Gasless laparoscopy versus conventional laparoscopy and laparotomy. A systematic review on the safety and efficiency

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Research

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Abstract

Background Gasless laparoscopy emerged to overcome the clinical and financial challenges of pneumoperitoneum and is often seen as a viable option for use in resource-limited settings as a means of saving costs and resources. This study aims to systematically review the evidence available on the safety and efficiency of gasless laparoscopy compared to conventional laparoscopy and laparotomy.

Methods Following PRISMA guidelines, Medline, Embase, Web of Science and Cochrane were searched. Variables of interest were determined a priori and Covidence software was used to screen studies for inclusion without demographic preference. The quality of studies was assessed using the Cochrane Risk Assessment tool.

Results Of 1080 screened studies a total of 43 studies were included. Laparoscopic cholecystectomy was by far the most studied intervention in randomized studies. In these, the mean set-up time for gasless and conventional laparoscopy was 13.14 (95% CI: -0.16–26.44) and 12.8 (95% CI: -10.86–36.47) minutes respectively; The mean duration of surgery for gasless and conventional laparoscopy was 89.39 (95% CI: 77.44-101.34) and 72.59 (95% CI: 63.44–81.74) minutes respectively and the mean length of stay was 4.25 (95% CI: 2.02–6.48) and 4.04 (95% CI: 1.72–6.36) days respectively. Most reported complications were hemorrhage and infection with no assessable statistical difference.

Conclusions Although gasless laparoscopy seems to be a feasible approach for many general surgery interventions, the observed outcomes based on safety and efficiency don’t suffice to recommend gasless laparoscopy as an alternative to conventional laparoscopy or laparotomy. Larger randomized trials with a low risk of bias are warranted.

Introduction

Around five billion people worldwide lack access to safe, timely and affordable surgical, obstetrics and anesthesia care (1). Due to lack of data, it becomes difficult to estimate the burden of abdominal surgical conditions (2). It is worth noting that a Global Burden of Disease study estimates the global mortality rate due to appendicitis is 0.7, biliary and liver conditions is 1.6 and intestinal obstruction is 3.9 per 100,000 population (3). A study in India showed that 1.1% of deaths (0-69 years) are attributed to acute abdominal conditions (72,000 deaths in 2020) (4). In high income settings, these conditions are managed using diagnostic imaging or diagnostic laparoscopy. The increased utilization of laparoscopy over laparotomy stems from several benefits such as reducing pain, reducing wound infection, promoting faster post-operative recovery and return to quality of life (5-9). However, laparoscopic abdominal surgery is resource intensive, requiring expensive surgical equipment, extensive training, general anesthesia and a ventilator to safely manage the abdominal insufflation.

In lower income settings, conventional laparoscopy is often unaffordable due to expensive air-tight trocars, limited availability of carbon dioxide gas and lack of general anesthesiologists needed for patients undergoing pneumoperitoneum and ventilator support (10). Patients may instead undergo laparotomy or go without surgery. Hence, many conditions are untreated, or undiagnosed because of the lack of diagnostic equipment and procedures. This leads to increased morbidity and mortality that could have been avoided by prompt access to resources.

In the early 1990’s gasless laparoscopy was introduced in a small scale primarily in resource limited settings, as a means to avoid the financial and clinical challenges associated with pneumoperitoneum and general anesthesia (11). The pneumoperitoneum is avoided by mechanical elevation of the anterior abdominal wall using a planar lifting system, inflatable balloon or other means to allow an overview of the abdominal organs. Several procedures such as gynecological (12-14), upper or lower gastrointestinal (15-20) and exploratory diagnostic procedures (21) have been performed through single or multiple incisions using a gasless technique.

The technique has been described and evaluated in several small studies and safety outcomes such as peri-operative complication rates (22-24) and efficiency outcomes (19, 25) have been compared with conventional intervention methods.

Gasless laparoscopy has been proposed to have a variety of potential benefits. One key benefit is the lower cost compared to conventional laparoscopy due to less expensive equipment, maintenance and anesthesia needs (24-26) as it can be used under spinal or local anesthesia (17, 27, 28). It could thereby act as a diagnostic option in resource-limited settings. Some studies have reported gasless laparoscopy to be associated with shorter duration of hospital stay for inpatients (26, 29). Others suggest that gasless laparoscopy decreases the hemodynamic burden due to abdominal insufflation in patients with hemodynamic compromise (e.g., exploratory laparoscopy for abdominal trauma) (17, 27, 28). Other suggested benefits are improved safety outcomes in pregnancy, reduced post-site metastasis rates and reduced contamination in some procedures (30-32). On the other hand, some authors have reported that gasless laparoscopy may carry a risk of poor visualization during the surgery, but suggest that there is no clinical significant difference in comparison to conventional laparoscopy (18, 31).

Since gasless laparoscopy has been developed only in the last two decades, the extent of utilization in resource limited settings is still limited. In addition, there have been several gasless products designed and trialed but it’s not yet clear which technique or design is better and in which contexts (12, 17, 33, 34). Also, only a few trials have used strict criteria in patient’s eligibility for surgery and presence of comorbidities and randomization when evaluating the technique (15, 26, 35). Moreover, it is not clear how the introduction of the technique and training for surgeons have been managed before performing the trials to help ensure safety and efficiency of gasless laparoscopy which is crucial when a new technique is being introduced (10).

This systematic review aims to comprehensively examine the available literature on the safety and the efficiency of gasless laparoscopy versus other treatment modalities such as conventional laparoscopy or laparotomy for various procedures across different study designs.

Methods

Study design

This systematic review is designed following the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocol guidelines (PRISMA) statement guidelines (36). The study was registered in the International Prospective Register for Systematic Reviews and Meta-analysis (PROSPERO) with registration number CRD42017078338 and the protocol of the study has been published (10).

Search strategy

A search across MEDLINE, Embase, Web of Science and Cochrane Central, Global Index Medicus from the World Health Organization (WHO), and the National Institutes of Health clinical trials database using both automated and manual search was used to identify studies and records were combined using the Boolean terms AND/OR. Covidence software (Covidence.org - Melbourne, Australia) was used to pool and manage all studies found. All duplicates were identified by the software and controlled manually. The combination search terms used is shown in *table 1* from MEDLINE. Endnote X9 reference manager software was used for citation.

Study selection

The inclusion criteria for the included studies follows the population, interventions, comparator, outcomes (PICO) tool where the population of interest are adults of 18 years or more without any restriction to race, gender or geography (table 2). Studies included all procedures that were done in a hospital from 1990 and onwards published in English. All excluded studies were tracked to understand how many studies were excluded based on language (table 3). The intervention used in this study is gasless laparoscopy. Gasless procedures were limited to general surgical procedures or conditions, or any trial involving diagnostic laparoscopy performed for general surgical investigation. It includes any variation of gasless technology and device design, any variation of gasless technique and any variation of a gasless training program. The comparison groups were general surgery patients who had conventional laparoscopy, laparotomy or received no interventions. All study designs were included; such as case-control, cohort, and randomized controlled trials (RCTs). The main outcomes this study investigates are the safety and efficiency of gasless laparoscopy.

Data extraction and analysis

Eight reviewers participated in the overall review process, with two independent reviewers reviewing each article, and a third senior reviewer to discuss discrepancies. Studies were initially screened based on titles and abstracts followed by full-text screening against the inclusion criteria. Data was extracted into Microsoft Excel and specific variables were identified to for data analysis. The Cochrane risk of bias assessment tool was used to assess the risk of bias across studies. RoB II was used for randomized control trials (RCTs) (37) and the (ROBINS-I) tool was used for bias risk assessment in non-randomized studies (38). Necessary tables and figures were developed based on descriptive statistics using Microsoft Excel and STATA Statistical Software Package.

Data synthesis

A mixed quantitative and qualitative synthesis was provided based on the strength of evidence for the outcomes of interest with specific focus on the varieties of outcomes between both the control and intervention groups. The data synthesis will include the strengths and limitations of the included studies, heterogeneity of the studies, generalizability of the results to other populations and the variety of settings and different patient outcomes. Furthermore, any alternate explanations from current literature and potential future developments were investigated and discussed.

Results

The search yielded 1080 studies from all the database searches. As shown in *figure 1*, 43 studies were selected for full data extraction and analysis. The variation of studies by study design, intervention used and procedures were as follows: gasless laparoscopy (GL) was most extensively studied in patients undergoing cholecystectomies where there were 24 RCTs and 5 cohort studies. The comparator was conventional laparoscopy (CL) in 24 of the RCTs and 4 cohort studies while open laparotomy (OL) was the comparator in 2 cohort gastrectomy procedures as shown in figure 2. Cholecystectomy was the procedure that was mostly reported as an indication for either GL, CL or OL or both (CL, OL). Due to the heterogeneity of the data, a meta-analysis was deemed non-feasible in this systematic review, however descriptive statistics were used to pool data for cholecystectomies due to relative homogeneity. For all other procedures a qualitative analysis only was made. Extracted data from all 43 included articles are shown in *table 4* (15, 16, 19, 28, 29, 33, 39-74) .

The main outcomes of the study examined both the efficiency and safety of GL in comparison to other interventions. Efficiency is reported as the mean set-up time (minutes) of the patient for the operation, mean duration of operation (minutes) and the total length of stay in the hospital (days) for those undergoing cholecystectomies across the 24 RCTs.

Efficiency

In patients undergoing cholecystectomies, the mean set-up time was 13.14 minutes (95% CI: -0.16 – 26.44) for GL from RCT studies reporting a total of 123 patients and it was 12.8 minutes (95% CI: -10.86 – 36.47 minutes) for CL from RCT studies reporting a total of 125 patients. The mean duration of operation for GL was 89.39 minutes (95% CI: 77.44 – 101.34) from RCT studies reporting a total 614 patients while it was 72.59 minutes (95% CI: 63.44 – 81.74) for CL from RCT studies reporting a total of 633 patients (figure 3a).

In patients undergoing GL, the mean length of stay in hospitals was 4.25 days (95% CI: 2.02 – 6.48) from RCT studies reporting a total of 423 patients while it was 4.04 days (95% CI: 1.72 – 6.36) from RCT studies reporting a total of 440 patients (figure 3b).

From non-RCT studies such as case-controls and cohorts (10 studies), there were several non-cholecystectomies (e.g.: abdominal trauma, intestinal neoplasm – wedge resection, subtotal gastrectomy, GIST removal, upper GIT stromal cancer, liver cystectomy, gastrectomy, colorectal lesions removal, inguinal hernia herniorrhaphy) that had a variety of duration of operation time. For example, colorectal lesions had the highest duration of operation for studies reporting GL and both (CL and OL) 220 minutes and 256.9 minutes respectively. This was followed by gastrectomy where studies reported a duration of operation for GL and both (CL and OL) to be 220.6 minutes and 245.8 minutes respectively. In contrast, liver cystectomies had the lowest duration of operation for GL and studies reporting both (GL and OL) 50.49 minutes and 70.8 minutes respectively. The remaining procedures' duration of operation ranged between 90.8 minutes and 143.8 minutes. Overall, GL had less duration of operation compared to both (CL and OL) except in inguinal hernia herniorrhaphy and upper GIT stromal cancer removal. The overall mean duration of operation was 152.66 minutes (95%CI: 101.01 – 204.3) for non-RCT studies reporting a total of 217 patients undergoing both OL and CL techniques. While, for GL the mean duration of operation was 135.8 minutes (95% CI: 93.37 – 178.23) for non-RCT studies reporting a total of 235 patients (figure 4a).

From non-RCT studies such as case controls and cohorts (10 studies), there were several non-cholecystectomies (e.g.: abdominal trauma, intestinal neoplasm – wedge resection, GIST removal, upper GIT stromal removal, liver cystectomy, gastrectomy, colorectal lesions removal) that had a variety of length of stay in hospitals as inpatients. Those who had a gastrectomy had the overall highest length of hospital stay for those who underwent GL and both OL and CL at 18.7 and 20.9 days respectively. In contrast, those who were admitted for liver cystectomy undergoing GL and both (OL and/or CL) had the lowest length of hospital stay at 3 days for each technique. The rest of the range of lengths of hospital stay across all admissions for all techniques was between 4.5 and 10 days. GL consistently had lower length of hospital stays across all admissions. The overall mean length of hospital stay was 7.54 days (95% CI: 2.78 – 12.31) for those who had GL (across 167 patients from the non-RCT studies) and for those who had both (CL and/or OL) it was 9.01 days (95% CI: 3.72 – 14.31) (across 155 patients from non-RCT studies) (figure 4b).

Safety

The safety of the surgical techniques has been structured into three main categories: surgical complications, readmissions to hospitals and all-cause mortality. There were five main complications identified as resulting from undergoing gasless laparoscopy, conventional laparoscopy, laparotomy or both including: wound infection, deep tissue infection, hemorrhage, hemodynamic instability and visceral injury.

Hemorrhage was the mostly reported complication in eight studies for patients undergoing GL, eight studies for patients undergoing CL, one study in OL and one study in those who had both (CL and/or OL). This was followed by visceral injuries where GL contributed to visceral injury in seven studies, CL in six studies and both (CL and/or OL) in two studies. Next was hemodynamic instability reported in six GL studies, six CL studies, one study in OL and one study in both (CL and/or OL). Deep tissue infection was then reported in seven GL studies, four CL studies and one both (CL and/or OL) study. Finally, wound infection was reported in seven GL studies, three CL studies and two both (CL and/or OL) studies.

Readmissions was reported equally in five studies for those who underwent GL and five studies for those who underwent CL. Only one study reported all-cause mortality in GL (figure 5).

Risk of bias assessment

More than 50% of the randomized control trial studies reported low risk of bias as shown in *figure 6a*, except in allocation concealment showing around 35% of studies had a low risk of bias, and per study risk of bias analysis is shown in *figure 6b*. Around 75% of non-randomized studies had low risk of bias except around 35% of studies showed low risk of confounding and selection bias shown in *figure 7a,* and the per study risk of bias analysis is shown in *figure 7b*.

Discussion

This systematic review identified 43 studies that were eligible for inclusion to look at the safety and efficiency of gasless laparoscopy in comparison to conventional laparoscopy or laparotomy or both. There was a total of 25 RCTs and 17 non-RCT studies.

Safety was assessed based on post-operative complications, readmissions and all-cause mortality. Overall post-operative complications and readmissions were reported very similar for GL, CL and OL across all study designs and procedures. The complications found were wound and deep tissue infections, hemorrhage, hemodynamic instability and visceral injury. However, in GL, there were three additional studies that reported wound and deep tissue infections compared to other interventions. There might not be a significant difference to warrant a reason of why there are more infections post GL compared to CL or OL, however, there might be a slightly increased risk during the use of the retractor, Laparo-lift or the Laparo-tensor that is introduced through the abdominal wall during the abdominal wall lifting in GL (75). Gurusamy et al (75) looked at GL only in cholecystectomy in a review study until 2011 while our study includes a wider span of conditions and compares GL to CL and OL including studies published over the last decade, hence suggesting this increased risk. Efficiency was assessed based on the set-up time, duration of operation in minutes and length of hospital stay in days. In those undergoing cholecystectomies, the set-up time of operation for GL and CL were almost the same. This shows that there is no much difference in setting up the patient for the procedure regardless of the type of laparoscopy.

RCT studies showed that in cholecystectomies only, the average duration of operation for GL was 89 minutes compared to 73 minutes for CL. GL for cholecystectomies might have taken a longer duration of operation due to the low surgical site exposure available for surgeons to navigate the blades during the procedure as also reported in a study by Vezakis et al who showed that intra-operative cholangiography was more successful in CL compared to GL (76). The inadequate exposure could be explained by the flat-topped pyramid space limited to the specific abdominal quadrant, particularly in obese and muscular patients and those with adhesions (76).

In non-RCT studies, the duration of operation in minutes was higher for those undergoing CL or OL or both for all other diseases (such as abdominal trauma, gastrectomy, tumor removal, hernia and colorectal lesions). On average the mean length of hospital stay in days was higher for those undergoing CL or OL or both compared to GL across most of the diseases. This could be explained by some of the adverse effects of pneumoperitoneum used such as increased intraabdominal pressure and absorption of carbon dioxide from the peritoneal cavity or adverse effects of open surgery. Increased intra-abdominal pressure causes cardiopulmonary effects including a push of the diaphragm upwards and hence reducing the pulmonary function (77, 78). In addition, it reduces the venous return and stroke volume through splanchnic vasoconstriction, reduction in inferior vena cava, renal and portal venous flow (79, 80).

The analysis was done comprehensively using several authors and explored the safety and efficiency of GL, CL and OL which was not embarked on before. In addition, the quality of all papers was assessed for bias and based on our analysis, the overall quality of the included studies was good based on the risk of bias assessment. However, this study still posits some limitations. A meta-analysis was deemed inappropriate due to the lack of quantitative metrics and homogeneity of data. Safety of such interventions could also reflect on the quality of life of the patient which was not explored in any of the studies reflecting a weakness in the studies themselves that were included. Since the risk of bias was relatively high in most RCTs,

Conclusion

In conclusion, GL seems to be a promising alternative to CL or OL in a variety of procedures. However, the lack of homogeneity of data precludes a comprehensive meta-analysis. Hence, the observed outcomes based on safety and efficiency do not suffice to recommend GL as a better alternative to CL for the admitted conditions. Data for cholecystectomies does seem to show non-inferiority and as the cost of GL is considerably lower, this technology should be further investigated. Larger randomized studies in homogenous patient populations with uncomplicated abdominal conditions, where detailed perioperative follow up and data on quality of life and cost is collected, are needed to address this.

List Of Abbreviations

CL: Conventional Laparoscopy

GL: Gasless Laparoscopy

OL: Open Laparotomy

PICO: Population, Intervention, Comparator, Outcomes

PRISMA: Preferred Reporting Items of Systematic Reviews and Meta-analysis

PROSPERO: International Prospective Register of Systematic Reviews

RCT: Randomized Control Trials

RoB II: Risk of Bias

ROBINS-I: Risk of Bias in Non-randomized Studies

WHO: World Health Organization

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Tables

Table 1: MEDLINE search strategy

Search number	Search terms	Results
1	(laparolift or abdolift).ab,ti.	21
2	(gasless or non insufflative or noninsufflative or non pneumoperiton* or nonpneumoperiton*).ab,ti.	632
3	(abdom* adj3 lift*).ab,ti.	307
4	(abdominal wall adj3 (suspen* or elevat*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	77
5	(laparos* or laparot* or peritoneoscop* or minimally invasive).ab,ti.	209927
6	1 or 2 or 3 or 4	925
7	5 and 6	572

Table 2: PICO Tool

Population	All races with no geographical restrictions. Human adults of at least 18 years old will be included from both genders.
Intervention	Gasless laparoscopy
Comparators	Conventional laparoscopy or open laparotomy
Outcomes	Safety and efficiency of gasless laparoscopy

Table 3: Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
● Articles published in English and Swedish ● Articles published on or after 1992 ● Adult humans of at least 18 years old of age from both genders with no restrictions to race or geographic distribution ● Any trial involving gasless laparoscopy ● Studies looking at the safety and efficiency of gasless laparoscopy	● Non-English and non-Swedish published articles ● Studies published before 1992 ● Patients less than 18 years of age ● Non-gasless laparoscopy procedure ● Gasless laparoscopy used for gynaecological surgery ● N<10 in any arm

Table 4: Data extraction of the outcomes of safety and efficiency of gasless versus conventional laparoscopy from all studies

Study	SAFETY						EFFICIENCY				
	Complication		Readmission		All-cause mortality		Length of stay		Set up time		Durat
	Gasless	Con.	Gasless	Con.	Gasless	Con.	Gasless	Con.	Gasless	Con.	Gasless
1. Koivusalo 1998		- Physio (increase in MAP, CVP, SPO_2, PO_2, Core temp, pulmonary dynamic compliance, minute volume, urine output									108 +/ 28 min
2. Koivusalo 1997	- *Metabolic* urine NAG lower - Tidal volume needed to be increased	urine NAG higher ($p<0.01$) 76 ± 29 minutes									76 ± 29 minutes
3. Koivusalo 1996	- *Metabolic:* $ETCO_2$ lower	-									108 +/- 28 min
4. Uen 2002	- Wound infection (1/48 patients)	here was a significant and sustained increase in both levels and a decrease in pH after CO_2insufflation until desufflation. higher $EtCO_2$, $PaCO_2$, and lower pH and compliance - Hemorrhage (2/47 patients)					89.66 +_ 26.2 (0.072)	74.86 +_ 27.5 (0.072)	11.56 +_ 3.8 (<0.001)	4.16 +_ 1.4 (<0.001)	95.96 +_ 24.1 (<0.012)
5. Chang 2011											
6. Vazquez-Rosales 2010							24 hrs	26 hrs			111.44 minutes
7. Wu 2010	Hemorrhage: 35.5+_11.7mL Average blood loss (0.099)	Hemorrhage: 40.3+_12.1 average blood loss (0.099)					5.8 +_ 1.2 (0.005)	7.2 +_ 1.2 (0.005)			129.6+_36 (p=0.532)
8. Uen 2007	Hemodynamic instability: the mean minute volume revealed a significant decrease in value during surgery for members of the GLC group($p<0.05$)	Hemodynamic instability: Pet CO_2, $PaCO_2$, Peak airway pressure: increase PH: decrease					3.3+_1.3 (0.512)	3.1±1.4 (0.512)	10.6±3.5 (0.008)	7.5±5.0 (0.008)	98.3±27.2 (0.008)
9. Ohta 1997	Subcutaneous emphysema Inguinal pain Inguinal seroma Subcutaneous bleeding Small bowel obstruction Paralytic ileus Testis swelling	Hemorrhage + Subcutaneous emphysema Inguinal pain Inguinal seroma Subcutaneous bleeding Small bowel obstruction Paralytic ileus Testis swelling		yes							94.7±23,4
10. Nanashima 1998							6.7 ± 2.1	6.1±1.5			141 ±31.5
11. Ortiz-Oshiro 2001			42 patients	42 patients							
12. Vezakis 1999		1 patient had wound	18 patients	18 patients			8 days	5 days			95 min

		infection									
13. Ninomiya 1998		Cardiac: CO, SV, %EF (decreased) HR increased									85.0 ± 11. (P>0.05)
14. Luo 2009	Hemorrhage: 64.13 +_ 163.66 (p=0.63)	Hemorrhage: 62.8 +_ 113.5 (p=0.63)					7.57 +_ 1.9 (6-15) p=0.63	8.3 +_ 1.9 (5-13) p=0.63			141.83 +_ 32.72 (106 200) p=0.4
15. Kitano 1993		Visceral perforation: CBD injury									52.9 min
16. Korkmaz 2002	1/20 intra-abdominal abscess, drained through laparotomy		1/20 intra-abdominal abscess, drained through laparotomy		1 death from intra-abdominal hemorrhage from gallbladder bed in a cirrhotic		3.7 days	1.7 days			
17. Cavina 1998			10 patients	20 patients							
18. Wu 2013	Hemorrhage: 139.1 (24.7) ml Deep tissue infection (1/23) 1 pneumonia, 2 fever, 1 lung atelectasis, 1 minor anastomotic leak	Hemorrhage: 185.8 (43.0) ml Deep tissue infection (1/12) 1 fever 1 lung atelectasis 1 minor anastomotic leak					18.7 ±1.4	20.9 ±1.7			220.6 ±13.
19. Larsen 2001		Hemodynamic instability: High (Systolic diameter, Diastolic diameter, HR) Lower (Fractional shortening)									102 (40-21 median (range)
20. Japanese Association of Abdominal Wall Lifting for Laparoscopic Surgery (JAAWLLS) Anonymous 1999	- minor: 3 patients with abnormal LFT, 1 mild bile leak, wound infection, asthma attack, wound dehiscence.		- 1 patient converted from peritoneal lift to open laparotomy due to bleeding (no further details provided)				8.6 +/- 4.6	8.3 +/- 3.9	13.7 ± 5.0	13.2 ± 5.3	100.0+/-46 mins
21. Jiang 2010	Hemorrhage: 97.1 ± 64.8ml	Hemorrhage: 105.0±95.3 - Delayed passing of flatus - Visceral perforation					6.3 ± 2.0 days	6.6 ± 2.5			220.0 ± 55 mins
22. Kim 2002											61 min +/- 11
23. Koivusalo 2008	Pneumonia		1 re-laparoscopy for internal bleeding from umbilical port site, 1 endoscopic retrograde cholangiopancreatography on postoperative day 12 due to bile duct stones				6.0 ± 2.1 (mean)	4.7 ± 1.0 (mean)			50.6 ± 17. min (mean)
24. Lee 2013							7.1	10.7			116.6
25. Chen 2012	Hemorrhage: 43.3mL +_ 59.4mL (p<0.05) (mean + SD)	Hemorrhage: 250.0 mL+_ 347.9mL (mean + SD)									141.1min + 52.6 (p<0.05) (mean +_ s
26. Ortiz-Oshiro 2001									25 mins (median)	35 mins (median)	60 mins (median)

27. Larsen 2002		1/26 bile leakage 1/26 intra-abdominal abscess formation		1 (endoscopic stenting)			1 (range 1–31) median	1 (range 1–31) median			102 mins
28. Larsen 2001		2 post-op fever (d/c after 1 and 3 days), 1 with aberrant duct - stented		1			5 days	8 days			102 mins
29. Ishikawa 2006	3/207 Bile duct injury, 0/224 bile duct leakage (no significant differences) - 2/207 wound infection - 1/207 abdominal abscess	2/224 abdominal bleeding, 23mL +_ 51 - 2/224 bile duct injury, 3/224 bile leakage (no significant difference) - 2/224 wound infection					10.4 +_8.8 days	10.9+_7.0 days			105 +_ 53 mins
30. Chou 2008	Hemorrhage: 95.63 ± 31.33 mL - Wound infection: 2 patients	Hemorrhage: 207.22 ± 73.31 mL - Wound infection: 1 patient					11.3 +/- 1.36 days	14.39 +/- 2.93 days			208.38 +/- 23.21 mins
31. Huang 2010							7.4	8.3			139.4 +- 76.2 (p=0.879)
32. Uemura 2002	Supraventricular or ventricular arrhythmia during procedure										85.0 (+_ 29.3)
33. Berberoglu 1999	Wound infection	Wound infection					3 days	3 days			50.49 +/- 10.9 (ranges, 30 75 min)
34. Talwar 2006	2 wound infections. Hemorrhage: 3 patients	Increase in MAP, PAP, Minute ventilation. Hemorrhage: 2 patients					48.9 hours	47.4 hours	5.4 ± 0.68 mins. p= <0.05	4.55 ± 0.51 mins p= <0.05	41.8 ± 7.89 mins p= <0.05
35. Andersson 2003	---	---	---	---	---	---	---	---	---	---	---
36. Egawa 2006	---	---	---	---	---	---	---	---	---	---	---
37. Giraudo 2001	1 omental injury (Visceral perforation)										
38. Hyodo 2012	Hemorrhage: 1 required Blood transfusion	Hemorrhage: 1 required Blood transfusion					6.9 +/- 2.5 days	6.3 +/- 2.0 days			182.1 +_ 9.21 (p < 0.05)
39. Ge 2014	Wound infection (1/50) Intrabdominal abscess 1/50	Wound infection (2/50) Intrabdominal abscess 1/50					4.36 +/- 1.74 (days)	5.68 +/- 4.43 days			70.6 +/- 30 (p=0.138) (minutes)
40. Lindgren 1997											102 min
41. Liao 2014	Visceral perforation: 2 Wound infection: 1 Deep tissue infection: 1	Visceral perforation: 3 Wound infection: 3 Deep tissue infection: 2 Pneumonia: 2					9.1 (4.5) days	16.3 (6.4) days			109.7 (33.5 min
42. Larsen	Visceral	Visceral									

2004	perforation (7/22)	perforation (10/28)									
43. Alijani 2004	Visceral perforation: bile leaks (2/20) 1/20 AMI Bradycardia (1/20)	1/20 Mild pancreatitis, 1/20 cholangitis. Decreased (COP, SV) Increase (PAP)					Median 2 days, IQR 1 day (p=0.71)	Median 1.5 days, IQR 1 day (p=0.71)			145.8+_11 (p = 0.22)

Figures

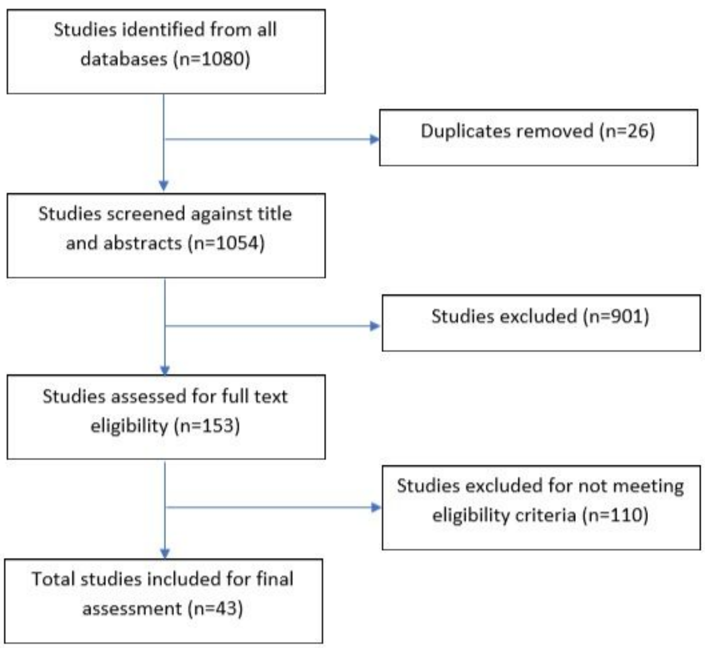
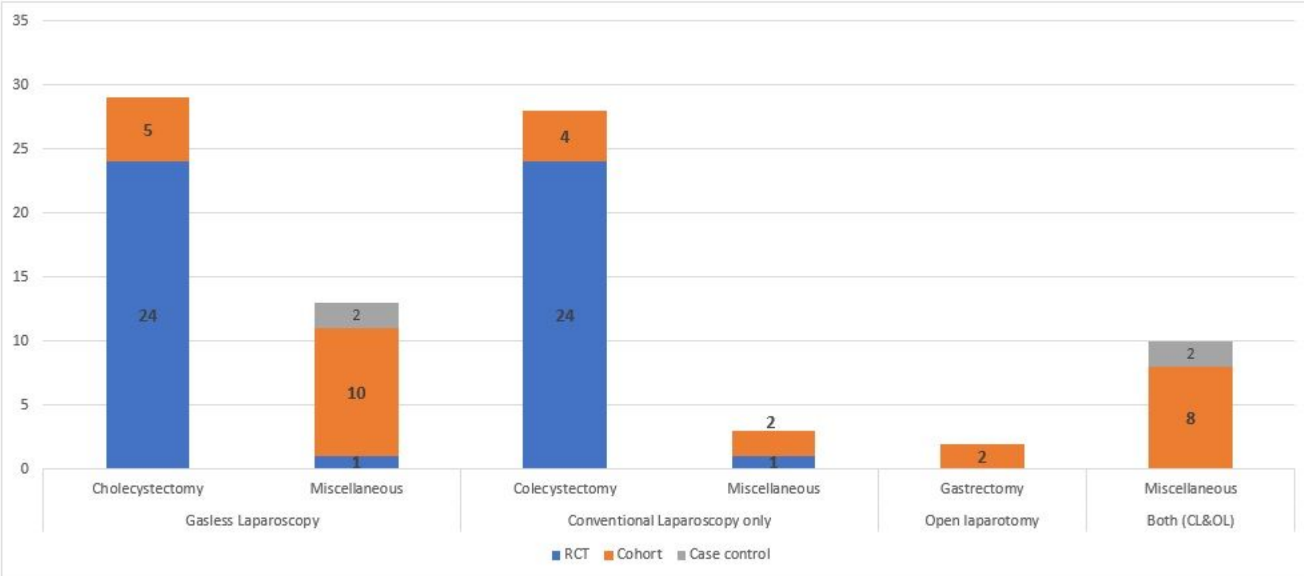


Figure 1

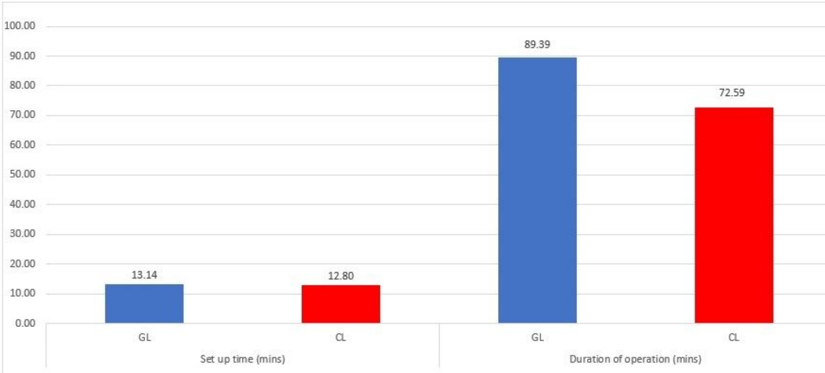
PRISMA Flowchart



Total number of patients across all studies reporting the following procedures					
Gasless laparoscopy		**Conventional laparoscopy**		**Open laparotomy**	**Both Open and Conventional**
Cholecystectomy	*Others*	*Cholecystectomy*	*Others*	*Gastrectomy*	*Others*
793 Cohort: 118 RCT: 675	366 Cohort: 281 RCT: 50 Case control: 35	864 Cohort: 159 RCT: 705	103 Cohort: 53 RCT: 50	56 Cohort: 56	269 Case control: 204 Cohort: 65

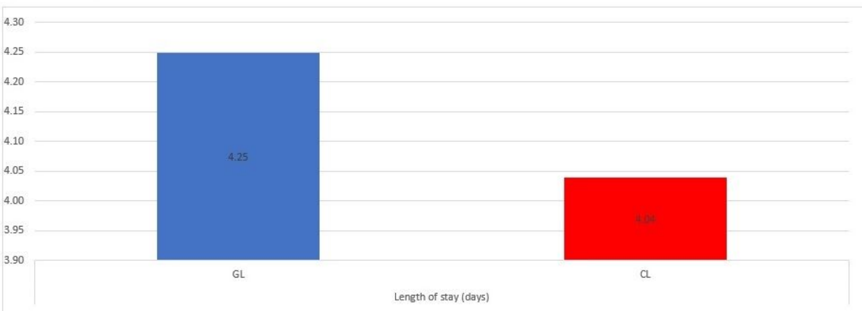
Figure 2

Distribution of the total number of studies across the main interventions in comparing gasless laparoscopy with either conventional laparoscopy or open laparotomy or both



	Set up time (mins)		Duration of operation (mins)	
Laparoscopy	Gasless	Conventional	Gasless	Conventional
Mean (95% CI)	13.14 (-0.16 - 26.44)	12.80 (-10.86 - 36.47)	89.39 (77.44 - 101.34)	72.59 (63.44 - 81.74)
Number of patients*	123	125	614	633

** The number of patients reported reflects the total number of patients across the studies presented in this graph*

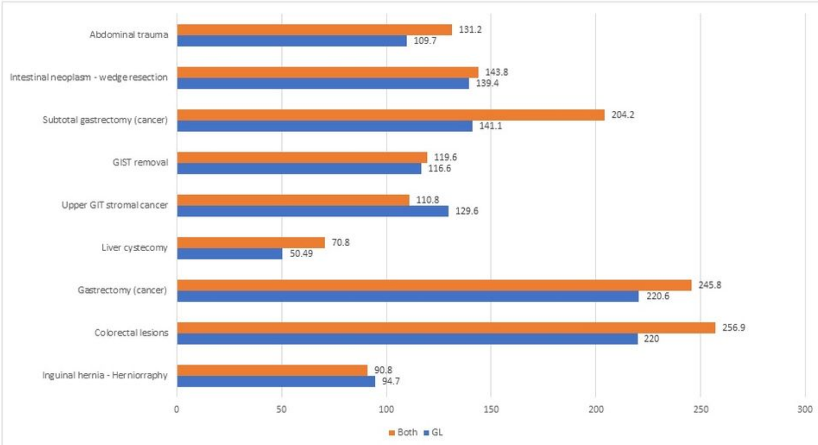


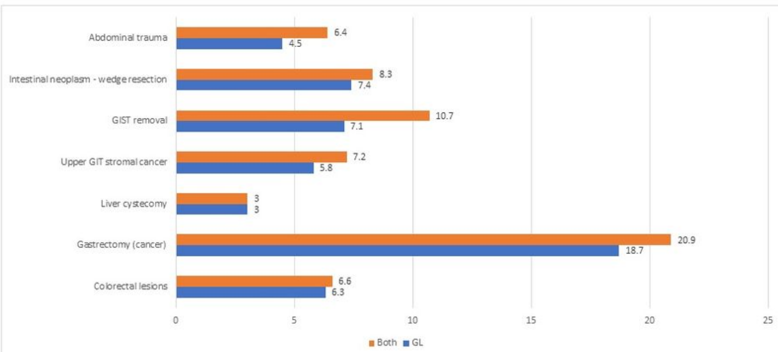
	Length of stay (days)	
Laparoscopy	Gasless	Conventional
Mean (95% CI)	4.25 (2.02 - 6.48)	4.04 (1.72 - 6.36)
Number of patients*	423	440

** The number of patients reported reflects the total number of patients across the studies presented in this graph*

Figure 3

a: Efficiency of Gasless Laparoscopy (GL) versus Conventional Laparoscopy (CL) presented as: mean set up time (mins), mean duration of operation (mins) – From 24 RCT studies that reported Cholecystectomies b: Efficiency of gasless laparoscopy (GL) versus conventional laparoscopy (CL) presented as: mean length of stay (days) – From 24 RCT studies that reported Cholecystectomies





	Length of stay (days)		Duration of operation (mins)	
Laparoscopy	Gasless	Both (OL, CL)	Gasless	Both (OL, CL)
Mean (95% CI)	7.54 (2.78 – 12.31)	9.01 (3.72 – 14.31)	135.8 (93.37 – 178.23)	152.66 (101.01 – 204.3)
Number of patients*	167	155	235	217

** The number of patients reported reflects the total number of patients across the studies presented in this graph*

Figure 4

a: Efficiency of gasless laparoscopy (GL) versus both conventional laparoscopy and open laparotomy from non-RCT studies (10 studies) presenting the duration of operation in minutes b: Efficiency of GL versus both CL and OL from non-RCT studies (10 studies) presenting the length of stay in days

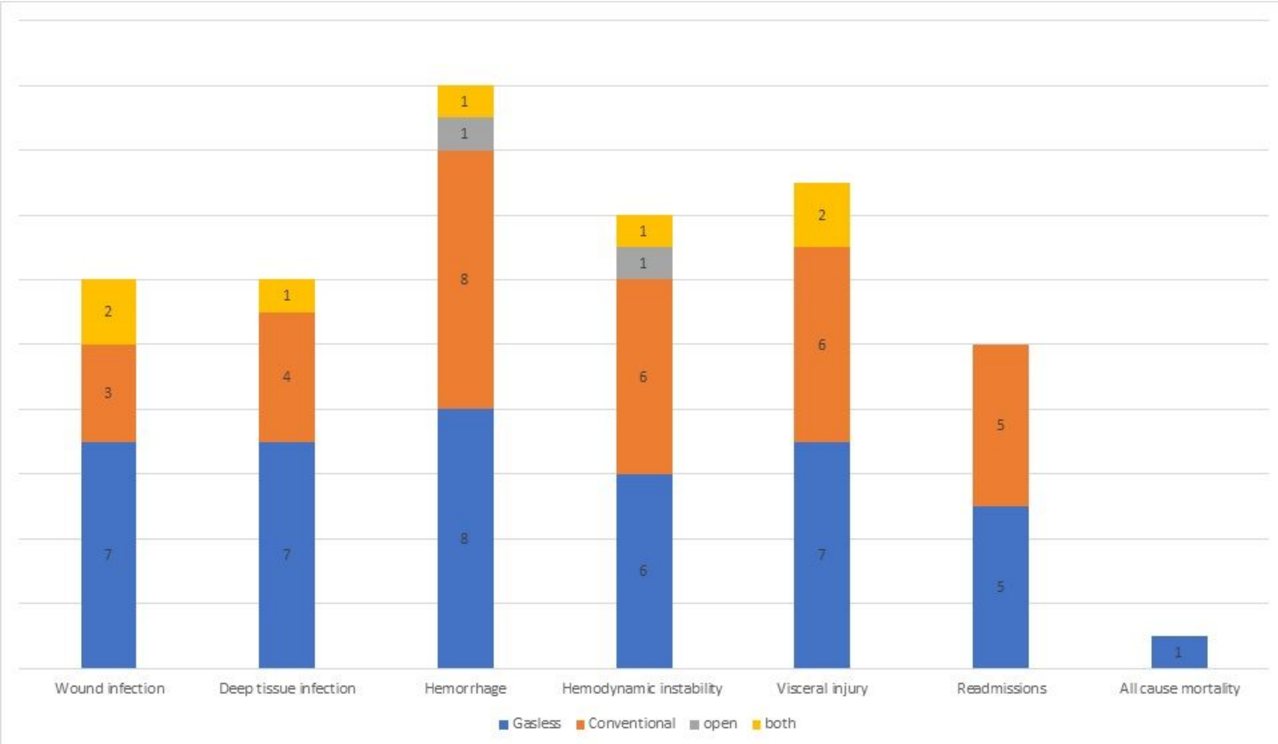


Figure 5

Bar graph showing the number of reported studies on the safety for gasless versus conventional laparoscopy, open laparotomy or studies reporting both; includes the 1) complications (wound infection, deep tissue infection, haemorrhage. Hemodynamic instability, visceral injury), 2) readmissions, and 3) all-cause mortality

Figure 6

a: Cochrane risk of bias graph - assessment of randomized studies b: Cochrane risk of bias summary of all randomized studies

Figure 7

a: Cochrane risk of bias graph - assessment of non-randomized studies b: Cochrane risk of bias summary of all non-randomized studies