70 [0.03, 15.07] 2.65 [1.5, 6.98] 1.50 [0.56, 3.99]	0.01 0.1 Favours [VO] Odds F	Favours [Non-VO] Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total events Heterogeneity: Chi ² = Test for overail effect: d Study or Subgroup Test for overail effect atki 2019 Sakir 2016 Shen B 2016 Shen B 2016 Shen B 2016 Shiomi 2017 Shi 2017 Sh	$\begin{array}{c} 1 \\ 1 \\ 21 \\ 1 \\ 6 \\ 511 \\ 7.77, df = (\\ 2 \\ 2 \\ 2 \\ 0 \\ 2 \\ 0 \\ 2 \\ 0 \\ 14 \\ 0 \\ 23 \\ 10 \\ 220 \\ 7.55, df = 1 \end{array}$	29 82 337 121 306 1145 6 (P = C P = 0.00 Fotal E 543 367 192 191 261 272 9 82 68 222 337 306 2650 1 (P = 0	2 5 2 1 7 .26); ² = 0 04) Non-VO 5 9 10 2 1 3 5 5 7 7 1 6 5 7 7 1 6 5 7 7	113 154 183 156 318 23% 1228 23% 0tal V 198 197 130 185 267 134 37 154 65 80 183 318 948 1	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% 100.0% 14.8% 13.2% 5.5% 7.0% 13.2% 1.0% 18.2% 1.6% 3.9% 1.6% 3.9% 9.6% 10.5%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] Odds Ratio CH. Fixed, 95% C1 2.65 [1.18, 5.95] 2.65 [1.18, 5.95] 2.65 [1.6, 5.80] 1.60 [0.41, 6.31] 5.67 [2.13, 15.12] 2.38 [1.06, 5.33] 2.08 [1.00, 4.30] 5.00 [0.60, 41.71] 0.62 [0.02, 15.40] 5.36 [1.46, 19.64] 0.70 [0.03, 15.07] 2.65 [1.5, 6.98] 1.50 [0.56, 3.99]	0.01 0.1 Favours (VO) Odds F M-H. Fixe	Favours [Non-VO] Ratio
Xang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Total (95% CI) Total events d Mmssaud 2019 Cakir 2015 Chen B 2016 Chen B 2016 Chen B 2016 Shiomi 2016 Faujinzaka 2008 Yu 2018 Zhai W 2023 Zhai W 2023 Zhai W 2023 Total 95% CI) Total 95% CI)	$\begin{array}{c} 1 \\ 1 \\ 21 \\ 1 \\ 6 \\ 511 \\ 7.77, df = (\\ 2 \\ 2 \\ 2 \\ 0 \\ 2 \\ 0 \\ 2 \\ 0 \\ 14 \\ 0 \\ 23 \\ 10 \\ 220 \\ 7.55, df = 1 \end{array}$	29 82 337 121 306 1145 6 (P = C P = 0.00 Fotal E 543 367 192 191 261 272 9 82 68 222 337 306 2650 1 (P = 0	2 5 2 1 7 .26); ² = 0 04) Non-VO 5 9 10 2 1 3 5 5 7 7 1 6 5 7 7 1 6 5 7 7	113 154 183 156 318 23% 1228 23% 0tal V 198 197 130 185 267 134 37 154 65 80 183 318 948 1	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% 100.0% 14.8% 13.2% 5.5% 7.0% 13.2% 1.0% 18.2% 1.6% 3.9% 1.6% 3.9% 9.6% 10.5%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0.04 [1.26, 3.44] 0.04 [1.26, 3.44] 0.05 [1.08, 5.80] 1.80 [0.41, 6.53] 2.08 [1.06, 5.33] 2.08 [1.00, 4.30] 5.07 [2.13, 15.12] 2.08 [1.06, 5.33] 2.08 [1.00, 4.30] 5.00 [0.60, 41.71] 0.62 [0.02, 15.40] 5.36 [1.4, 9.64] 1.50 [0.56, 3.99] 1.50 [0.56, 3.94]	0.01 0.1 Favours (VO) Odds F M-H. Fixe	Favours [Non-VO] atio , 95% Cl , 95% Cl ,
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total events Heterogeneity: Chi ² = Test for overail effect: d Study or Subgroup Test for overail effect atki 2019 Sakir 2016 Shen B 2016 Shen B 2016 Shen B 2016 Shiomi 2017 Shi 2017 Sh	$\begin{array}{c} 1 \\ 1 \\ 21 \\ 1 \\ 6 \\ 511 \\ 7.77, df = (\\ 2 \\ 2 \\ 2 \\ 0 \\ 2 \\ 0 \\ 2 \\ 0 \\ 14 \\ 0 \\ 23 \\ 10 \\ 220 \\ 7.55, df = 1 \end{array}$	29 82 337 121 306 1145 6 (P = C P = 0.00 Fotal E 543 367 192 191 261 272 9 82 68 222 337 306 2650 1 (P = 0	2 5 5 2 1 7 0.26); ² = 04) Non-VO Events T 7 7 3 5 9 10 2 1 3 2 5 7 7 1 5 9 10 2 1 3 5 9 10 2 1 3 5 9 10 2 1 3 5 9 10 2 1 1 1 2 1 2 1 2 1 2 1 2 1 2 1 2 1	113 154 183 156 318 1228 23% 0141 <i>V</i> 198 197 130 267 134 185 267 134 37 154 80 183 37 154 80 183 37 154 948 1 948 1	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% 100.0% 14.8% 13.2% 5.5% 7.0% 13.2% 1.0% 18.2% 1.6% 3.9% 1.6% 3.9% 9.6% 10.5%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0.000 [1.08, 5.00] 2.65 [1.18, 5.95] 2.50 [1.08, 5.80] 1.60 [0.41, 6.51] 5.67 [2.13, 15.12] 2.08 [1.06, 5.33] 2.08 [1.00, 4.30] 5.50 [0.02, 15.40] 5.50 [0.02, 15.40] 5.50 [0.02, 15.40] 5.51 [1.45, 15.61] 2.58 [1.09, 7, 6.80] 1.50 [0.56, 3.99] 2.58 [1.92, 3.47]	0.01 0.1 Favours [VO] Odde F M-H. Fixe 	Favours [Non-VO] attice
Kang 2012 Shiomi 2016 Zhau V2023 Total (95% CI) Total events Heterogeneity: Ch ² = Total 2019 Study or Subgroup Almasaudi 2019 Zakir 2015 Zhen 2022 Hom Saudi 2018 Zong 2022 Hom 2016 Shiomi 2016 Shiomi 2016 Shalow 2023 Total 405% CI) Total 405% CI) <td>1 1 1 1 1 1 1 1 1 1 1 1 1 1</td> <td>$\begin{array}{c} 29\\ 82\\ 337\\ 121\\ 306\\ 6 \ (P=0.0)\\ 6 \ (P=0.0)\\ 1145\\ 6 \ (P=0.0)\\ 102\\ 102\\ 102\\ 102\\ 102\\ 102\\ 102\\ 102$</td> <td>2 5 2 2 2 2 2 3 2 3 3 5 7 7 1 3 2 1 3 2 1 3 2 5 7 7 1 3 2 1 3 2 5 7 7 1 3 5 5 7 7 1 3 3 2 7 7 7 7 7 7 7 7 9 9 102 6); ² = 9 4) 102 7 102 7 102 103 102 102 102 102 102 102 102 102 102 102</td> <td>113 154 183 156 318 1228 23% 1228 23% 1228 23% 197 198 197 193 185 267 134 37 154 65 80 183 318 48 1 83 48 48 1</td> <td>3.6% 15.5% 11.0% 3.9% 30.3% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%</td> <td>1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0.04 Ratio 0.44, Fixed, 95% C1 2.65 [1.18, 5.95] 2.65 [1.18, 5.95] 2.65 [1.6, 5.93] 2.65 [1.6, 5.33] 2.08 [1.00, 4.30] 5.07 [0.02, 15.40] 5.00 [0.04, 17.11] 0.62 [0.02, 15.40] 5.36 [1.46, 19.64] 1.50 [0.56, 3.99] 2.58 [1.92, 3.47] .01 0.01 0.01 [0.05, 0.02]</td> <td>0.01 0.1 Favours [VO] Odds F M-H. Fixe 1 Favours [experimental]</td> <td>Favours [Non-VO] atio 1.95% Cl 1.95% Cl 10 10 Favours [control] 5 Ratio</td>	1 1 1 1 1 1 1 1 1 1 1 1 1 1	$\begin{array}{c} 29\\ 82\\ 337\\ 121\\ 306\\ 6 \ (P=0.0)\\ 6 \ (P=0.0)\\ 1145\\ 6 \ (P=0.0)\\ 102\\ 102\\ 102\\ 102\\ 102\\ 102\\ 102\\ 102$	2 5 2 2 2 2 2 3 2 3 3 5 7 7 1 3 2 1 3 2 1 3 2 5 7 7 1 3 2 1 3 2 5 7 7 1 3 5 5 7 7 1 3 3 2 7 7 7 7 7 7 7 7 9 9 102 6); ² = 9 4) 102 7 102 7 102 103 102 102 102 102 102 102 102 102 102 102	113 154 183 156 318 1228 23% 1228 23% 1228 23% 197 198 197 193 185 267 134 37 154 65 80 183 318 48 1 83 48 48 1	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0.04 Ratio 0.44, Fixed, 95% C1 2.65 [1.18, 5.95] 2.65 [1.18, 5.95] 2.65 [1.6, 5.93] 2.65 [1.6, 5.33] 2.08 [1.00, 4.30] 5.07 [0.02, 15.40] 5.00 [0.04, 17.11] 0.62 [0.02, 15.40] 5.36 [1.46, 19.64] 1.50 [0.56, 3.99] 2.58 [1.92, 3.47] .01 0.01 0.01 [0.05, 0.02]	0.01 0.1 Favours [VO] Odds F M-H. Fixe 1 Favours [experimental]	Favours [Non-VO] atio 1.95% Cl 1.95% Cl 10 10 Favours [control] 5 Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total events Test for overall effect: d Budy or Subgroup Zakir 2019 Zakir 2019 Zakir 2019 Zhen B 2016 Zhen B 2016 Zhen W 2018 Zhou 2023 Flouga 2028 Zhou 2023 Total (95% CI) Total events Total events Total events	1 1 1 1 1 1 1 1 1 1 1 1 1 1	$\begin{array}{c} 29\\ 82\\ 337\\ 121\\ 306\\ 6 \ (P=0.0)\\ 6 \ (P=0.0)\\ 1145\\ 6 \ (P=0.0)\\ 102\\ 102\\ 102\\ 102\\ 102\\ 102\\ 102\\ 102$	2 5 2 2 2 2 2 3 2 3 3 5 7 7 1 3 2 1 3 2 1 3 2 5 7 7 1 3 2 1 3 2 5 7 7 1 3 5 5 7 7 1 3 3 2 7 7 7 7 7 7 7 7 9 9 102 6); ² = 9 4) 102 7 102 7 102 103 102 102 102 102 102 102 102 102 102 102	113 154 183 156 318 1228 23% 1228 23% 1228 23% 134 130 185 267 130 185 267 37 130 185 337 155 80 183 318 948 1)%	3.6% 15.5% 11.0% 30.3% 30.3% 100.0% feight 1 14.8% 13.2% 5.5% 7.0% 13.2% 5.5% 1.6% 3.9% 1.6% 1.0% 1.6% 3.9% 0.0%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0.000 [1.08, 5.00] 2.65 [1.18, 5.65] 2.50 [1.08, 5.60] 2.26 [1.18, 5.65] 2.26 [1.08, 5.60] 2.26 [1.08, 5.63] 2.26 [1.08, 5.63] 2.26 [1.08, 5.33] 2.08 [1.00, 4.30] 5.07 [2.3, 15.12] 2.08 [1.00, 4.30] 5.07 [2.0, 15.07] 0.26 [1.09, 7, 6.86] 1.50 [0.56, 3.99] 2.58 [1.92, 3.47]	0.01 0.1 Favours [VO] Odds F M-H. Fixe 0.1 1 Favours [experimental] Odds 1	Favours [Non-VO] attice
Kang 2012 Shiomi 2016 Zhau V2023 Total (95% CI) Total events Heterogeneity: Chi² = Test for overall effect: Massaudi 2019 Jour 2018 Shiomi 2016 Shaim 2016 Shaima 2016 Shaim 2017 Shaim 2018 Shaim 2019 Shaim 2018	1 1 21 1 6 7.77, df = (2 = 2.87 (f) VO Events 220 7.55, df = 11 220 7.55, df = 12 VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO V VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VO VV VV VV VV VV VV VV VV VV VV VV VV VVV VVV VVV VVV VVV VVVVVVVVVVVVV	299 82 337 121 36 (P = 0.0 P = 0.0 P = 0.0 P = 0.0 P = 0.0 Total E P = 0.0 State 2 9 82 68 82 272 982 68 82 2337 306 2250 (1 (P = 0.00) 1 (P = 0.00)	2 5 2 2 1 7 7 2 2 7 7 7 3 5 9 9 10 2 2 1 3 2 5 7 1 61 .75); l ² = 0 4) 7 7 7 3 5 9 9 10 2 1 3 2 5 7 1 1 8 9 9 10 2 11 8 9 9 10 2 10 10 10 10 10 10 10 10 10 10 10 10 10	113 154 183 156 318 1228 23% 1228 23% 1228 23% 197 198 197 193 185 267 134 37 154 65 80 183 318 48 1 83 48 48 1	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0.41, Fixed .95% C1 2.65 [1.18, 6.56] 1.60 [0.41, 6.53] 2.65 [1.16, 5.33] 2.08 [1.00, 4.30] 5.09 [0.60, 4.1.71] 0.53 [1.46, 19.64] 0.53 [1.46, 19.64] 0.70 [0.03, 16.07] 2.61 [0.97, 6.89] 2.58 [1.92, 3.47] 0.00 0.040s Ratio M-H, Fixed, 95% C 0.64 (0.11, 3.89]	0.01 0.1 Favours [VO] Odds F M-H. Fixe 1 Favours [experimenta] 1 Favours [experimenta] 1 Odds 1 M-H. Fixe	Favours [Non-VO] atio 1.95% Cl 1.95% Cl 10 10 Favours [control] 5 Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total events Heterogeneity: Chi ² = Test for overail effect: d Study or Subgroup Jakir 2015 Chen W 2018 Shiomi 2016 Shiomi 2016	$\begin{array}{c} 1 \\ 1 \\ 21 \\ 1 \\ 6 \\ 511 \\ 7.77, df = ($	299 82 337 121 306 6 (P = 0 P = 0.00 Total E P = 0.00 Total E 24 367 9 82 68 82 68 82 68 22 337 306 2650 1 (P = 0 9 82 261 27 261 27 261 27 261 27 261 27 261 2650 2650 2650 2650 2650 2650 2650 2650	2 5 2 2 1 7 7 7 7 3 5 9 9 10 2 1 3 2 5 7 1 61 61 61 61 7 7 1 61 8 7 7 1 8 9 9 10 2 5 7 10 1 9 10 1 1 1 3 2 5 5 7 10 10 10 10 10 10 10 10 10 10 10 10 10	113 154 183 156 318 1228 23% 1228 23% 1228 197 198 197 130 185 65 80 183 318 948 1 154 65 80 183 318 948 1 154 65 154 154 65 154 154 154 154 154 156 156 156 156 156 156 156 156 156 156	3.6% 15.5% 11.0% 3.9% 30.3% 100.0% 100.0% 100.0% 100.0% 100.0% 100.0% 00.0% Weight 21.3%	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0.000 [1.08, 5.00] 2.65 [1.18, 5.65] 2.50 [1.08, 5.60] 2.26 [1.18, 5.65] 2.26 [1.08, 5.60] 2.26 [1.08, 5.63] 2.26 [1.08, 5.63] 2.26 [1.08, 5.33] 2.08 [1.00, 4.30] 5.07 [2.3, 15.12] 2.08 [1.00, 4.30] 5.07 [2.0, 15.07] 0.26 [1.09, 7, 6.86] 1.50 [0.56, 3.99] 2.58 [1.92, 3.47]	0.01 0.1 Favours [VO] Odds F M-H. Fixe 1 Favours [experimenta] 1 Gdt 0.1 Favours [experimenta] 1 Odds M-H. Fixe	Favours [Non-VO] atio 1.95% Cl 1.95% Cl 10 10 Favours [control] 5 Ratio
Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total (95% CI) Total (95% CI) Total events Heterogeneity: Chi ² = Test for overail effect Mmasaudi 2019 Jakir 2015 Chen B 2016 Chen W 2018 Shiori 2016 Shiori 2016 Shiori 2016 Chai 0006 Cher 0023 Total (95% CI) Total events -test for overail effect: ; C Study or Subgroup Chen WZ 2018 Dong 2022 Study or Subgroup Chen WZ 2018 Dong 2022 Shiomi 2016 Shiomi 2016	1 1 21 1 6 7.77, df = (2 = 2.87 (f) VO Events 220 7.55, df = 11 220 7.55, df = 12 VO VO Events 2 4 4 20 2 2 4 4 2 2 2 2 4 4 2 2 2 2 2 4 2 2 2 2 2 2 2 2 2 2 2 2 2	299 82 337 121 306 6 (P = 0 P = 0.00 total E 543 367 192 192 192 192 82 261 2261 2261 263 307 306 (P = 0 (C = 0) 9 82 68 82 22 337 306 (P = 0) 9 82 68 82 26 337 121 192 192 192 192 192 192 203 205 192 192 192 192 192 192 192 192 192 192	2 2 5 2 2 1 7 7 2,26); I ² = 04) 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	1113 154 183 156 318 1228 23% 1228 23% 1228 1228 1228 1197 130 197 130 197 134 197 134 197 133 185 267 154 80 948 1 185 267 154 185 318 318 199 199 199 199 199 199 199 199 199 1	3.6% 3.15.5% 111.0% 30.3% 100.0% 100.0% 100.0% 100.5% 1.0% 3.9% 3.9% 3.9% 3.0% 1.0% 3.9% 3.9% 3.9% 3.0% 1.0% 3.9% 3.0% 1.0% 3.0% 1.0% 3.0% 1.0% 5.5% 3.0% 1.0% 5.5% 3.0% 5.5% 5.5% 5.5% 5.5% 5.5% 5.5% 5.5% 5	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0.44 Eixed, 95% CI 2.50 [1.68, 5.69] 2.50 [1.68, 5.69] 2.50 [1.68, 5.69] 2.50 [1.68, 5.63] 2.08 [1.06, 5.33] 2.08 [1.06, 5.33] 2.08 [1.06, 5.33] 2.08 [1.07, 5.80] 1.50 [0.56, 3.99] 2.58 [1.92, 3.47] 0.70 [0.56, 3.99] 2.58 [1.92, 3.47] 0.64 [0.11, 3.89] 0.68 [0.9, 2.43] 9.60 [0.46, 202.28] 3.76 [0.23, 62.69]	0.01 0.1 Favours [VO] Odds F M-H. Fixe 1 Favours [experimental] Odds M-H. Fixe	Favours [Non-VO] atio 1.95% Cl 1.95% Cl 10 10 Favours [control] 5 Ratio
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Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhou 2023 Total (95% CI) Total (95% CI) Total (95% CI) Total events Heterogeneity: Chi ² = Test for overail effect Mmasaudi 2019 Jakir 2015 Chen B 2016 Chen W 2018 Shiori 2016 Shiori 2016 Shiori 2016 Chai 0006 Cher 0023 Total (95% CI) Total events -test for overail effect: ; C Study or Subgroup Chen WZ 2018 Dong 2022 Study or Subgroup Chen WZ 2018 Dong 2022 Shiomi 2016 Shiomi 2016	1 1 21 1 6 7.77, df = (2 = 2.87 (f) VO Events 220 220 7.55, df = 11 2 = 6.25 (P VO Events 2 4 4 2 0 0 2 2 4 4 2 1 2 4 2 2 1 2 2 2 2 1 2 2 2 2 2 2 2 2 2 2 2 2 2	299 82 337 121 306 6 (P = 0 P = 0.00 total E 543 367 192 192 192 192 82 261 2261 2261 263 307 306 (P = 0 (C = 0) 9 82 68 82 22 337 306 (P = 0) 9 82 68 82 26 337 121 192 192 192 192 192 192 203 205 192 192 192 192 192 192 192 192 192 192	2 2 5 2 2 1 7 7 2,26); I ² = 04) 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	1113 154 183 156 318 1228 23% 1228 23% 1228 1228 1228 1197 130 197 130 197 134 197 134 197 133 185 267 154 80 948 1 185 267 154 185 318 318 199 199 199 199 199 199 199 199 199 1	3.6% 3.15.5% 111.0% 30.3% 100.0% 100.0% 100.0% 100.5% 1.0% 3.9% 3.9% 3.9% 3.0% 1.0% 3.9% 3.9% 3.9% 3.0% 1.0% 3.9% 3.0% 1.0% 3.0% 1.0% 3.0% 1.0% 5.5% 3.0% 1.0% 5.5% 3.0% 5.5% 5.5% 5.5% 5.5% 5.5% 5.5% 5.5% 5	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0.44 Eixed, 95% CI 2.50 [1.6, 5.55] 2.50 [1.6, 5.55] 2.50 [1.6, 5.55] 2.50 [1.6, 5.55] 2.50 [0.6, 4.5, 53] 3.20 [0.0, 4.5, 53] 3.50 [0.5, 6, 33] 2.08 [1.0, 5, 33] 2.08 [1.0, 5, 33] 2.08 [1.0, 7, 6, 86] 1.50 [0.5, 6, 399] 2.58 [1.92, 3.47] 0.00 [0.5, 2.347] 0.64 [0.11, 3.89] 0.68 [0.9, 2.43] 9.60 [0.46, 202.28] 3.76 [0.2, 3.6, 26.9]	0.01 0.1 Favours [VO] Odde F M-H. Fixe Favours [experimenta] 1 Favours [experimenta] 1 Odde M-H. Fixe	Favours [Non-VO] atio 1.95% Cl 1.95% Cl 10 10 Favours [control] 5 Ratio
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Kang 2012 Shiomi 2016 Zhai W 2023 Zhao 2024 Zhao 2024 Zhao 2023 Total (95% CI) Total events Heterogeneity: Chi ² = Test for overall effect: Mmasaud 2019 Zakir 2015 Chen B 2016 Chen WZ 2018 Jong 2022 Hous 2019 Shiomi 2016 Shai W 2023 Zhau V 2023 Zhau V 2023 Chen WZ 2018 Dong 2022 Fost (95% CI) Total events Chen WZ 2018 Dong 2022 Shiomi 2016 Frast for overall effect: 1 Chen WZ 2018 Dong 2022 Shiomi 2016 Thao 2024 Zhou 2023 Total (95% CI) Total events Chea (95% CI) Total events Total (95% CI) Total events Fost for overall effect:	1 1 1 1 1 1 1 1 1 1 1 1 1 1	299 82 337 121 306 F = 0.0 F =	2 2 5 2 2 1 7 7 2 2 2 1 7 7 7 7 3 3 5 9 9 10 2 1 1 7 7 7 3 3 5 9 9 10 2 2 1 1 7 7 7 3 3 5 5 9 9 10 2 1 1 7 7 7 7 7 7 7 3 3 5 5 7 9 9 10 7 1 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	113 154 183 154 183 318 1228 23% 011 Y 198 197 185 183 130 185 267 134 65 80 183 37 154 65 80 183 37 184 80 948 1 185 267 154 80 156 65 80 183 318 948 1 188 183 197 198 197 194 198 197 194 198 197 194 197 194 198 197 194 198 197 194 197 194 198 197 194 198 197 194 198 197 194 198 197 194 198 197 194 197 194 198 197 194 197 194 198 197 194 197 194 197 194 197 194 198 197 194 197 194 198 197 194 198 197 194 198 197 194 198 197 194 198 197 194 198 197 194 197 194 197 194 197 194 197 194 197 194 197 194 197 194 197 194 197 194 197 194 197 194 197 194 197 194 197 194 197 194 197 194 194 197 194 197 194 194 194 194 194 194 194 194 194 194	3.6% 3.6% 11.0% 3.9% 30.3% 100.0% 441.4% 1.6% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0.44 Eixed, 95% Cl 2.65 [1.48, 5.45] 2.65 [1.46, 15.42] 2.85 [1.09, 7, 6.38] 2.58 [1.92, 3.47] 0.62 [0.02, 15.40] 2.58 [1.92, 3.47] 0.64 [0.11, 3.89] 0.66 [0.11, 3.89] 0.66 [0.14, 5.21] 0.66 [0.22, 32, 62.69] 0.86 [0.14, 5.21] 0.66 [0.24, 5.22] 0.66 [0.14, 5.21]	0.01 0.1 0.01 0.1 0.01 0.1 0.01 0.1 1 Favours [VO] 0.01 0.1 1 Favours [experimenta]] 0.01 0.1	Favours [Non-VO] atio atio by 5% Cl by
Kang 2012 Shiomi 2016 Zhai W 2023 Total (95% CI) Total events Heterogeneity: Chi ² = Test for overail effect: d Mmsaud 2019 Zakir 2019 Zakir 2019 Zakir 2019 Zakir 2019 Zakir 2019 Zakir 2019 Zakir 2019 Zakir 2016 Shiomi 2016 Shiomi 2016 Shiomi 2016 Shiomi 2016 Shiomi 2016 Shiomi 2016 Shiomi 2016 Shiomi 2016 Chet (95% CI) Total events Heterogeneity: Chi ² = Che WZ 2018 Zhao 2024 Zhao 2024 Zhao 2024 Zhao 2024 Zhao 2024 Zhao 2024 Chet (95% CI) Total (95% CI) Total (95% CI)	1 1 1 1 1 1 1 1 1 1 1 1 1 1	299 82 337 121 306 F = 0.0 F =	2 2 5 2 2 3 7 3 7 4 8 4 7 7 7 7 7 7 7 7 7 7 8 9 9 10 2 1 7 7 7 3 3 5 9 9 10 2 2 1 1 7 7 7 3 8 5 9 9 10 2 2 1 1 7 7 7 3 8 5 9 9 10 2 2 1 1 7 7 7 3 8 5 7 7 7 1 7 7 7 3 8 5 7 9 9 10 2 2 1 1 7 7 7 3 8 5 7 9 9 10 2 2 1 1 7 7 7 3 8 5 7 9 9 10 2 2 1 1 7 7 7 3 8 5 7 7 7 1 7 7 7 3 8 5 7 7 9 10 9 10 9 10 9 10 9 10 9 10 9 10 9 10	1113 154 183 156 318 1228 23% 01228 23% 01228 23% 01228 197 130 197 130 197 130 197 130 197 130 197 133 338 338 338 338 338 338 338 338 348 10% 0 7 0 7 0 156 267 154 267 154 267 154 267 154 267 154 267 154 267 154 267 154 267 154 267 155 267 156 267 156 267 156 267 156 267 156 267 156 267 156 267 156 267 156 267 156 267 156 267 156 267 156 267 156 267 156 267 267 156 267 267 267 267 267 267 267 267 267 26	3.6% 3.6% 11.0% 3.9% 30.3% 100.0% 441.4% 1.6% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2	1.98 [0.17, 22.65] 0.37 [0.04, 3.20] 6.01 [1.39, 25.95] 1.29 [0.08, 20.86] 0.89 [0.30, 2.67] 2.08 [1.26, 3.44] 0.41 [1.26, 3.44] 0.42 [1.26, 3.44] 0.42 [1.26, 3.44] 0.42 [1.26, 3.44] 0.44 [1.46, 3.41] 0.45 [1.46, 5.45] 1.45 [1.46, 5.45] 1.45 [1.46, 6.33] 2.08 [1.06, 5.33] 2.08 [1.06, 5.33] 2.08 [1.06, 5.33] 2.08 [1.06, 5.33] 0.45 [1.46, 4.54] 0.70 [0.03, 15.07] 0.45 [1.46, 4.54] 0.70 [0.46, 2.02, 10] 0.68 [0.14, 5.24] 0.86 [0.14, 5.24] 0.86 [0.14, 5.24] 1.56 [0.26, 9.43] 1.13 [0.55, 2.30]	0.01 0.1 Favours [VO] Odds F M-H. Fixed Favours [experimenta] Odds Odds M-H. Fixed Odds Odds Odds M-H. Fixed Favours [VO]	Favours [Non-VO] atio 4.95% Cl
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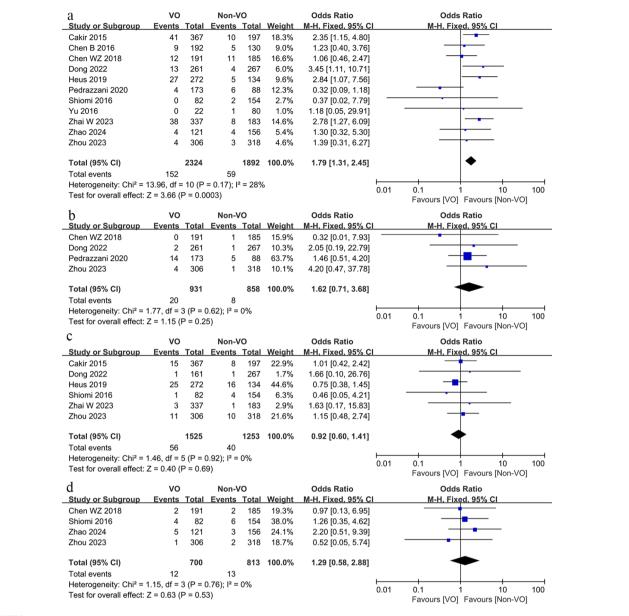
Forest plot describing the differences in (a) anastomotic leak, (b) intestinal obstruction, (c) intra-abdominal abscess, (d) wound infection, (e) bleeding and (f) gastrointestinal dysfunction between VO and non-VO.

3.10 Prognosis

OS (HR = 0.97, 95%CI = 0.85-1.09, p = 0.524; Figure 6a) and DFS (HR = 0.98, 95%CI = 0.85-1.14, p = 0.154; Figure 6a) did not differ statistically significantly between the VO and non-VO groups.

3.11 Publication bias

Using the comprehensive complication data, Begg's (p = 0.174; Figure 7a) and Egger's tests (p = 0.061; Figure 7b) were performed, and no discernible publication bias was found.

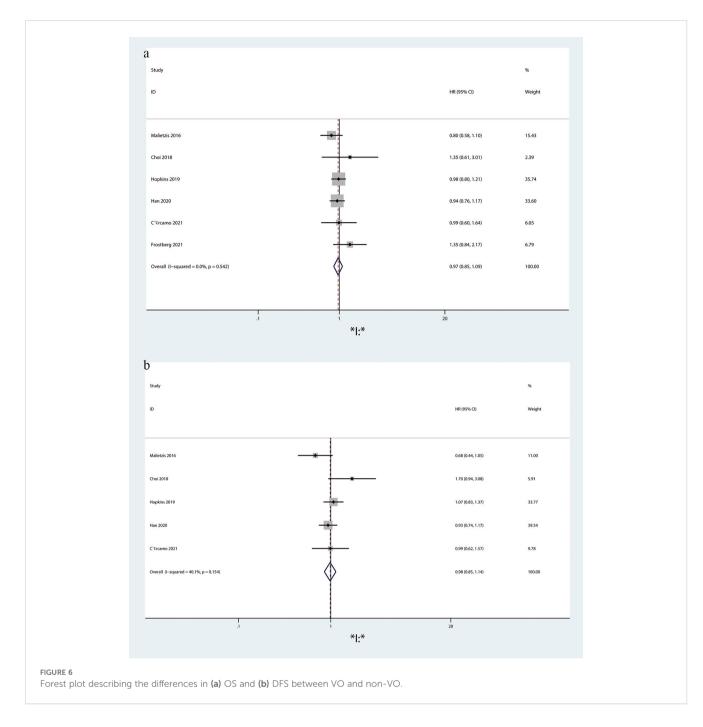


Forest plot describing the differences in (a) pulmonary problems, (b) cardiac issues, (c) urinary tract infections and (d) urine retention between VO and non-VO.

4 Discussion

Obesity, being directly linked to several chronic illnesses and cancers, is a major global public health concern (40). Although BMI has long been the most commonly used metric for diagnosing obesity, it does not adequately reflect the distribution of fat in obese individuals. This is because obesity is characterized by an uneven distribution of fat tissue throughout the body, along with localized disruptions in fat and glucose metabolism (41). Obesity can be classified into two categories based on the location of fat accumulation: visceral obesity and peripheral obesity. The assessment of VFA through CT scanning is considered the gold standard for diagnosing visceral obesity, which is predominantly found in the abdominal region (42). Early studies have linked visceral fat to the incidence of CRC, the second most common cancer worldwide (43). However, the impact of VO on survival and surgical complications in colorectal cancer patients remains inconclusive (44, 45). Therefore, we conducted this meta-analysis to evaluate the effect of visceral obesity on postoperative outcomes in colorectal cancer.

We compared the data of colorectal cancer surgery patients with and without VO. We found that patients with VO experienced a longer recovery time for bowel movements, had fewer lymph nodes harvested, and had higher conversion rates. Additionally, the overall incidence of complications-including anastomotic leaks, intestinal obstruction, intra-abdominal abscesses, wound infections, and pulmonary complications-was significantly higher

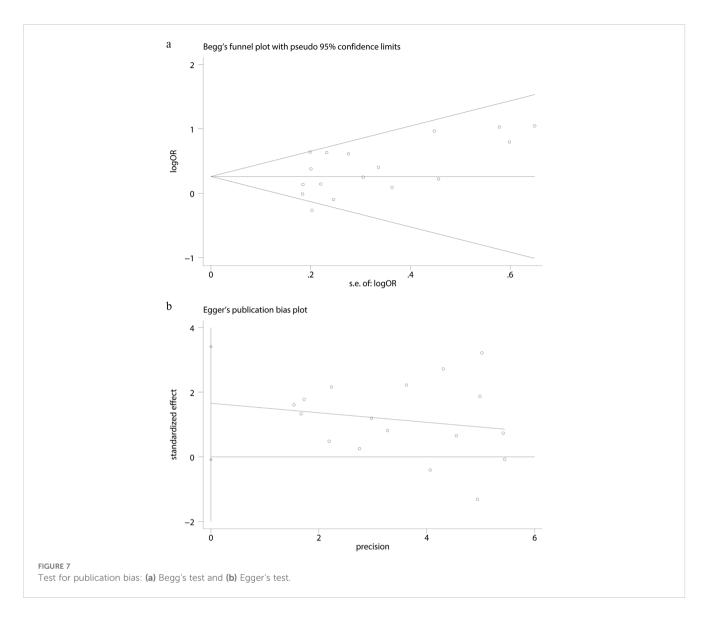


in patients with VO compared to those without. However, there was no difference in OS and DFS between the two groups.

The quantity of lymph nodes removed during tumor excision is a crucial predictor of oncological results in addition to demonstrating the surgeon's ability. VFA influences the number of lymph nodes harvested, either because visceral obese patients have thicker mesenteries, which can make it difficult to see anatomical planes during surgery, making the surgical field more difficult and making it more difficult to dissect lymph nodes and identify blood vessels, which leads to fewer lymph nodes being harvested (14), or because fat tissue adheres to the mesentery, making it more difficult to identify lymph nodes in visceral obese patients (16). Despite the difficulty of dissecting lymph nodes, the operating time did not increase appreciably. The findings of metaanalyses that have already been published contradict this (46). We think that even with obese patients, the operational time can be reduced after a long learning period and overcoming the learning curve, even though the process is more complex.

In general, obesity, tumor size, and pelvic anatomical characteristics are the primary factors that contribute to the transition to open surgery (47, 48). Visceral obesity can further complicate the surgical field and operability, in addition to the challenges posed by limited anatomical features (49). This is specifically verified by our research.

Postoperative problems serve as critical indicators for evaluating short-term surgical outcomes, particularly in colorectal



cancer surgery, where anastomotic leakage is a significant postoperative complication. Thickened mesentery, oversized omentum, and excessive visceral fat are frequently seen in patients with VO. VO is a significant predictor of surgical difficulties and patient outcomes because of these characteristics (50). Anastomotic leaking is more common in VO patients due to the increased technical difficulties of surgery caused by the growth in intra-abdominal fat. Furthermore, obesity raises intra-abdominal pressure for an extended period of time, which may hinder anastomotic site microcirculation and recovery (51). Metabolic problems are strongly associated with obesity, and the inflammatory state that these abnormalities cause may have a detrimental effect on anastomotic healing and tissue repair (52). Excess belly fat increases the risk of bowel blockage because it can impede or disrupt normal intestinal movement, which in turn increases the mechanical pressure on the intestines. Patients who are obese usually have thicker mesentery, which increases the risk of obstruction by causing insufficient blood flow to the intestines. According to research, inflammatory factors such IL-1 α , IL-1 β , and IL-1 receptor antagonists are more prevalent in human visceral fat tissue than subcutaneous fat tissue (53–55). Bowel obstruction is more likely to occur when the intestines are altered intraoperatively since this causes the release of these inflammatory substances. This also explains the delayed recovery of bowel function in the VO group, as evidenced by the prolonged time to first bowel movement after surgery. Furthermore, too much fat raises the danger of fat liquefaction and infection, which explains why wound and intra-abdominal infections are more common (56, 57).

Some negative outcomes can be improved with thorough preoperative evaluation and therapy. According to studies, visceral obesity can be successfully decreased by pharmaceutical therapies, dietary changes, exercise, and behavioral counselling (58). In addition to greatly reducing the risk of problems from surgery, preoperative reduction of visceral fat may also be taken into consideration for patients who have pneumonia or other pulmonary risk factors, especially if they are unable to bear additional respiratory harm. However, it takes time to reduce visceral fat, which may have negative consequences including tumor growth. As a result, it is crucial to perform a comprehensive evaluation of the patient's general health and carefully consider the risks and timing of the intervention.

There is ongoing discussion over the effect of VFA on the longterm prognosis following colorectal cancer surgery. According to some research, VFA is a significant predictor of DFS following surgery for colorectal cancer (59) and is regarded as a separate risk factor for OS in patients undergoing adjuvant chemotherapy for the disease (60). Contrary to the above findings, new research indicates that patients with greater VFA scores actually have longer OS (44). Notably, our study's findings indicate that there were no appreciable variations in long-term outcomes (OS and DFS) between the VO and non-VO groups among patients who had colon cancer surgery. There are several factors that affect the association between visceral fat and the long-term prognosis of colorectal cancer, some of which are not well supported by clinical data. We think that this association may be significantly influenced by variables including hormone levels (61), patient gender (62), and tumor stage (9). Visceral fat's endocrine effects may encourage tumor growth and recurrence in patients with early and intermediatestage cancer, which would lower OS and DFS. On the other hand, since cancer patients frequently have a negative energy balance and a larger visceral fat content may be advantageous for survival, a higher visceral fat content typically suggests superior nutritional reserves for patients with advanced disease. The long-term prognosis of patients with colorectal cancer may also be impacted by the notable variations in steroid hormone levels (such as testosterone and estradiol) between women before and after menopause. These hormones are strongly linked to fat deposition. Nevertheless, there is currently little clinical evidence to validate these putative determinants, and the study's data set is small. To evaluate the effect of these factors on the long-term prognosis of patients with colorectal cancer, more extensive prospective studies are therefore required.

Considering the potential impact of our findings on clinical practice for colorectal cancer patients, this study highlights the importance of distinguishing between visceral and non-visceral obesity, which may lead to more targeted and effective interventions. By identifying visceral obesity as a key metabolic risk factor in colorectal cancer patients, clinicians can prioritize interventions such as lifestyle modifications or pharmacotherapy, especially for those with higher visceral fat accumulation. Furthermore, our findings may assist in the early identification of high-risk colorectal cancer patients for obesity-related comorbidities such as diabetes, cardiovascular diseases, and fatty liver, enabling more timely interventions and improving long-term outcomes. Moreover, incorporating the measurement of visceral fat into routine screening for colorectal cancer patients can help healthcare providers better stratify patient risks and personalize treatment strategies. Overall, this study emphasizes the importance of personalized obesity management, which could significantly improve clinical decision-making, patient outcomes, and public health interventions for colorectal cancer patients.

Among the limitations of this study are the following: (1) the definition of visceral obesity differed among the included studies

(some defined it as VFA \geq 100 cm², others as VFA \geq 130 cm², and some studies classified it based on gender), (2) the surgical approaches used in the included studies varied (open surgery, laparoscopic surgery, and robotic surgery were used, which is another source of high heterogeneity and potential bias), and (3) there may be publication bias because the studies only included patients who had completed preoperative CT scans, while those without CT scans were excluded.

5 Conclusions

In summary, patients with VO who have colorectal cancer and have surgery tend to have fewer lymph nodes removed, higher conversion rates to open surgery, and more postoperative problems. Nevertheless, OS nor DFS seem to be substantially impacted by these factors. Large-scale, prospective research from other nations and areas are still required to confirm these findings and investigate the underlying mechanisms, though, because of sample size limits and regional diversity.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material. Further inquiries can be directed to the corresponding author.

Author contributions

YW: Conceptualization, Data curation, Formal Analysis, Supervision, Writing – original draft, Writing – review & editing. XL: Investigation, Methodology, Software, Writing – original draft, Writing – review & editing. XF: Validation, Writing – original draft, Writing – review & editing. XJ: Formal Analysis, Writing – original draft, Writing – review & editing. LH: Conceptualization, Data curation, Visualization, Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fonc.2025.1538073/ full#supplementary-material

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