PRACE POGLĄDOWE

Readmission to hospital following laparoscopic cholecystectomy: a meta-analysis

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Abstract

Background: Laparoscopic cholecystectomy (LC) is one of the most commonly performed surgical procedures. Despite this, patterns of readmission following LC are not well defined. This meta-analysis aimed to determine rates and predictors of readmission.

Methods: An ethically approved International Prospective Register of Systematic Reviews (PROSPERO)-registered meta-analysis was undertaken searching PubMed, Scopus, Web of Science and Cochrane Library databases from January 2013–June 2018 adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Published literature potentially suitable for data analysis was graded using methodological index for non-randomised studies (MINORS) criteria; papers scoring ≥ 16/24 for comparative and ≥ 10/16 for non-comparative studies were included. A meta-analysis of potential risk factors was performed by computing the odds ratio using Mantel-Haenszel method and fixed-effects model with 95% confidence intervals.

Results: Three thousand and eight hundred thirty-two articles were reduced to 44 studies qualifying for a final analysis of 1,573,715 laparoscopic cholecystectomies from 25 countries. Overall readmission rate was 3.3% (range: 0.0–11.7%); 52,628 readmissions out of 1,573,715 LCs. Surgical complications accounted for 76% of reported reasons for readmission, predominantly bile duct complications (33%), wound infection (17%) and nausea and vomiting (9%). Pain (15%) and cardiorespiratory complications (8%) account for the remainder. Obesity, single port LC and day case LC were not associated with increased rates.

Conclusions: Pain, nausea and vomiting and surgical complications, particularly bile duct obstruction are the most common causes for readmission. Intra-operative cholangiography may reduce readmission rates. Causes for readmission were inconsistently reported throughout. The mean readmission rate of 3.3% may act as a quality benchmark for improving LC, and clearer reporting of reasons for readmission are required to advance care.

Key words: laparoscopic cholecystectomy, readmission, surgical outcomes, quality care.

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Biliary disease and cholecystitis remain one of the most significant surgical challenges. Over 1,000,000 cholecystectomies are performed in the US every year [1, 2], and over 50,000 in the UK [3]. While minimally invasive laparoscopic cholecystectomy (LC) has afforded great advantages over open cholecystectomy, reducing variability and improving outcomes remains a challenge [4, 5]. It is only recently that operative classifications and grading of cholecystitis have been published [6]. LC related peri-operative complications, while infrequent may result in potential readmission to hospital [7]. Understanding the process of readmission, its prevalence and potential associated factors would be important in improving the delivery of care for patients undergoing biliary surgery. A number of key publications on readmission following cholecystectomy have been reported but to date, to our best knowledge, no meta-analysis has been published [8–11]. The aim of this study was to evaluate the prevalence of readmission after LC and if possible, factors predisposing to it.

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METHODS

Search strategy and study eligibility

An ethically approved, PROSPERO registered meta-analysis of all published English articles pertaining to unplanned readmission following LC was undertaken at Letterkenny University Hospital searching PubMed, Scopus, Web of Science and Cochrane Library electronic databases over a 5-and-a-half-year period from January 2013 to June 2018. The search terms 'readmission', 'laparoscopic cholecystectomy', 'outcome', 'return', 'readmitted' 'rates', not 'open laparoscopic cholecystectomy' and not 'conversion to open' were used in combination with Boolean operators AND or OR. The primary outcome of interest was unplanned readmission of patients post index LC.

The method of analysis and inclusion criteria were specified in advance to avoid selection bias and documented in a protocol which was prospectively registered and published with the International Prospective Register of Systematic Reviews (PROSPERO) on 25/07/2018 (ID: CRD42018104960). This meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Studies were included in the systematic review if the following criteria were met; studies that involved LC which reported readmission rates post-laparoscopic cholecystectomy, and observational studies and randomized control trials whose full text articles were available in the English language.

Studies were not included if they were systematic reviews, meta-analyses, case reports, letters or protocols, studies that did not report key outcomes, related to interval laparoscopic cholecystectomies, obstetric and paediatric studies, and those which data was inadequate for interpretation via meta-analysis. Publications relating to open cholecystectomy were not included.

Definitions

Hospital readmission was defined as any unplanned readmission to hospital within 30 days of discharge following LC. When the timing of readmission was not defined in the study it was assumed to be within 30 days of discharge. Readmission rate was expressed as the number of readmissions as a percentage of the overall number of laparoscopic cholecystectomies performed. Where reported, causes of readmission and contributing factors were recorded.

Data extraction and quality assessment

The descriptive and quantitative data from the screened studies were extracted by the same reviewer and were entered into a computerized spreadsheet for analysis. Once the data extraction was completed a quality assessment tool was chosen to determine the studies with highly rated methodologies suitable for inclusion in the final analysis. The tool chosen for the quality assessment was the Methodological Index for Non-Randomised Studies (MINORS) criteria [12]. This tool is designed for the quality assessment of comparative and non-comparative surgical studies using a 3-point scale (0 – not reported, 1 – reported but inadequate, 2 – reported and adequate) on eight items for non-comparative studies and twelve items for comparative studies. The global ideal score being 16 for non-comparative studies and 24 for comparative studies.

Quality assessment was performed independently in a blinded standardised manner by two reviewers. Disagreements between reviewers were resolved by discussion between the two review authors (CM, DF). If no agreement could be reached, a third reviewer (JL) analysed the publication and decided on inclusion. Comparative studies with a MINORS score of > 15, and non-comparative studies with a MINORS score of > 10 were included in the final analysis.

Statistical analysis

The overall readmission rate was based on the cumulative rates of readmission in included studies. Risk factors and their potential relationship to readmission rates was analysed using odds ratio (OR) and 95% confidence intervals (CI) for each possible risk factor was calculated, along with the *P*-value with < 0.05 representing statistical significance. The Mantel-Haenszel method and fixed-effects models were used due to low heterogeneity. Heterogeneity was assessed using the I^2 statistic where a value greater than 75% was considered high and a less than 25% was considered low.

RESULTS

This meta-analysis reviewed 3832 articles, 67 meeting inclusion criteria, and 44 [8–10, 13–52] were finally enrolled after applying the MINORS score. Figure 1 shows the modified PRISMA flowchart for identification and inclusion of relevant papers. Twenty-three studies were excluded from the meta-analysis; 10 papers were deemed low quality [53–61] and 13 papers did not provide readmission rates specific to LC [62–74].

Readmission rate

A total of 1,573,715 LC were reported, with 52,628 readmissions within 30 days. The overall readmission rate was 3.3%, ranging from 0% to 11.7%. Reported readmission rates for all studies are shown in Figure 2.

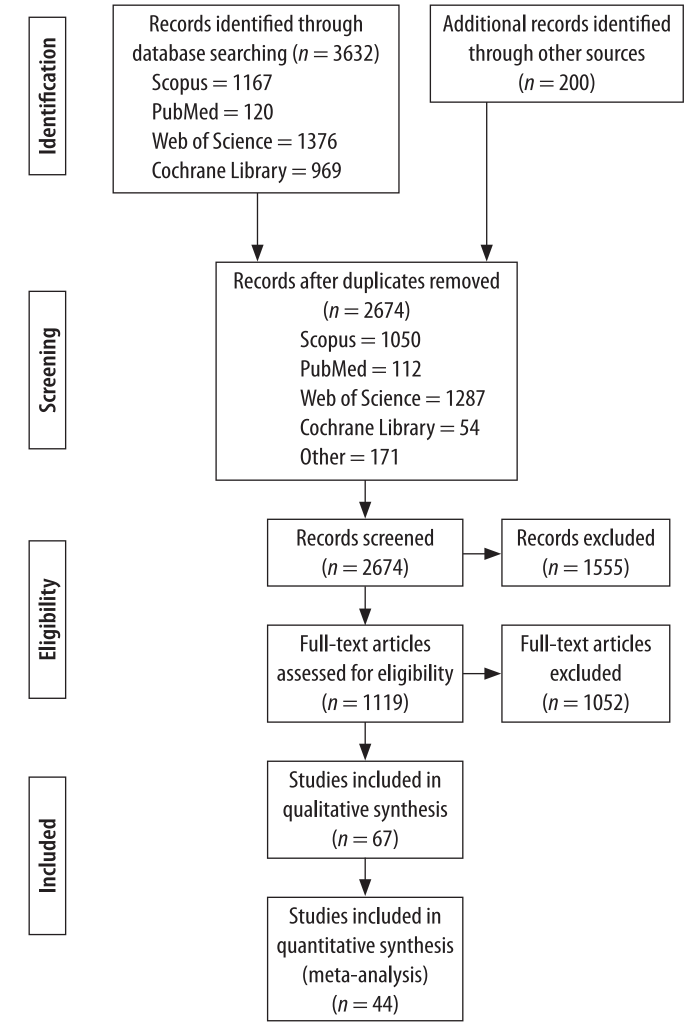

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FIGURE 1. Modified PRISMA 2009 flow diagram

The difference in readmission rate did not differ between large studies (sample size of > 1000 patients, see Table 1) and small studies (sample size of < 1000 patients, see Table 2), with an average of 3.3% in both groups.

Studies analysed were from 25 countries, with 20/44 carried out in Europe (total cohort 30,583) and 8/44 carried out in North America (total cohort 1,257,910) with readmission rates of 7.7% and 3.6% respectively.

Out of the 44 studies included, 12 reported a readmission rate of ≥ 5%, and 32 studies reported a readmission rate of < 5%. Studies reporting a readmission rate of ≥ 5% had an average cohort size of 15,000, whereas studies reporting a readmission rate of < 5% had an average cohort size of 44,000. There were three studies that reported a readmission rate > 7%; these include Vohra *et al*. [43] based in the UK and Ireland (7.1%), Fuks *et al*. [19] based in France (9.5%) and Nielsen *et al*. [31] based in Denmark (11.7%).

Causes of readmission

Of the 44 studies, 25 reported the reasons for patient readmission post-LC, accounting for only 4,002 out of 52,628 readmissions. Causes of all readmissions were reported in only 19 of these studies, with the remaining 6 studies partially reporting. Rosero *et al.* [8] provided 3,712 out of the 4,002 reasons for readmission, and reported on day case procedures in the USA. For this reason, Figure 3 shows reasons for readmission reported in Rosero *et al.* [8] and those reported in all other studies (which consisted of a mix of both day case and inpatient procedures) separately. Surgical complications accounted for 56% of reported reasons for readmission, predominantly bile duct complications (46%), other (16%), nausea and vomiting (11.8%) and bleeding (8%). Bile duct complications reported by Rosero *et al*. [8] included bile duct obstruction in 995 cases accounting for 21.3% of their readmission. Nine hundred and three of these cases were treated with endoscopic procedures. Bile duct injury accounted for 30 cases. Bile leak was not reported as a complication in Rosero *et al*. [8] However, it was reported in a number of other studies as a cause for readmission and accounted for 32 cases [9, 10, 20, 22, 34, 39, 41, 42, 50–52, 75]. Pain (16%), surgical site occurrence (14%) cardiorespiratory complications (9%), and unrelated medical (6%) account for the remainder.

Risk factors associated with increased readmission

None of the risk factors analysed for readmission post-LC were found to be significant. Obesity (BMI > 30) was the only pre-operative patient factor for readmission analysed and was not statistically significant [20, 50] (OR = 0.76, CI = 0.49–1.16, P = 0.20) (Figure 4).

Surgical factors analysed included single port LC vs. four port LC [13, 29, 42] (OR = 1.27, CI = 0.83–1.96, P = 0.27) (Figure 5), and day case LC vs. inpatient LC [17, 37] (OR = 0.50, CI = 0.16–1.53, P = 0.23) (Figure 6).

DISCUSSION

This meta-analysis reviewing 44 publications dealing with over 1.5 million patients undergoing LC identified that, on average one in thirty patients are readmitted within 30 days. This reflects the findings of Tang *et al*. [75], in their meta-analysis comparing day case and inpatient LC, which reported a mean post discharge readmission rate of 2.4%, and an in-patient admission rate of 13.1%. Readmission rates were not found to be statistically significantly different between large studies and small studies (Tables 1 and 2), nor whether the surgery was undertaken in Europe [31, 50] or North America [8, 33].

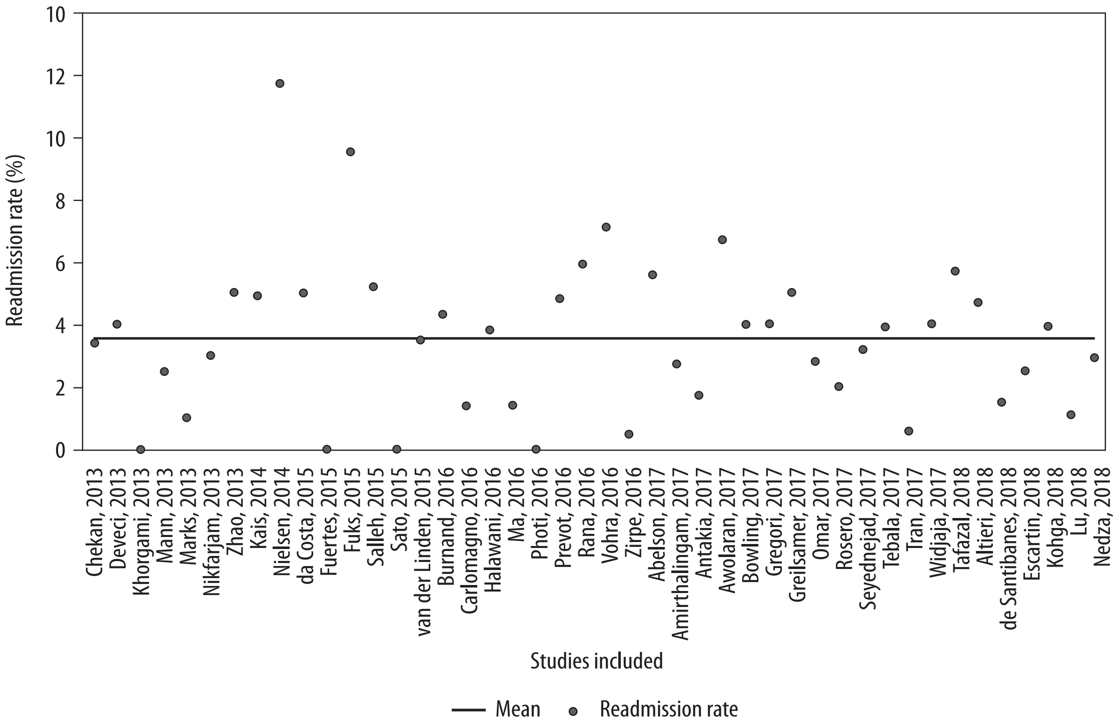

FIGURE 2. Readmission rates post-laparoscopic cholecystectomy

Readmission has become a quality indicator in the delivery of medical care [70, 75]. This relates to both the inconvenience to patients, the cost, resource utilisation and the associated morbidity and potential mortality. Cholecystectomy itself is one of the commonest procedures undertaken with over one million cholecystectomy's performed in the US annually [1, 2]. A readmission rate of 3% would have significant impact on utilization of resources, accounting for potentially 30,000 patients readmitted annually in the US alone, which equates to almost all index cholecystectomies performed in the UK. One of the challenges relating specifically to cholecystectomy is the variation that occurs both within patient cohorts and also the variation in actual operative findings.

Understandably, complex medical patients with increased co-morbidities are potentially more likely to have adverse outcomes and either prolonged hospitalization time or increased readmission rates. Attempts at defining operative grading have only recently been achieved. Sugrue *et al*. [6] in 2015 reported one of the first operative scoring systems in an attempt to define benchmarks for streamlining outcome analysis. Since then other scoring and grading systems have been reported including the AAST [76] and Cairns [77] scoring systems. This may aid in the comparison of patients' operative severity and grade.

Increasingly, health insurance companies will penalize hospitals where readmissions have occurred. It is therefore important to have common denominators in determining acceptable or anticipated outcomes versus excess variability that is no longer acceptable. Some of the studies in this group had high readmission rates approaching 12%. The Surgical Variance Report 2017 [78] by the Royal Australasian College of Surgeons, reported a readmission rate of 8% with marked variation.

Limitations of this meta-analysis include the exclusion of papers not providing adequate data, most

TABLE 1. Readmission rates of large studies with a cohort size greater than 1000 patients

Large study (> 1000 patients)	Cohort size, *N*	No. of readmissions	Readmission rate, %
Abelson, 2017	150,938	7918	5.2
Altieri, 2018	392,485	18,933	4.8
Bowling, 2017	1646	63	3.8
Chekan, 2013	116,823	3291	2.8
Halawani, 2016	52,825	2043	3.9
Kais, 2014	1658	80	4.8
Lu, 2018	225,558	2475	1.1
Ma, 2016	2031	29	1.4
Nedza, 2018	364,716	10,697	2.9
Nielsen, 2014	14,417	1463	10.1
Photi, 2016	1005	0	0.0
Rosero, 2017	230,745	4675	2.0
Seyednejad, 2017	1256	40	3.2
Vohra, 2015	8909	633	7.1
Total	1,565,012	52,340	3.3

TABLE 2. Readmission rates of small studies with a cohort size less than 1000 patients

Small study (< 1000 patients)	Cohort size, *N*	No. of readmissions	Readmission rate, %
Amirthalingam, 2017	149	4	2.7
Antakia, 2014	476	8	1.7
Awolaran, 2017	328	22	6.7
Burnand, 2016	46	2	4.3
Carlomagno, 2016	207	3	1.4
da Costa, 2015	264	8	3.0
de Santibanes, 2018	201	3	1.5
Deveci, 2013	86	4	4.7
Escartin, 2018	915	25	2.7
Fuertes, 2015	100	0	0.0
Fuks, 2015	414	25	6.0
Gregori ,2017	730	30	4.1
Greilsamer, 2017	80	4	5.0
Khorgami, 2013	90	0	0.0
Kohga, 2018	486	15	3.1
Mann, 2013	233	7	3.0
Marks, 2013	200	2	1.0
Nikfarjam, 2013	386	13	3.4
Omar, 2017	187	5	2.7
Prevot, 2016	414	20	4.8
Rana, 2016	747	44	5.9
Salleh, 2015	58	3	5.2
Sato, 2015	360	0	0.0
Tafazal, 2018	266	14	5.3
Tebala, 2017	223	9	4.0
Tran, 2017	486	3	0.6
van der Linden, 2015	200	7	3.5
Widjaja, 2017	100	4	4.0
Zhao, 2013	60	3	5.0
Zirpe, 2016	211	1	0.5
Total	8703	288	3.3

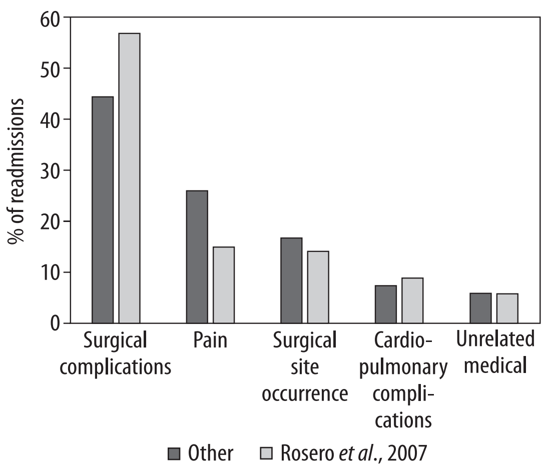

FIGURE 3. Causes for readmission, Rosero ($n = 3712$) compared to others ($n = 289$)

commonly due to failure to specify if readmission was following LC or open cholecystectomy. Authors of these studies were not contacted to obtain this data. A second limitation is, when not specified by studies, readmission was assumed to mean readmission to hospital within 30 days of discharge. The reasons for readmissions unfortunately, are not widely reported. This indicates the need to have a robust international data reporting system for biliary disease. These modules could be built into existing inpatient surgical registries or emergency surgery registries. Coccolini *et al.* [79] has proposed a mechanism whereby the World Society of Emergency Surgery (WSES) would develop a worldwide emergency general surgery formation and evaluation project. This will determine common benchmarks for training and education programmes worldwide in an effort to standardize management, improve outcomes and ultimately save lives. At one of the world's first emergency surgery performance improvement programs in emergency general surgery [80] key performance indicators for LC did not include readmission rate.

The causes for readmission identified in this meta-analysis predominately related to biliary complications. Nausea, vomiting and peri-operative pain were not infrequent followed by surgical site occurrence. Reported reasons for readmission come from day case procedure cohort studies [8]. In the Rosero *et al.* [8] series, many readmissions are a result of the underestimation of post-operative pain expected in this procedure in an outpatient setting [81]. An aggressive procedure-specific multimodal analgesia and concomitant antiemetic therapy regimen should be determined for use both immediately following surgery and following discharge home to address this potential cause for readmission [82]. Rosero *et al.* [8] discovered several risk factors for increased readmission using hierarchical mixed regression analyses. These included co-morbidities such as chronic renal failure, chronic pulmonary disease, liver disease and cancer, and patient demographics such as male sex, increasing age, non-Hispanic white race/ethnicity and non-private insurance type. They also identified surgical risk factors for readmission, which included the type of procedure and the indication for surgery. Patients presenting with acute cholecystitis had a 30% higher chance of being readmitted in comparison to those presenting with chronic cholecystitis. Similar findings are described by Giger *et al.* [83]. Also, patients undergoing surgery on a weekend were also associated with significantly increased readmission rates. Interestingly, the risk of readmission was reduced when intra-operative cholangiogram was implemented by about 15% which is supported by the findings of Halawani *et al.* [29] following analysis of

Study of subgroup	Obese Events	Obese Total	Non-obese Events	Non-obese Total	Body mass	Odds ratio M–H, Fixed, 95% CI
Bowling, 2017	25	727	40	900	68.9%	0.77 (0.46–1.27)
Gregori, 2017	10	294	20	436	31.1%	0.73 (0.34–1.59)
Total (95% CI)		**1021**		**1336**	**100.0%**	**0.76 (0.49–1.16)**
Total events	35		60			

Heterogeneity: $\chi^2 = 0.01$, df = 1 ($P = 0.93$); $I^2 = 0\%$

Test for overall effect: $Z = 1.29$ ($P = 0.20$)

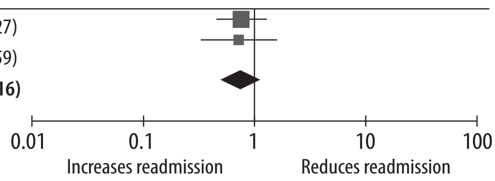

FIGURE 4. Effect of obesity on readmission

Study of subgroup	Single port LC Events	Single port LC Total	Four ports LC Events	Four ports LC Total	Body mass	Odds ratio M–H, Fixed, 95% CI
Chekan, 2013	20	527	3200	114,356	84.8%	1.37 (0.88–2.15)
Marks, 2013	1	119	1	81	3.5%	0.68 (0.04–11.00)
Van der Linden, 2015	3	100	4	100	11.7%	0.74 (0.16–3.41)
Total (95% CI)		**746**		**114,537**	**100.0%**	**1.27 (0.83–1.96)**
Total events	24		3205			

Heterogeneity: $\chi^2 = 0.78$, df = 2 ($P = 0.68$); $I^2 = 0\%$

Test for overall effect: $Z = 1.10$ ($P = 0.27$)

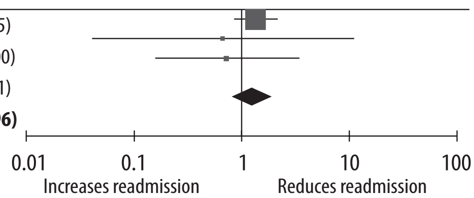

FIGURE 5. Effect of single port laparoscopic cholecystectomy on readmission

Study of subgroup	Day case LC Events	Day case LC Total	Inpatient LC Events	Inpatient LC Total	Body mass	Odds ratio M–H, Fixed, 95% CI
Escartin, 2018	3	147	22	768	65.3%	0.71 (0.21–2.39)
Salleh, 2015	0	31	3	27	34.7%	0.11 (0.01–2.25)
Total (95% CI)		**178**		**795**	**100.0%**	**0.50 (0.16–1.53)**
Total events	3		25			

Heterogeneity: $\chi^2 = 1.27$, df = 1 ($P = 0.26$); $I^2 = 21\%$

Test for overall effect: $Z = 1.21$ ($P = 0.23$)

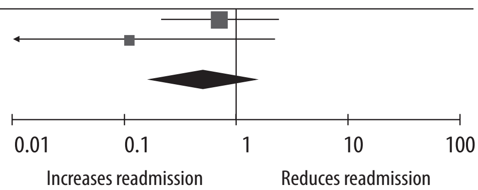

FIGURE 6. Effect of day case laparoscopic cholecystectomy on readmission

the National Surgical Quality Improvement Program database (NSQIP). Due to the potential seriousness of biliary complications, it begs the question of the current global approach to intra-operative cholangiography and single stage bile duct clearance. A recent meta-analysis by Pan *et al*. [84] found performance of intra-operative cholangiography to have superior outcomes in managing cholecysto-choledocholithiasis.

Attempts to improve safety and reduce biliary complications including identification of the critical view of safety, the use of Rouviere's sulcus as a landmark and the use of intra-operative cholangiography have not been uniformly adapted. They are prone to misinterpretation and false reporting. Obesity was not significantly associated with readmission in this meta-analysis, which may indicate the need to have more robust gradings for different BMI categories – a BMI > 30 does not fit all. This study cannot overcome the limitations of the original studies. Obesity is a continuous outcome; however it is reported as a dichotomous outcome in original studies. This "obesity paradox" is currently a widely discussed issue in surgical literature. While the categorisation of continuous variables simplifies outcomes for presentation of results, for example in tables, it is unnecessary for statistical analysis and reduces the power of the statistical analysis as a result [85, 86].

We identified a baseline rate for readmission with significant variation. This suggests that there is an onus on the surgical community to help standardize the metrics of cholecystectomy.

CONCLUSIONS

While overall readmission following LC is uncommon, there are opportunities to reduce this through attention to operative strategies including use of intra-operative cholangiography and attention to post-operative analgesia and reduction in nausea. Focusing on high risk groups, including acute cholecystitis patients and surgery performed at weekends could enhance outcomes. Some crucial data concerning perioperative course and outcomes in cholecystectomy should be implemented into large international registries in order to improve our understanding of potential risk factors for complications.

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