Review Article

The Safety of Laparoscopic Cholecystectomy in the Day Surgery Unit Comparing with That in the Inpatient Unit: A Systematic Review and Meta-Analysis

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We aimed to perform a systematic review and meta-analysis on the safety of laparoscopic cholecystectomy performed in the day surgery unit versus those performed in the inpatient unit. Several databases including Ovid Embase, Medline Ovid, Cochrane Central, Web of Science, and Google Scholar were searched from inception through February 2019. Our results revealed that laparoscopic cholecystectomy can be conducted safely and effectively in day surgery units, helping bed shortage.

1. Introduction

Laparoscopic cholecystectomy (LC) is considered the "gold standard" for the surgical treatment of gallstone disease because it results in less postoperative pain, better cosmesis, and shorter hospital stays and recover faster than open cholecystectomy [1–5]. Currently, approximately 750,000 laparoscopic cholecystectomies are performed annually in the United States, which accounts for roughly 90 percent of all cholecystectomies [6, 7]. Routine LC requires patients to admit at least one night in the inpatient units. With the development of day surgery, patients with good home support can leave the hospital within six hours after surgery [8, 9].

Day surgery LC is known for many benefits, including overcoming inpatient bed shortage and cost effective, compared to routine LC [10, 11]. However, the growth of day surgery LC is till slow and even has not developed in most developing countries like China mainland [12, 13]. Concerns about safety, not the lack of adequate techniques and facilities, have curbed the wide-scale development of LC as day surgery [14, 15]. Thus, we aim to assess the safety of LC in day surgery units through an updated systematic review and meta-analysis, which will raise an important reference value to promote the establishment and development of day surgery LC in developing countries.

2. Methods

2.1. Literature Search. The search strategy and subsequent literature search were developed and performed with the assistance of an experienced medical reference librarian (W.M.B) following five "PICOS" components (supplementary S1). The search strategies were developed in Ovid Embase and translated to match the subject headings and keywords for Medline, Ovid, Cochrane Central, Web of Science, and Google Scholar, from inception through February 2019. The following items were used: day surgery, day-case surgery, day stay, hospitalization, outpatient surgery, ambulatory surgery, and laparoscopic cholecystectomy. The details of the search strategy are provided in Supplementary S2. Electronic searches were supplemented by manual searches for references to the included studies and review articles. All results were downloaded from a bibliographic database manager, EndNote 9.0 (Thomson ISI ResearchSoft, Philadelphia, Pennsylvania, USA).

2.2. Selection. A single reviewer (W.X) screened the titles and abstracts. Full articles were assessed by two pairs of independent reviewers (W.X and M.W), and discrepancies were resolved through adjudication.

Inclusion criteria were (1) studies compared day surgery LC with inpatient with randomization or not and case series about day surgery LC with more than 10 patients; (2) studies included patients who consented to participate day surgery LC before operation; (3) day surgery was defined as patients underwent operation and discharged within the same day, and overnight stay was defined as patients stayed more than one night after operation; (4) adult patients aged younger than 75 years and with BMI less than 35; (5) patients with no significant comorbidities before LC; and (6) patients did not have history of open abdominal surgeries.

Exclusion criteria were (1) studies that did not meet the inclusion criteria for day surgery or no definite criteria for day surgery, (2) patients that had previous abdominal surgery, (3) no definition or differentiation between inpatient and outpatient surgery, (4) with no relevant data or insufficient data, (5) sample size of fewer than 10 patients, (6) animal studies or non-English-language articles, (7) laparoscopic cholecystectomy for pregnant or diabetic patients, and (8) letters, comments, conference abstracts, and reviews.

2.3. Quality Assessment. This study was conducted following the preferred reporting items for systematic review and metaanalysis (PRISMA). The Cochrane Collaboration tool was used to assess the quality of the RCTs by two reviewers independently. All different opinions about quality assessment were discussed with a third reviewer (Q.Y) to reach an agreement on consensus.

2.4. Data Extraction. Study characteristics were extracted from two reviewers (M.W and W.X) with structured data extraction forms, including study design, country, year of publication, sample size, diseases at LC, patient demographics, American Society of Anesthesiologists (ASA) scores, trial duration, interview time, postoperative complications, postoperative nausea and vomiting (PONV), Visual Analogue Score (VAS), discharge time, time to normal activity, operation time, readmission, patients' satisfaction, and total cost. Outcome measures including percentages, mean, or median values with standard deviations or ranges were recorded.

Any disagreement between reviewers was to be discussed with a third reviewer (Q.Y) to reach an agreement. The corresponding author of the identified paper was contacted to request incomplete or unpublished data.

2.5. Statistical Analysis. Heterogeneity across the studies was assessed using the Q statistic test and I^2 statistic. The presence of heterogeneity was considered significant if the p value of the Q test was less than 0.01 or the I^2 value was more than 50%. If the interstudy heterogeneity was significant, a DerSimonian-Laird random-effects model was used, or a fixed-effects model was conducted. Pooled Risk Ratio (RR) or Odds Ratio (OR) with 95% confidence interval (CI) was

estimated for dichotomous data, and Mean Difference (MD) with 95% CI was estimated for continuous data. All statistical analyses were performed using RevMan software (version 5.3, Cochrane Collaboration). Statistical significance was assessed at the $\alpha = 0.05$ level.

3. Results

3.1. Search Results. In total, 1859 unique articles were included after the search of several databases. Eighty-eight articles were identified for full-text review after the title and abstract screening, and 64 of them were excluded with reasons. The remaining 24 articles included 8 RCTs for quantitative synthesis and the other 16 case series or controlled studies only for qualitative analysis (Figure 1).

3.2. Baseline Characteristics. The eligible 24 studies including 8 RCTs and 14 case series and 2 retrospective controlled studies were published from 1998 to 2018 [16–39]. These studies reported the day surgery LC performed on cholelithiasis or gallbladder polyps with the trial duration ranged from 6 months to 72 months. Only two studies [24, 25] reported more male patients underwent day surgery LC (90% and 52% males, respectively). The female patients accounted for 52% to 88.5% in the other 22 studies (Table 1).

There were 10 studies [32–39] that compared the LC in the day surgery unit versus inpatient unit, and 2 of them [18, 26] were retrospective controlled studies which were excluded from quantitative synthesis. Of the remaining 8 RCTs, there were 301 patients that underwent LC in day surgery units and 308 patients underwent LC in the inpatient units. All patients were given prophylactic analgesia, except that data was not available in the two studies. All the patients in the day surgery group were discharged 4-8 hours after surgery if they meet the discharge criteria, and the patients in the inpatient group were scheduled to discharge the following day after surgery (Table 2).

3.3. Outcomes

3.3.1. Postoperative Complications. Postoperative complications were reported in seven trials [32, 33, 35–39] with 287 patients in the day surgery group and 294 patients in the inpatient group. In total, 15 out of 287 (5.2%) participants had postoperative complications in the day surgery group compared with 21 out of 294 (7.1%) in the inpatient group. The pooled RR was 0.73 with 95% CI 0.4-1.34, and no significant difference was observed (p = 0.3) (Figure 2).

3.3.2. Postoperative Nausea and Vomiting (PONV) and Visual Analogue Score (VAS). There were three studies [37–39] that reported the PONV with 196 participants in total. One study reported a higher PONV rate in the inpatient group (18.2% vs. 12.5%) than that in the day surgery group. The other two studies reported higher PONV rates in the day surgery group (26.5% vs. 12.8%; 17.2% vs. 6.9%) than those in the inpatient group. The heterogeneity was not significant (p = 0.28; $I^2 = 21\%$), and the pooled RR was 1.49 with no significant difference between two groups (p = 0.24; 95% CI 0.77-2.86) (Figure 2).

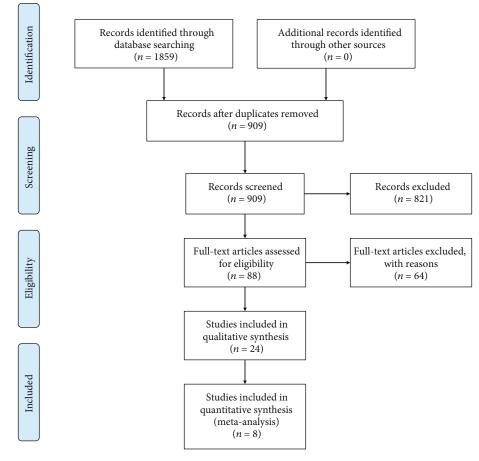


FIGURE 1: Preferred reporting items for systematic reviews and meta-analysis (PRISMA) flow chart for this study.

Five trials [32, 35, 37–39] assessed the VAS of patients after operation, including 175 patients in each group. The heterogeneity was significant (p < 0.001; $I^2 = 95\%$), but the exclusion of any one of the five studies did not change the results. So, the random model was used to estimate the pooled effect (MD = -0.39; 95% CI -0.64, 0.13), and the VAS in the day surgery group was significantly lower than that in the inpatient group (p = 0.003) (Figure 2).

3.3.3. Prolongation of Hospital Stay. The rate of successful discharge of patients after day surgery LC ranged from 82% to 100% in all the included studies (Table 1). Five RCTs [33–36, 39] including 397 patients reported the prolongation of hospital stay. Two of them reported nil prolongation in each group, and the other three studies had 5.4% to 18.3% of patients that prolonged the hospital stay. There was no heterogeneity (p = 0.35; $I^2 = 4\%$) between these five trials, and the pooled RR was 1.05 (95% CI 0.6-1.85) with no significant difference (p = 0.87) (Figure 3).

3.3.4. Return to Normal Activity. There were four studies reported that patients returned to normal activity or those returned to work after surgery. Two of them [32, 33] showed the time of patients return to normal activity after surgery, and the other two [38, 39] reported the number of patients who returned to normal activity less than one week. So, we

analyzed them separately and estimated the OR for dichotomous data and MD for continuous data. The two studies with patient number had significant heterogeneity (p = 0.001). The similar percentage of patients who returned to normal activity less than one week in the two groups (day surgery 75% versus overnight stay 75.8%) was reported in one study [38] while a much higher percentage of that in the day surgery group was observed in the other study (day surgery 100% versus inpatient 37.9%) [39]. The pooled OR (OR = 8.12; 95% CI 0.05-1213.9) was calculated from the randomized model, and the overall effect was not significant (p = 0.41) (Figure 4).

The other two studies [32, 33] showed that patients took a shorter time to return to normal activity for patients in the day surgery group than those in inpatient group (MD -1.2; 95% CI -1.82, -0.59; p = 0.0001), and there was no significant heterogeneity (p = 0.2; $I^2 = 39\%$) between these two studies (Figure 4).

3.3.5. Patients' Satisfaction. The patients' satisfaction of day surgery LC varied from 78% to 97% for all the included studies (Table 1). Five trials [32–35, 38, 39] compared the patients' satisfaction in the day surgery group with that in the inpatient group. One of them [35] showed satisfaction scores with mean 3.4 in the day surgery group and 3.1 in the inpatient group. The other four studies reported the

First author	Year	Study type	Country	Diseases	Duration (mo.)	DSLC no.	Age (year)	Female no. (%)	Operation time (min)	Discharge, no. (%)	Satisfaction (%)
Studies only for qualitative analysis	qualitatı	ive analysis									
Rabi [31]	2018	Case series	Pakistan	Cholelithiasis	12	113	37.9 ± 8.5	100, 88.5%	44.5 ± 12.8	99, 87.6%	NA
Tiryaki [30]	2016	Case series	Turkey	Symptomatic chronic cholelithiasis	48	60	40.6 ± 8.1	45, 75%	NA	55, 91.7%	89.6%
Al-Qahtani [29] 2015	2015	Case series	Saudi Arabia	Symptomatic cholelithiasis	48	487	41.9 ± 8	426, 87.5%	NA	465, 95.5%	96.90%
AI-Omani [28]	2015	Case series	Saudi Arabia	Symptomatic cholelithiasis	60	1140	34.2 ± 8	1004, 88%	40.6 ± 12	1094, 96%	NA
Gelmini [27]	2013	Case series	Italy	Gallstone	36	43	49 ± 11.7	28, 65	48.9 ± 14.9	37, 86%	95.30%
Sato [26]	2012	Controlled study	Japan	Symptomatic gallstone	21	50	53.6 ± 14.5	26, 52%	108.4 ± 41.7	41, 82%	NA
Zarour [25]	2009	Case series	Qatar	Symptomatic gallbladder diseases	24	56	NA	27, 48%	NA	48, 85.7%	78.60%
Ali [24]	2009	Case series	Pakistan	Symptomatic cholelithiasis	18	50	43 ± 13.3	5, 10%	NA	46, 92%	NA
Victorzon [23]	2007	Case series	Finland	Not mentioned	72	567	48 ± 9.5	419, 74%	56 ± 18	356, 62.8%	NA
Chauhan [22]	2006	Case series	India	Symptomatic gallstone	12	287	37 ± 7.7	NA	NA	270, 94.1%	NA
Bueno [21]	2006	Case series	Spain	Symptomatic cholelithiasis	62	448	53.1 ± 14.5	338, 75.4%	45 ± 22.4	397, 88.6%	NA
Chok [20]	2005	Case series	China	Symptomatic gallbladder diseases	28	135	47.5	97, 72%	¢69	125, 92.6%	NA
Barut [19]	2005	Case series	Turkey	Symptomatic cholelithiasis	60	70	37.8 ± 9.9	55, 78.6%	36.6 ± 6.3	70, 100%	NA
Sharma [18]	2004	Controlled study	UK	Cholelithiasis	9	42	47.8 ± 9.6	32, 76.2%	35 ± 12	41, 97.6%	88.10%
Fassiadis [17]	2004	Case series	UK	Symptomatic cholelithiasis	30	100	44 ± 10.2	91, 91%	38 ± 9.2	99, 99%	92.60%
Siu [16]	2001	Case series	China	Symptomatic gallbladder diseases	26	60	40.5 ± 10.5	39, 65%	45.8 ± 21.6	54,90%	78%
Studies for quantitative synthesis	titative :	synthesis									
Salleh [39]	2015	RCT	Malaysia	Symptomatic gallstones	12	29	49.8 ± 13	21, 67.7%	NA	29, 100%	96.6%
Kumar [38]	2015	RCT	India	Symptomatic gallstones	NA	32	35.9 ± 12.4	26, 81%	NA	31, 96.9%	84.40%
Barthelsson [37]	2008	RCT	Sweden	Cholelithiasis	40	34	44.2 ± 10.6	NA	NA	34, 100%	NA
Johansson [36]	2006	RCT	Sweden	Gallstone	12	52	NA	NA	NA	48, 92.3%	NA
Curet [35]	2002	RCT	USA	Symptomatic cholelithiasis	19	43	34.7 ± 11	33, 76.7%	65 ± 15	37, 86%	$NA^{@}$
Young [34]	2001	RCT	Australia	Not mentioned	10	14	38.3 ± 6.4	NA	NA	14, 100%	85.7%
Hollington [33]	1999	RCT	Australia	Not mentioned	20	09	49 ± 14.3	NA	NA	49, 81.7%	NA
Keulemans [32]	1998	RCT	Netherlands	Symptomatic cholelithiasis	22	37	39.4 ± 9.7	28, 70%	76 ± 5	34, 91.9%	92%

TABLE 1: Characteristics of the included studies.

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Study	Group	No. initially randomized	No. accomplished the trial	Age	Prolong stay	Prophylactic analgesia	Cholangiogram	Discharge
Salleh et al. [39]								
	DS OS	31 31	29 29	49.8 (21-75) 49.8 (21-75)	0% 0%	Yes	Selectively	After 6 hours of postsurgical observation The following day after
Kumar et al.[38]								surgery
	DS	32	32	35.94 ± 12.4	3.1%	X7	NTA	After 6-8 hours of postsurgical observation
	OS	33	33	42.72 ± 11.9	NA	Yes	NA	Stay more than one night
Barthelsson et al	. [37]							
	DS	50	34	44 (22-68)	0%	Yes	Routinely	After 5-6 hours of postsurgical observation
	OS	50	39	45 (22-68)	NA			The next morning
Johansson et al.	[36]							
	DS	54	52	(18-70)	7.7%	Yes	Routinely	After 4-8 hours of postsurgical observation
	OS	53	48	(18-70)	12.5%			The following day after surgery
Curet et al. [35]								
	DS	43	43	33 (18-68)*	14%	Yes	Selectively	After 4 hours of postsurgical observation
	OS	37	37	43 (19-66)*	5.4%		,	The following day after surgery
Young and O'Co	onnell [34	£]						Mithin 9 hours often
	DS	14	14	39 (26-48)	0%	NA	None	Within 8 hours after surgery
	OS	14	14	40 (21-50)	0%			23 h postsurgery
Hollington et al.	[33]							The evening of the
	DS	74	60	45 (17-83)	18.3%	NA	Routinely	operation day with at least 4 h of postsurgical observation
	OS	76	71	49 (17-83)	18.3%			The following day after surgery
Keulemans et al.	[32]							
	DS	40	37	39 (20-62)	8.1%	Yes	Selectively	Discharged before 7 PM within the operation day
	OS	40	37	48 (19-65)	NA			At least one-night stay after surgery

DS: day surgery; OS: overnight stay; [#]mean \pm standard deviation; NA: not available; ^{*}p < 0.05.

patients' number of satisfaction with surgery. These four trials had no significant heterogeneity (p = 0.48; $I^2 = 0\%$). The patients' satisfaction rate in the day surgery group was significantly higher than that in the inpatient group (RR = 2.24; 95% CI 1.03-4.9; p = 0.04) (Figure 5).

3.3.6. *Readmission and Cost.* All the included RCTs reported patients' readmission, and 4 of them [32, 34, 36, 38] reported 0% readmission in both groups. The other 4 trials [33, 35, 37,

39] reported 0% to 3.3% readmission rates in the day surgery group and 0% to 10.3% readmission rates in the inpatient group. There was no significant heterogeneity among these studies (p = 0.49; $I^2 = 0$ %). The pooled effect was not significantly different between the two groups (RR = 0.57; 95% CI 0.19, 1.72; p = 0.32) (Figure 6).

Three RCTs [32, 33, 36] reported the cost of LC as day surgery and overnight stay procedure. All the three trials reported less cost by day surgery LC than by inpatient LC,

Postoperative complications

Study or subgroup	Day sur	gery LC	Overnight	t stay LC	Weight	Risk ratio		Risk	ratio	
	Events	Total	Events	Total	weight	M-H, fixed, 95% CI	Year	M-H, fix	ed, 95% CI	
Keulemans 1998	3	37	1	37	4.5%	3.00 [0.33, 27.53]	1998			
Hollington 1999	2	60	3	71	12.2%	0.79 [0.14, 4.57]	1999		•	
Curet 2002	4	43	6	37	28.7%	0.57 [0.18, 1.88]	2002		<u> </u>	
Johansson 2006	2	52	0	48	2.3%	4.62 [0.23, 93.91]	2006		•	
Barthelsson 2008	0	34	2	39	10.4%	0.23 [0.01, 4.60]	2008			
Salleh 2015	0	29	2	29	11.1%	0.20 [0.01, 3.99]	2015			
Kumar 2015	4	32	7	33	30.7%	0.59 [0.19, 1.82]	2015			
Total (95% CI)		287		294	100.0%	0.73 [0.40, 1.34]				
Total events	15		21							
Heterogeneity: $chi^2 = 4$.60, df = 6 (j	p = 0.60);	$I^2 = 0\%$				0.001	0.1	1 10	1000
Test for overall effect: 2	Z = 1.02 (<i>p</i> =	= 0.31)						s day surgery LC	Favors inpatient	

Postoperative nausea and vomitting

Study or subgroup	Experi	mental	Con	itrol	Weight	Risk ratio	Risk ratio
	Events	Total	Events	Total	,, eight	M-H, fixed, 95% CI	M-H, fixed, 95% CI
Barthelsson 2008	9	34	5	39	37.1%	2.06 [0.77, 5.57]	+=-
Curet 2002	0	43	0	37		Not estimable	_
Kumar 2015	4	32	6	33	47.0%	0.69 [0.21, 2.21]	
Salleh 2015	5	29	2	29	15.9%	2.50 [0.53, 11.86]	
Total (95% CI)		95		101	100.0%	1.49 [0.77, 2.86]	•
Total events	18		13				
Heterogeneity: $chi^2 = 2$.	52, df = 2 (<i>p</i> =	0.28); I ² =	= 21%			Г	
Test for overall effect: Z	-1.18(p-0)	24)				0.00	01 0.1 1 10 1000
rest for overall effect. Z	– 1.10 (<i>p</i> – 0	-27)					Favors day surgery LC Favors inpatient unit LC

Postoperative visual	analogue pain score (VAS)
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Study or subgroup	Day sı	urgery	LC	Overni	ght sta	ıy LC	Weight	Mean difference			Me	an differenc	e	
	Mean	SD	Total	Mean	SD	Total	0	IV, random, 95% CI	Year		IV, 1	andom, 95%	6 CI	
Keulemans 1998	2.4	0.3	37	2.8	0.3	37	20.3%	-0.40 [-0.54, -0.26]	1998		-	-		
Curet 2002	4.2	0.4	43	4.3	0.3	37	20.0%	-0.10 [-0.25, 0.05]	2002					
Barthelsson 2008	3.85	0.2	34	4	0.2	39	21.0%	-0.15 [-0.24, -0.06]	2008			*		
Salleh 2015	2.9	0.2	29	3.6	0.2	29	20.8%	-0.70 [-0.80, -0.60]	2015					
Kumar 2015	2	0.4	32	2.6	0.6	33	17.9%	-0.60 [-0.85, -0.35]	2015			-		
Total (95% CI)			175			175	100.0%	-0.39 [-0.64, -0.13]						
Heterogeneity: $tau^2 = 0$	0.08; chi ² =	= 76.80), df = 4	(<i>p</i> < 0.00	0001);	$I^2 = 95$	%		_	-2	-1	0	1	2
Test for overall effect:	Z = 2.95 (j	p = 0.0	003)							-	s day surgery		s inpatient i	unit LC

FIGURE 2: Meta-analysis forest plot concerning postoperative complications. VAS: significant difference in favor of day surgery unit versus inpatient unit. There was no significant difference of postoperative complications and PONV between day surgery and inpatient groups.

and the pooled effect was significantly different (MD -250.8; 95% CI -396, -105.6; p = 0.0007). However, the heterogeneity among them was significant (p < 0.001) and one study [32] affected the stability of the overall effect obviously. So, the subgroup analysis without this study was performed, and the reestimated result showed that there was no significant difference between day surgery and inpatient LC (p = 0.07) (Figure 7).

3.4. Quality Assessment. The quality of the 8 RCTs was assessed with the Cochrane Collaboration tool, and the risk

of bias was shown as Figure S1 in the supplementary. Six of the 8 RCTs reported the randomization sequence, and 8 of them reported the allocation concealment. None of them reported blinding.

4. Discussion

This study was conducted to assess the safety and benefits of LC as a day surgery procedure compared to an inpatient procedure. Our results showed that LC can be performed safely and cost effectively in day surgery units for selective patients.

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Prolongation of hospital stay

C (Day sur	gery LC	Overnigh	it stay LC	147 1 1 4	Risk ratio		Ri	sk ratio		
Study or subgroup	Events	Total	Events	Total	Weight	M-H, fixed, 95% CI	Year	М-Н,	fixed, 95% CI		
Hollington 1999	11	60	13	71	58.7%	1.00 [0.48, 2.07]	1999	_	-		
Young 2001	0	14	0	14		Not estimable	2001				
Curet 2002	6	43	2	37	10.6%	2.58 [0.55, 12.03]	2002	-			
Johansson 2006	4	52	6	48	30.7%	0.62 [0.18, 2.05]	2006				
Salleh 2015	0	29	0	29		Not estimable	2015				
Total (95% CI)		198		199	100.0%	1.05 [0.60, 1.85]			•		
Total events	21		21								
Heterogeneity: $chi^2 = 2$.09, df = 2 (<i>f</i>	<i>v</i> = 0.35);	$I^2 = 4\%$				0.02	0.1	1	10	50
Test for overall effect: 2	Z = 0.17 (<i>p</i> =	0.87)						Favors day surgery LC	Favors inpa		

FIGURE 3: Meta-analysis forest plot concerning the prolongation of hospital stay. No significant difference was observed between two groups (day surgery group versus inpatient group).

o. 1 1	Exper	imental		Cont	rol	117 . 1		Odds ratio			0	dds ratio)		
Study or subgroup	Events	Tota	al Ev	vents	Total	Weigh	nt N	1-H, random, 95% CI	Year		M-H, r	andom,	95% CI		
Kumar 2015	24	32		25	33	53.5%	%	0.96 [0.31, 2.97]	2015		_	-	-		
Salleh 2015	29	29		11	29	46.5%	%	94.91 [5.27, 1708.60]	2015						
Total (95% CI)		61			62	100.0%	%	8.12 [0.05, 1213.79]							
Total events	53		3	36											
Heterogeneity: tau ² =	11.86; chi ² =	10.47, 0	df = 1 ((p = 0.00)	()); $I^2 =$	90%							1		
									0.001		0.1		10		1000
Test for overall effect:	Z = 0.82 (p	= 0.41)										-			
Test for overall effect:	Z = 0.82 (p	= 0.41)								Favors day sur		Fav	ors inpatie	nt unit LC	
Test for overall effect: Time to normal activit	ty			0				March			gery LC		ors inpatie	nt unit LC	
Time to normal activit	ty Day su	rgery LO		Overniş		W	Veight	Mean difference			gery LC Me:	an differ	ors inpatie	nt unit LC	
Time to normal activit	ty	rgery LO		Overnią Mean		LC V Fotal	Veight	Mean difference IV, fixed, 95% CI			gery LC Me:		ors inpatie	nt unit LC	
Time to normal activit	ty Day su	rgery LC SD T				V Total					gery LC Me:	an differ	ors inpatie	nt unit LC	
Time to normal activit Study or Subgroup	ty Day su Mean	rgery LC <u>SD T</u> 3	otal	Mean	SD 7	Total W 37 2	20.2%	IV, fixed, 95% CI	Year		gery LC Me:	an differ	ors inpatie	nt unit LC	
Time to normal activi Study or Subgroup Keulemans 1998 Hollington 1999	ty Day su <u>Mean</u> 14	rgery LC SD T 3 2	'otal 37	Mean 16	<u>SD</u> 7 3 2	Total W 37 2 71 7	20.2% 79.8%	IV, fixed, 95% CI -2.00 [-3.37, -0.63]	Year 1998		gery LC Me:	an differ	ors inpatie	nt unit LC	
Time to normal activi Study or Subgroup Keulemans 1998 Hollington 1999 Total (95% CI)	Day su Mean 14 12	rgery LC SD T 3 2	<u>otal</u> 37 60 9 7	Mean 16 13	<u>SD</u> 7 3 2	Total W 37 2 71 7	20.2% 79.8%	IV, fixed, 95% CI -2.00 [-3.37, -0.63] -1.00 [-1.69, -0.31]	Year 1998	Favors day sur	gery LC Me: IV,	an differ fixed, 99	ence 5% CI		
Time to normal activi Study or Subgroup Keulemans 1998	ty Day su <u>Mean</u> 14 12 1.64, df = 1 (rgery LC <u>SD T</u> 3 2 (p = 0.20)	$\frac{1}{37}$ 60 97 0); $I^2 =$	Mean 16 13	<u>SD</u> 7 3 2	Total W 37 2 71 7	20.2% 79.8%	IV, fixed, 95% CI -2.00 [-3.37, -0.63] -1.00 [-1.69, -0.31]	Year 1998		mery LC Meri IV,	an differ	ors inpatie	nt unit LC	

FIGURE 4: Meta-analysis forest plot concerning time to return to normal activity. Time to normal activity: significant difference in favor of day surgery versus inpatient unit.

Similar postoperative complications, PONV, and prolongation of hospital stay and readmission rates of patients after LC were observed in the day surgery group and the inpatient group. Significant smaller VAS and shorter time to return to normal activity were observed in the day surgery group than those in the inpatient group, which could increase the patients' satisfaction. Besides, the inclusion criteria for selective patients, easy reach to the hospital, and the schedule of operation which should be in the morning are also required for day surgery LC.

The LC can be performed safely in both inpatient units and day surgery units.

There were rare severe complications after LC in either day surgery units or inpatient units. The most common postoperative complications included fever, wound infection, diarrhea, PONV, and pain. The postoperative complication rates were similar in the day surgery group (5.2%) with that in the inpatient group (7.1%). PONV and postoperative pain are common in patients after LC and directly influence the hospital stay, readmission, and postoperative satisfaction. Six of the 8 RCTs [32, 35–39] performed prophylactic analgesia to relieve PONV and postoperative pain in this study, and 12.5%-26.5% of patients experienced PONV in the day surgery group compared to 6.9%-18.2% of patients in the inpatient group. But there was no significant difference between the two groups in PONV (RR = 1.49; p = 0.24; 95% CI 0.77-2.86), which was consistent with the previous study [40, 41]. The mean VAS after LC was lower in the day surgery group than that in the inpatient group. Five RCTs in this study reported VAS within 24h after LC, and the MD was

Patients' satisfaction

Study or subgroup	Day surg	gery LC	Overnight	stay LC	Weight	Odds ratio		Odds r	ratio	
	Events	Total	Events	Total	weight	M-H, fixed, 95% CI	Year	M-H, fixed	l, 95% CI	
Keulemans 1998	34	37	30	37	27.8%	2.64 [0.63, 11.15]	1998			
Young 2001	12	14	8	14	13.1%	4.50 [0.72, 28.15]	2001		•	
Salleh 2015	28	29	25	29	9.9%	4.48 [0.47, 42.79]	2015		•	
Kumar 2015	27	32	28	33	49.3%	0.96 [0.25, 3.71]	2015			
Total (95% CI)		112		113	100.0%	2.24 [1.03, 4.90]		-	•	
Total events	101		91							
Heterogeneity: $chi^2 = 2$	2.47, df = 3 (<i>p</i>	= 0.48); I	$^{2} = 0\%$				0.01	0.1 1	10	100
Test for overall effect: 2	Z = 2.02 (p = 0)	0.04)					0.01	Favors day surgery LC	Favors inpatient ur	

FIGURE 5: Meta-analysis forest plot concerning patients' satisfaction. Significant difference in favor of inpatient unit versus day surgery unit after LC.

Study on sub-succes	Day surg	gery LC	Overnigh	t stay LC	Mainhe	Risk ratio		Risk	ratio	
Study or subgroup	Events	Total	Events	Total	Weight	M-H, fixed, 95% CI	Year	M-H, fix	ed, 95% CI	
Keulemans 1998	0	37	0	37		Not estimable	1998			
Hollington 1999	2	60	3	71	33.0%	0.79 [0.14, 4.57]	1999			
Young 2001	0	14	0	14		Not estimable	2001			
Curet 2002	0	43	1	37	19.3%	0.29 [0.01, 6.86]	2002 -	•		
Johansson 2006	0	52	0	48		Not estimable	2006			
Barthelsson 2008	1	34	0	39	5.6%	3.43 [0.14, 81.49]	2008			_
Kumar 2015	0	32	0	33		Not estimable	2015			
Salleh 2015	0	29	3	29	42.0%	0.14 [0.01, 2.65]	2015			
Total (95% CI)		301		308	100.0%	0.57 [0.19, 1.72]				
Total events	3		7							
Heterogeneity: $chi^2 = 2$		= 0.49); I	$^{2} = 0\%$				0.002	0.1	1 10	500
Test for overall effect: 2	Z = 1.00 (<i>p</i> =	0.32)						s day surgery LC	Favors inpatient	

FIGURE 6: Meta-analysis forest plot concerning readmission. No significant difference between two groups.

estimated as -0.39 (95% CI -0.64, 0.13; p = 0.003). In other words, patients in the day surgery group had less postoperative pain than those in the inpatient group. The patients in the day surgery group might feel more comfortable at home the night after surgery so that they got lower VAS than those staying in the hospital in the inpatient group. Readmission rate is another critical factor to assess the safety of the surgical procedure. In this study, 8 RCTs [32–39] reported the readmission rate after discharging ranged from 0% to 10.3% in total. The main reasons for readmission are still PONV, fever, pain, and wound infection. Therefore, we revealed that patients that underwent LC in the day surgery units had lower VAS than those in the inpatient units.

The LC can be performed as a day surgery procedure effectively. In total, 82%-100% of the patients after LC discharged the same day successfully in the 24 studies included in this study. The main reasons for prolonging the hospital stay include postoperative pain, PONV, and conversion to open surgery [30, 31, 42]. In addition, some patients that lived far from the hospital would choose to prolong the hospital stay, and similar rates were observed in both day surgery

and inpatient groups. The rates of prolongation of hospital stay are both about 0% to 18% in the two groups, and there was no significant difference between them (RR = 1.05; 95%) CI 0.6-1.85; p = 0.87). Most patients can return to normal activities or work within one week either in the day surgery group or in the inpatient group. One study [38] reported that 75% of patients returned to work after LC in both groups. However, the other study [39] reported 100% of patients in the day surgery group versus 28% of patients in the inpatient group who returned to work less than one week. Another two studies [32, 33] reported the time to normal activity, and we estimated the pooled MD. The result revealed that patients after LC in the day surgery units took less time to normal activity than those in the inpatient units (p = 0.0001). Given the above, patients after LC in the day surgery units need less recovery time than those in the inpatient units; thus, it is effective to perform LC as a day surgery procedure.

Day surgery LC increased patients' satisfaction but did not reduce cost significantly compared to the overnight stay procedure. The satisfaction rate of patients after day surgery LC ranged from 78% to 97%, and it was not significantly

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Subgroup analysis

Cturder on such susses	Day s	urgery	LC	Overni	ight sta	iy LC	Weight	Mean difference				Mean di	fference		
Study or subgroup	Mean	SD	Total	Mean	SD	Total		IV, random, 95% CI	Year		Ι	V, rando	om, 95%	CI	
Keulemans 1998	188	14	37	488	76	37	33.7%	-300.00 [-324.90, -275.10]	1998		•				
Hollington 1999	2,732	76	60	2,835	110	71	33.5%	-103.00 [-135.01, -70.99]	1999			+			
Johansson 2006	3,513	120	52	3,864	120	48	32.8%	-351.00 [-398.08, -303.92]	2006						
Total (95% CI)			149			156	100.0%	-250.82 [-396.03, -105.61]							
Heterogeneity: tau ² =					(<i>p</i> < 0.	.00001)	; $I^2 = 98\%$			-500	-250	()	250	500
Test for overall effect:	Z = 3.39	(p=0)	.0007)							Favor	s day surg	ery LC	Favors	inpatien	t unit LC

Study or subgroup	Day surgery LC Ov				Overnight stay LC			Mean difference		Mean difference				
	Mean	SD	Total	Mean	SD	Total	Weight 1	IV, random, 95% CI	Year	IV, random, 95% CI				
Hollington 1999	2,732	76	60	2,835	110	71	50.3%	-103.00 [-135.01, -70.99]	1999		1	ŀ		
Johansson 2006	3,513	120	52	3,864	120	48	49.7%	-351.00 [-398.08, -303.92]	2006	-	-			
Total (95% CI)			112			119	100.0%	-226.37 [-469.41, 16.66]						
Heterogeneity: $tau^2 = 30330.19$; $chi^2 = 72.91$, $df = 1$ ($p < 0.00001$); $I^2 = 99\%$									-500	-250	0	250	500	
Test for overall effect: $Z = 1.83 (p = 0.07)$									Favors day surgery LC Favors inpatient unit LC					

FIGURE 7: Meta-analysis forest plot concerning cost. Significant difference in favor of day surgery versus inpatient unit.

different to those in the inpatient units, which was consistent with the previous study. There were 6 studies [23, 24, 27, 36, 38, 39] that reported less cost of LC in day surgery units than that in the inpatient units. However, we quantitatively analyzed the two RCTs and the results showed no significant difference between the two groups (p = 0.07). However, in our opinion, the day surgery saved the bed cost to reduce the total cost and more studies would be required to document this conclusion.

In conclusion, our results revealed that patients that underwent LC in the day surgery units had similar postoperative complications, readmission rates, and prolongation of hospital stay comparing with those in the inpatient units, and these results were consistent with previous studies [40, 42, 43]. Furthermore, our study firstly revealed that patients after LC had lower VAS in the day surgery group than that in the inpatient group. Furthermore, we firstly estimated the cost of these two procedures, and the result revealed less cost in day surgery units than that in the inpatients units with no significant difference. Although we only synthesized RCTs with no significantly different results, three other non-RCT studies [23, 24, 27] had reported less cost for day surgery LC. Thus, we believe that LC performed in day surgery units is cost effective than routine LC procedures.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Supplementary Materials

Supplementary Figure S1: risk of bias summary and risk of bias graph. Supplementary S2: search strategy for "The Safety of Laparoscopic Cholecystectomy in Day Surgery Unit Comparing with That in the Inpatient Unit: A Systematic Review and Meta-Analysis." (*Supplementary Materials*)

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