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Robot assistant versus human or another robot assistant in patients undergoing laparoscopic cholecystectomy

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Abstract

Background—The role of a robotic assistant in laparoscopic cholecystectomy is controversial. While some trials have shown distinct advantages of a robotic assistant over a human assistant others have not, and it is unclear which robotic assistant is best.

Objectives—The aims of this review are to assess the benefits and harms of a robot assistant versus human assistant or versus another robot assistant in laparoscopic cholecystectomy, and to assess whether the robot can substitute the human assistant.

Search methods—We searched the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library*, MEDLINE, EMBASE, and Science Citation Index Expanded (until February 2012) for identifying the randomised clinical trials.

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CONTRIBUTIONS OF AUTHORS: K Gurusamy is the lead author and identified the trials for inclusion; extracted the data; and wrote the review. K Samraj independently identified trials for inclusion; and extracted the data for all the trials. G Fusai and BR Davidson critically commented on the review and suggested improvements.

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DECLARATIONS OF INTEREST

None known

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The aims have been revised to provide a more focused question. The outcomes have been ordered by clinical importance. Conversion to open cholecystectomy has been added as a new outcome.

Differences between previous version and current version

The risk of bias and the outcomes have been modified according to the recommendations of version 5.1 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). A summary of findings table has been provided.

Selection criteria—Only randomised clinical trials (irrespective of language, blinding, or publication status) comparing robot assistants versus human assistants in laparoscopic cholecystectomy were considered for the review. Randomised clinical trials comparing different types of robot assistants were also considered for the review.

Data collection and analysis—Two authors independently identified the trials for inclusion and independently extracted the data. We calculated the risk ratio (RR) or mean difference (MD) with 95% confidence interval (CI) using the fixed-effect and the random-effects models based on intention- to-treat analysis, when possible, using Review Manager 5.

Main results—We included six trials with 560 patients. One trial involving 129 patients did not state the number of patients randomised to the two groups. In the remaining five trials 431 patients were randomised, 212 to the robot assistant group and 219 to the human assistant group. All the trials were at high risk of bias. Mortality and morbidity were reported in only one trial with 40 patients. There was no mortality or morbidity in either group. Mortality and morbidity were not reported in the remaining trials. Quality of life or the proportion of patients who were discharged as day-patient laparoscopic cholecystectomy patients were not reported in any trial. There was no significant difference in the proportion of patients who required conversion to open cholecystectomy (2 trials; 4/63 (weighted proportion 6.4%) in the robot assistant group versus 5/70 (7.1%) in the human assistant group; RR 0.90; 95% CI 0.25 to 3.20). There was no significant difference in the operating time between the two groups (4 trials; 324 patients; MD 5.00 minutes; 95% CI -0.55 to 10.54). In one trial, about one sixth of the laparoscopic cholecystectomies in which a robot assistant was used required temporary use of a human assistant. In another trial, there was no requirement for human assistants. One trial did not report this information. It appears that there was little or no requirement for human assistants in the other three trials. There were no randomised trials comparing one type of robot versus another type of robot.

Authors' conclusions—Robot assisted laparoscopic cholecystectomy does not seem to offer any significant advantages over human assisted laparoscopic cholecystectomy. However, all trials had a high risk of systematic errors or bias (that is, risk of overestimation of benefit and underestimation of harm). All trials were small, with few or no outcomes. Hence, the risk of random errors (that is, play of chance) is high. Further randomised trials with low risk of bias or random errors are needed.

Medical Subject Headings (MeSH)

Cholecystectomy, Laparoscopic [*methods; mortality]; Randomized Controlled Trials as Topic; Robotics [*methods]; Safety

MeSH check words

Humans

BACKGROUND

About 10% to 15% of the adult western population have gallstones (Jørgensen 1987; NIH 1992; Muhrbeck 1995; Halldestam 2004). Between 1% and 4% become symptomatic in a

year (NIH 1992; Halldestam 2004). More than half a million cholecystectomies (removal of the gallbladder) are performed per year in the United States alone (NIH 1992; Livingston 2004). Regional differences exist in the cholecystectomy rates (Mjäländ 1998). Laparoscopic ('key-hole') cholecystectomy is now the preferred method of cholecystectomy (NIH 1992; Fullarton 1994; Bakken 2004).

During laparoscopic cholecystectomy, a camera inserted into the abdominal cavity acts as the surgeon's eyes and is controlled by a trained human assistant in conventional laparoscopic cholecystectomy. In order to overcome the difficulty of the availability of trained assistants due to the laws limiting working hours (Kraft 2004), and to overcome the problems of an unsteady camera (Aiono 2002), robot-assisted camera control has been suggested as an alternative. There are different methods by which the camera can be controlled using a robot.

1. 'EndoAssist' is a freestanding laparoscopic camera manipulator controlled by infrared signals from a headset worn by the operator (Aiono 2002).
2. 'Aesop' is a voice-controlled robot which responds to the surgeon's voice (Den Boer 2002).
3. 'Passist' is a manually controlled mechanical arm that is capable of locking the laparoscope and an additional grasper in the desired position, allowing for adjustments of position using one hand (Den Boer 2002).
4. The 'Zeus system' (Zhou 2006) and the 'Da Vinci system' (Heemskerk 2005) are systems in which the surgeon controls the robotic arms using a console (tele-robotic surgery) (Zhou 2006).

Robot assistants can help in the workforce planning, avoiding the need for a trained assistant. They may also avoid surgeons' tremors, which can be magnified because of the use of long instruments with the abdominal wall acting as the fulcrum.

This review is an update of the previous Cochrane systematic review about the role of a robot assistant in laparoscopic cholecystectomy (Gurusamy 2009).

OBJECTIVES

- To compare the benefits and harms of a robot assistant versus human assistant in laparoscopic cholecystectomy, and to assess whether the robot can substitute the human assistant.
- To compare the benefits and harms of different robot assistants in laparoscopic cholecystectomy.

METHODS

Criteria for considering studies for this review

Types of studies—We included all randomised clinical trials that compared a robot assistant with the human assistant in patients undergoing laparoscopic cholecystectomy (irrespective of language, blinding, publication status, sample size, or whether the trials were

adequately powered or not). We also intended to include randomised trials that compared different robot assistants in laparoscopic cholecystectomy.

Quasi-randomised studies (where the method of allocating participants to a treatment group are not strictly random, for example, date of birth, hospital record number, alternation) and observational studies were excluded for the assessment of benefits because of the very high risk of bias associated with such trials. However, such studies were retrieved for the assessment of harms of the robot and were included in the discussion.

Types of participants—Patients undergoing laparoscopic cholecystectomy (elective or emergency) for any condition (symptomatic gallstones, acalculous cholecystitis, gallbladder polyp, or any other condition).

Types of interventions—We planned to include the following interventions.

- Robot assistant (irrespective of the method of control) versus human assistant.
- Robot assistant (one type) versus robot assistant (another type).

Types of outcome measures

Primary outcomes

1. Mortality.
2. Morbidity.
3. Serious adverse events. Adverse events are defined as any untoward medical occurrence not necessarily having a causal relationship with the treatment but resulting in a dose reduction or discontinuation of treatment (ICH-GCP 1996). Serious adverse events are defined as any event that would increase mortality; is life-threatening; requires inpatient hospitalisation; results in a persistent or significant disability; or any important medical event which might have jeopardised the patient or requires intervention to prevent it.
4. Quality of life.

Secondary outcomes

1. Conversion to open cholecystectomy.
2. Proportion discharged as day-patient laparoscopic cholecystectomy patients.
3. Total operating time.
4. Return to work.

Search methods for identification of studies

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library*, MEDLINE, EMBASE, and Science Citation Index Expanded (Royle 2003) until February 2012. We also searched the World Health Organization International Clinical Trials Registry Platform search portal, which searches various trial registers

including ISRCTN and [ClinicalTrials.Gov](http://apps.who.int/trialsearch/Default.aspx) (<http://apps.who.int/trialsearch/Default.aspx>), to identify further trials (until February 2012). We have given the search strategies in Appendix 1 with the time span for the searches.

We also searched the references of the identified trials as well as contacted manufacturers of robots to identify further relevant trials.

Data collection and analysis

Trial selection and extraction of data—KSG and KS identified the trials for inclusion independently of each other. KSG and KS have also listed the excluded studies with the reasons for their exclusion.

KSG and KS, independently of each other, extracted the following data.

1. Year and language of publication.
2. Country.
3. Year of publication.
4. Inclusion and exclusion criteria.
5. Sample size.
6. Population characteristics such as age and sex ratio.
7. Antibiotic prophylaxis.
8. Pressure of pneumoperitoneum.
9. Description of robot assistant.
10. Experience of surgeons.
11. Experience of the surgeons with the robot assistant.
12. Experience of human assistants.
13. Outcomes (mentioned above).
14. Risk of bias (described below).

We sought any unclear or missing information by contacting the authors of the individual trials. We planned to contact the authors of the trials to clarify whether a trial report has been duplicated or if there was any doubt whether the trials shared the same patients, completely or partially (by identifying common authors and centres).

We resolved any differences in opinion through discussion. BRD adjudicated any differences in opinion.

Assessment of risk of bias—We followed the instructions given in the *Cochrane Handbook for Systematic Reviews of Intervention* (Higgins 2011) and the Cochrane Hepato-Biliary Group Module (Gluud 2012). According to empirical evidence (Schulz 1995; Moher 1998; Kjaergard 2001; Wood 2008), the risk of bias of the trials was assessed based on the

following domains: sequence generation, allocation concealment, blinding of participants and outcome assessors, incomplete outcome data, selective outcome reporting, and vested interest bias. Risk of bias domains were classified as follows.

Allocation sequence generation

- Low risk of bias: sequence generation was achieved using computer random number generation or a random number table. Drawing lots, tossing a coin, shuffling cards, and throwing dice are adequate if performed by an independent adjudicator.
- Uncertain risk of bias: the trial is described as randomised, but the method of sequence generation was not specified.
- High risk of bias: the sequence generation method is not, or may not be, random. Quasi-randomised studies, those using dates, names, or admittance numbers in order to allocate patients, are inadequate and will be excluded for the assessment of benefits but not for assessing harms.

Allocation concealment

- Low risk of bias: allocation was controlled by a central and independent randomisation unit, sequentially numbered opaque and sealed envelopes or similar, so that intervention allocations could not have been foreseen in advance of, or during, enrolment.
- Uncertain risk of bias: the trial was described as randomised, but the method used to conceal the allocation was not described so that intervention allocations may have been foreseen in advance of, or during, enrolment.
- High risk of bias: if the allocation sequence was known to the investigators who assigned participants, or if the study was quasi-randomised. Quasi-randomised studies were excluded for the assessment of benefits but not for assessing harms.

Blinding of participants and personnel

- Low risk of bias: blinding was performed adequately, or the outcome measurement is not likely to be influenced by lack of blinding.
- Uncertain risk of bias: there is insufficient information to assess whether the type of blinding used is likely to introduce bias in the estimate of effect.
- High risk of bias: no blinding or incomplete blinding, and the outcome or the outcome measurement is likely to be influenced by lack of blinding.

Blinding of outcome assessors

- Low risk of bias: blinding was performed adequately, or the outcome measurement is not likely to be influenced by lack of blinding.
- Uncertain risk of bias: there is insufficient information to assess whether the type of blinding used is likely to introduce bias in the estimate of effect.

- High risk of bias: no blinding or incomplete blinding, and the outcome or the outcome measurement is likely to be influenced by lack of blinding.

Incomplete outcome data

- Low risk of bias: the underlying reasons for missing data are unlikely to make treatment effects depart from plausible values, or proper methods have been employed to handle missing data.
- Uncertain risk of bias: there is insufficient information to assess whether the missing data mechanism in combination with the method used to handle missing data are likely to introduce bias in the estimate of effect.
- High risk of bias: the crude estimate of effects (eg, complete case estimate) will clearly be biased due to the underlying reasons for missing data, and the methods used to handle missing data are unsatisfactory.

Selective outcome reporting

- Low risk of bias: pre-defined, or clinically relevant and reasonably expected outcomes are reported on.
- Uncertain risk of bias: not all pre-defined or clinically relevant and reasonably expected outcomes are reported on, or are not reported fully, or it is unclear whether data on these outcomes were recorded or not.
- High risk of bias: one or more clinically relevant and reasonably expected outcomes were not reported on; data on these outcomes were likely to have been recorded.

Vested interest bias

- Low risk of bias: if the trial is conducted by a party without any vested interests in the outcome of the trial.
- Uncertain risk of bias: if it is not clear if the trial is conducted by a party with vested interest in the outcome of the trial.
- High risk of bias: if the trial is conducted by a party with vested interests in the outcome of the trial (such as robotic assistant manufacturer).

We considered trials which were classified as low risk of bias in all the above domains as trials with low risk of bias. In all other cases, trials were classified as at high risk of bias.

Statistical methods—For dichotomous variables, we calculated the risk ratio (RR) with 95% confidence interval (CI). We reported the risk difference if this was different from risk ratio (that is, if the risk difference was statistically significant and the risk ratio was not statistically significant, and vice versa). Risk difference includes the ‘zero event trials’ while the risk ratio does not. For continuous variables, we calculated the mean difference (MD) or standardised mean difference (SMD) with 95% CI. For serious adverse events we reported the rate ratio (RaR) with 95% CI.

We performed an intention-to-treat analysis whenever possible (Newell 1992). If this was not possible, we imputed data for binary outcomes using various scenarios such as the best-worst case scenario, worst-best case scenario, best-best case scenario, and worst-worst case scenario (Gurusamy 2009a; Gluud 2012).

For continuous outcomes, we planned to use available-case analysis. For continuous outcomes, we imputed the standard deviations from P values according to the instructions given in the *Cochrane Handbook for Systematic Reviews of Intervention* (Higgins 2011) and used the median for the meta-analysis when the mean was not available. If it was not possible to calculate the standard deviation from P values or confidence intervals, we planned to impute the standard deviation as the highest standard deviation noted for that group under that outcome.

We performed the meta-analyses according to the recommendations of The Cochrane Collaboration (Higgins 2011) and the Cochrane Hepato-Biliary Group Module (Gluud 2012) using the software package Review Manager 5 (RevMan 2011). We use a random-effects model (DerSimonian 1986) and a fixed-effect model (DeMets 1987). In the case of discrepancy between the two models, we have reported both results; otherwise we have reported only the results from the fixed-effect model.

Assessment of heterogeneity: We explored heterogeneity by the χ^2 test with significance set at a P value of 0.10, and measured the quantity of heterogeneity by the I^2 statistic (Higgins 2002).

Subgroup analysis: We intended to perform the following subgroup analyses.

- Trials with low risk of bias compared to trials with high risk of bias.
- Different types of robot assistant (eg, tele-robotic, voice-controlled, head-controlled, manual control).

However, we performed none of these due to the fact that all trials had high risk of bias and none compared different robots.

Reporting bias: We planned to use a funnel plot to explore bias (Egger 1997; Macaskill 2001) and to use asymmetry in a funnel plot of trial size against treatment effect to assess this bias in the case where more than 10 trials were included. We also planned to perform the linear regression approach described by Egger 1997 to determine the funnel plot asymmetry. However, we performed neither of these because few trials were included under each outcome.

Summary of findings table: Although we planned to report all the outcomes in the summary of findings table using GradePro 3.6 (<http://ims.cochrane.org/revman/other-resources/gradepr>), we have reported only conversion to open cholecystectomy and operating time as these were the only outcomes that provided information for the summary of findings table.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

We identified a total of 80 references through electronic searches of the Cochrane Hepato-Biliary Group Controlled Trials Register and the Cochrane Central Register of Controlled Trials in *The Cochrane Library* (n = 8), MEDLINE (n = 28), EMBASE (n = 11), and Science Citation Index Expanded (n = 33). We excluded 21 duplicates and 50 clearly irrelevant references through reading abstracts. Nine references were retrieved for further assessment. One reference was identified through scanning reference lists of the identified randomised trials (Gracia 1996). We excluded four references for the reasons listed in the table 'Characteristics of excluded studies'.

Six randomised trials involving 560 patients, randomised to robot assistants (212 patients) versus human assistants (219 patients), fulfilled the Inclusion criteria. The reference identified by scanning the reference lists was a conference abstract of a trial involving 129 patients, but it did not provide the number of patients randomised to each group (Gracia 1996). All six trials were completed trials and compared robot assistants versus human assistants. The flow of references is shown in Figure 1. Details about the types of devices used, sample size, patient characteristics, surgeons' previous experience with the robot assistant, and the inclusion and exclusion criteria used in the trials are shown in the table 'Characteristics of included studies'.

There were no randomised clinical trials comparing one type of robot assistant with another.

Participants

All the trials included patients undergoing laparoscopic cholecystectomy mainly for gallstones. When sufficient information was available, it was clear that only patients undergoing elective laparoscopic cholecystectomy were included. The average age in the trials ranged from 51 years to 56 years, in the trials that reported the average age. The proportion of females in the trials that provided this information ranged from 37.5% to 78.2%.

Interventions

The robotic assistant used in the trials and the methods of control of the robotic assistants are shown in the table 'Characteristics of included studies'.

Risk of bias in included studies

The risk of bias in the included trials is summarised in the risk of bias graph (Figure 2) and risk of bias summary (Figure 3). All the trials were at high risk of bias.

Effects of interventions

See: Summary of findings for the main comparison Robotic assistant compared to human assistant for patients undergoing laparoscopic cholecystectomy

The results are reported as relative risk (RR), standardised mean difference (SMD) or mean difference (MD) with 95% confidence intervals (CI). The main results are reported in the Summary of findings for the main comparison.

Mortality

Only one trial explicitly stated this outcome (Zhou 2006). There was no mortality in either group (Zhou 2006).

Morbidity

Only one trial explicitly stated morbidity as an outcome (Zhou 2006). There was no serious morbidity in either group (Zhou 2006).

Adverse events

No trial reported adverse events.

Quality of life

This outcome was not reported in any trial.

Conversion to open cholecystectomy—Two trials could be included for this outcome (Aiono 2002; Zhou 2006). Based on the meta-analysis of these two trials, we observed no significant difference in the proportion of patients who required conversion to open cholecystectomy (RR 0.90; 95% CI 0.25 to 3.20) (Analysis 1.1). Gracia et al stated that there was no difference in the conversion to open cholecystectomy without providing further information on the proportion of patients who underwent conversion to open cholecystectomy (Gracia 1996).

Operating time

Four trials could be included in the meta-analysis of this outcome (Aiono 2002; Den Boer 2002; Kraft 2004; Zhou 2006). There was no significant difference in the operating time between the two groups (MD 5.00 minutes; 95% CI -0.55 to 10.54). The other two trials also reported some information on operating time but could not be included in the meta-analysis (Gracia 1996; White 2003). Gracia et al stated that there was no difference in the operating time between the two groups (Gracia 1996). White et al stated that the operating time was about 30 minutes longer in the robotic assistant group (White 2003). The statistical significance of the finding is not known.

Day-patient laparoscopic cholecystectomy

None of the trials reported the proportion of patients discharged as day-patient laparoscopic cholecystectomy patients.

Supplementary information: requirement for human assistants in the robotic group

In one trial, 11 of 60 patients allocated to the robot assistant group required a human assistant at least temporarily (Kraft 2004). White et al reported that all the operations in the robot assistant group were completed without requirement for a human assistant. Gracia et al

did not report this directly nor could we infer this from the discussion (Gracia 1996). While the other three trials did not report this explicitly, it appears that all or nearly all the robot-assisted laparoscopic cholecystectomies were completed successfully.

Variations in statistical analysis

The interpretation of the effect estimate did not change by adopting the random-effects model or using risk difference.

Subgroup analysis

All the trials were at high risk of bias. This is why a subgroup analysis of low risk of bias trials could not be carried out. The other subgroup analysis could not be performed as each trial used a different type of robot.

Reporting bias

Exploration of reporting bias by a funnel plot was not performed because few trials were included in this review.

DISCUSSION

This review has shown that robot-assisted laparoscopic cholecystectomy does not seem to offer any significant advantages over human-assisted laparoscopic cholecystectomy. The robot assistants assessed in this review were 'Endoassist' (Aiono 2002), 'Aesop' (Den Boer 2002; Kraft 2004), 'Passist' (Den Boer 2002), and 'Zeus' (White 2003; Zhou 2006). There was no difference in the proportion of patients who underwent conversion to open cholecystectomy or in the operating time. Not enough direct information on morbidity is available from the randomised clinical trials. Only one trial reported mortality and morbidity (Zhou 2006).

Three observational studies were identified from the searches performed (Nio 2004; Heemskerk 2005; Tanoue 2006). These studies included 20 patients (10 underwent surgery using a robotic assistant and 10 underwent surgery with a human assistant) (Nio 2004), 24 patients (12 underwent surgery by robot assistant and 12 underwent surgery by human assistant) (Heemskerk 2005), and 51 patients (10 underwent surgery by robot assistant and 41 underwent surgery by human assistant) (Tanoue 2006). All three studies reported surgical morbidity. None of the morbidities were related to the robot in any of these observational studies (Nio 2004; Heemskerk 2005; Tanoue 2006) and there was no difference in the overall surgical morbidities in the robot assistant group and human assistant group in the two observational studies that reported overall surgical morbidities (Nio 2004; Heemskerk 2005).

In the previous version of this review, we demonstrated that the errors were potentially fewer with the robot assistant compared with a human assistant (not statistically significant) (Gurusamy 2009). Given that laparoscopic cholecystectomy has a very low incidence of mortality, and the lack of difference in the error rate (such as gallbladder perforations) between the human assistant and robotic assistant (Gurusamy 2009), 10s of 1000s of

patients will be necessary to demonstrate any difference in mortality or morbidity between a human assistant and robot assistant. Taking all the information including indirect evidence into account, it appears that a robotic assistant is safe, although one cannot completely rule out the small possibility of increased morbidity with a robot assistant unless trials at low risk of bias and including 1000s of patients are performed.

Furthermore, it must be noted that the surgeons' experience in using the robotic assistant was much less than using the human assistant. The previous experience of the surgeons in the use of a robot assistant varied from no experience to good experience. The set-up time and total operation time decreases even after performing 32 robot-assisted laparoscopic cholecystectomies (Kraft 2004). However, such experienced assistants are not available in all hospitals. Thus, the information provided in the trials included in this review is insufficient to arrive at an unbiased conclusion.

One of the important consequences of a robot assistant could be workforce planning. This could enable a surgeon to perform laparoscopic cholecystectomy even in the absence of an experienced human assistant. One trial reported that around 18% of the patients in which robot assistants were used also required human assistance (although only temporarily in the majority of the patients) (Kraft 2004). Although the previous experience of the surgical trainees has not been quantified in this trial, this is an issue of considerable importance for people who plan to substitute or supplement the human workforce with a robotic workforce. If human assistants must be available during the use of a robot assistant, there would be major cost and training implications. In another trial, there was no requirement for human assistants in the robotic assistant group (White 2003). We were not able to infer the proportion of robot-assisted laparoscopic cholecystectomies that required human assistants in one trial (Gracia 1996). In the other three trials, it appears that there was no need for human assistance other than the occasional help of the nurse in positioning the robot in the robot-assisted group. It must also be noted that all the trials included only elective laparoscopic cholecystectomy. Emergency laparoscopic cholecystectomy for acute cholecystitis is a more complex procedure, with a higher proportion of patients who develop complications and undergo conversion to open cholecystectomy, than elective laparoscopic cholecystectomy for biliary colic (Rutledge 2000). Trials are necessary to assess the value of robot-assisted laparoscopic cholecystectomy for acute cholecystitis.

It appears that robotic-assisted laparoscopic cholecystectomy does not offer any benefit over human assisted laparoscopic cholecystectomy. A formal cost-effectiveness analysis should be performed to assess whether robot assistants can supplement or replace human assistants in different settings such as previous availability of a robot for use in other operations, a human assistant available in case of necessity, and the use of a robot assistant in the setting of service provision where surgical training is not the main focus.

AUTHORS' CONCLUSIONS

Implications for practice

Robot-assisted laparoscopic cholecystectomy does not seem to offer any significant advantages over human-assisted laparoscopic cholecystectomy in patients undergoing elective laparoscopic cholecystectomy.

Implications for research

Further randomised clinical trials are needed to compare robot-assisted and human-assisted elective and emergency laparoscopic cholecystectomy.

Future randomised clinical trials should ensure that the surgeons are well experienced in robot-assisted laparoscopic cholecystectomy or, alternatively, patients should be randomised to experts in the respective form of cholecystectomy.

Future randomised clinical trials should include more patient oriented and healthcare planning oriented outcomes (that is, to enable cost-effectiveness measures).

More trials on robot assistants in laparoscopic cholecystectomy need to adopt blinded assessments of outcome measures.

Future trials need to describe the need for additional human assistant in the robotic group (type of assistant, duration of assistant) as well as describe the level of experience of the human assistant in the control group including type of assistant and duration of assistant.

Trials need to be conducted and reported according to the CONSORT statement (www.consort-statement.org).

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Additional statements

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Disclaimer of the Department of Health: "The views and opinions expressed in the review are those of the authors and do not necessarily reflect those of the National Institute for Health Research (NIHR), National Health Services (NHS), or the Department of Health."

Appendix 1. Search strategies

Database	Period of Search	Search Strategy
Cochrane Central Register of Controlled Trials (CENTRAL) in	Issue 2, 2012.	#1 MeSH descriptor Cholecystectomy, Laparoscopic explode all trees

Database	Period of Search	Search Strategy
The Cochrane Library (Wiley)		<p>#2 (laparoscop* OR coelioscop* OR celioscop* OR perito-neoscop*) AND cholecystectom*</p> <p>#3 (#1 OR #2)</p> <p>#4 MeSH descriptor Robotics explode all trees</p> <p>#5 “remote operations” OR telerobotics OR “robot-assisted” OR “robot assisted” OR robotics</p> <p>#6 (#4 OR #5)</p> <p>#7 (#3 AND #6)</p>
MEDLINE (Pubmed)	1987 to February 2012	((laparoscop* OR coelioscop* OR celioscop* OR peritoneoscope) AND (cholecystectom*)) OR cholecystectomy, laparoscopic[MeSH] AND (“Robotics”[MeSH] OR “remote operations” OR telerobotics OR “robot-assisted” OR “robot assisted” OR robotics) AND ((randomised controlled trial [pt] OR controlled clinical trial [pt] OR randomised [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab]) NOT (animals [mh] NOT humans [mh]))
EMBASE (OvidSP)	1987 to February 2012	<p>1 exp crossover-procedure/or exp double-blind procedure/or exp randomised controlled trial/or single-blind procedure/</p> <p>2 (((((random* or factorial* or crossover* or cross over* or cross-over* or placebo* or double*) adj blind*) or single*) adj blind*) or assign* or allocat* or volunteer*).af.</p> <p>3 1 or 2</p> <p>4 (laparoscop* or coelioscop* or celioscop* or peritoneoscop*).af.</p> <p>5 exp laparoscopic surgery/</p> <p>6 4 or 5</p> <p>7 cholecystectom*.af.</p> <p>8 exp cholecystectomy/</p> <p>9 7 or 8</p> <p>10 6 and 9</p> <p>11 (remote operations or telerobotics or robot-assisted or robot assisted or robotics).af.</p> <p>12 exp robotics/</p> <p>13 11 or 12</p> <p>14 3 and 10 and 13</p>
Science Citation Index Expanded (Web of Knowledge)	1987 to February 2012	<p>#1 TS=(laparoscop* OR coelioscop* OR celioscop* OR peri-toneoscop*)</p> <p>#2 TS=(cholecystectomy)</p> <p>#3 TS=(“remote operations” OR telerobotics OR “robot-assisted” OR “robot assisted” OR robotics)</p> <p>#4 TS=(random* ORblind* ORplacebo* OR meta-analysis)</p> <p>#5 #4 AND #3 AND #2 AND #1</p>
International Clinical Trials Registry Plat-form (http://apps.who.int/trialsearch/Default.aspx)	February 2012	robot OR robotic AND cholecystectomy

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON

Robotic assistant compared to human assistant for patients undergoing laparoscopic cholecystectomy

Patient or population: patients undergoing laparoscopic cholecystectomy.

Settings: secondary and tertiary care.

Intervention: robotic assistant.

Comparison: human assistant.

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Human assistant	Robotic assistant			
Conversion to open cholecystectomy	71 per 1000	64 per 1000 (18 to 229)	RR 0.9 (0.25 to 3.2)	133 (2 studies)	⊗○○○ very low 1,2,3,4,5
Operating time	The mean operating time in the control groups was 55 minutes	The mean operating time in the intervention groups was 5 minutes higher (0.55 lower to 10.54 higher)		324 (4 studies)	⊗○○○ very low 1,2,6,7

CI: Confidence interval;

RR: Risk ratio.

GRADE Working Group grades of evidence.

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

* The basis for the **assumed risk** is the mean control group risk across studies. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

¹ High risk of bias.

² Because of the few trials, we were unable to assess publication bias by funnel plot.

³ Only one trial had patients who required conversion to open cholecystectomy.

⁴ The confidence interval overlaps 1 and either/or 0.75 and 1.25.

⁵ There were fewer than 300 events in both groups.

⁶ The heterogeneity was high.

⁷ The confidence intervals include no difference and minimal clinically important difference.

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Aiono 2002

Methods	Randomised clinical trial.
Participants	Country: UK. Number randomised: 93. Post-randomisation drop-outs: 7 (7.5%) (included for conversion to open cholecystectomy but not for operating time). Revised sample size: 86. Average age: 56 years. Females: 48 (55.8%). Inclusion criteria 1 Elective laparoscopic cholecystectomy.
Interventions	Participants were randomly assigned to two groups. Group 1: robotic assistant (n = 43). Group 2: human assistant (n = 50).
Outcomes	The outcomes reported were conversion to open cholecystectomy and operating time
Notes	Attempts were made to contact the author in February 2012. The author provided additional information in March 2012

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: This information was not available.
Allocation concealment (selection bias)	Unclear risk	Quote: "Once it was confirmed that the operation was feasible by the laparoscopic technique, patients were randomised by the closed envelope method". "There were a batch of numbered sealed envelopes in theatre and the next numbered envelope was opened" (author replies) Comment: Further details were not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: This information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: This information was not available.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: There were post-randomisation drop-outs.
Selective reporting (reporting bias)	High risk	Comment: Some important outcomes which will generally be assessed were not reported
Free of vested interest bias?	Low risk	Quote: "There was no external funding and no conflict of interest" (author replies)
Free of expertise bias?	High risk	Quote: "Surgeons were included in the trial after one practice operation using the EndoAssist" Comment: The surgeons were well experienced in performing laparoscopic cholecystectomy with human assistants

Den Boer 2002

Methods	Randomised clinical trial.
Participants	Country: The Netherlands. Number randomised: 78. Post-randomisation drop-outs: not stated.

	Revised sample size: 78. Average age: 51 years. Females: 61 (78.2%). Inclusion criteria <div><div>1</div>Elective laparoscopic cholecystectomy for symptomatic cholelithiasis</div> <div><div>2</div>ASA I to III.</div> Exclusion criteria <div><div>1</div>Age younger than 18 years.</div> <div><div>2</div>BMI > 40.</div> <div><div>3</div>Pregnancy.</div> <div><div>4</div>Previous upper abdominal surgery.</div> <div><div>5</div>Recent pancreatitis.</div> <div><div>6</div>Clinical, chemical, or radiologic suspicion of cholestasis/stones in the CBD.</div> <div><div>7</div>Cholecystitis.</div> <div><div>8</div>Other infection in the right upper abdominal quadrant.</div> <div><div>9</div>Suspicion of perforation or empyema of the gallbladder.</div> <div><div>10</div>Porcelain gallbladder.</div> <div><div>11</div>Diagnosed cancer.</div> <div><div>12</div>Bleeding disorders.</div>	
Interventions	Participants were randomly assigned to two groups. Group 1: robotic assistant (n = 39). Group 2: human assistant (n = 39).	
Outcomes	The outcomes reported were operating time.	
Notes	Attempts were made to contact the author in February 2012.	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "All the surgeons randomly performed group as decided by the drawing of lots".
Allocation concealment (selection bias)	Unclear risk	Quote: "All the surgeons randomly performed group as decided by the drawing of lots".
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: This information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: This information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: This information was not available.
Selective reporting (reporting bias)	High risk	Comment: Some important outcomes which will generally be assessed were not reported
Free of vested interest bias?	Unclear risk	Quote: "This search is part of the Minimally Invasive Surgery and Interventional Techniques (MISIT) program of the Delft Interfaculty Research Centre on Medical Engineering (DIOC-9)" Comment: Further details were not available.
Free of expertise bias?	High risk	Quote: "None of the surgeons were experienced in solo surgery"

Gracia 1996

Methods	Randomised clinical trial.
Participants	Country: USA. Number randomised: 129. Post-randomisation drop-outs: not stated. Revised sample size: 129. Average age: not stated. Females: not stated. Inclusion criteria 1 Laparoscopic cholecystectomy.
Interventions	Participants were randomly assigned to two groups. Group 1: robotic assistant (n = not stated). Group 2: human assistant (n = not stated).
Outcomes	The outcomes reported were operating time and conversion to open cholecystectomy
Notes	The only information available was that there was no difference in the operating time or conversion to open cholecystectomy. Attempts were made to contact the author in February 2012. The author does not work at the hospital anymore and there were no forwarding contact details available

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: This information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: This information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: This information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: This information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: This information was not available.
Selective reporting (reporting bias)	High risk	Comment: Some important outcomes which will generally be assessed were not reported
Free of vested interest bias?	Unclear risk	Comment: This information was not available.
Free of expertise bias?	High risk	Quote: "The cases performed with the robot were similar to the human assistant in terms of operating time even though the users were inexperienced in the technology"

Kraft 2004

Methods	Randomised clinical trial.
Participants	Country: Germany. Number randomised: 120.

	<p>Post-randomisation drop-outs: not stated. Revised sample size: 120. Average age: 52 years. Females: 89 (74.2%). Inclusion criteria</p> <p>1 Patients undergoing laparoscopic cholecystectomy for cholelithiasis.</p> <p>Exclusion criteria</p> <p>1 Expected adhesions.</p> <p>2 Emergency procedures.</p>	
Interventions	Participants were randomly assigned to two groups. Group 2: human assistant (n = 60). Group 1: robotic assistant (n = 60).	
Outcomes	The outcome reported was operating time.	
Notes	Attempts were made to contact the author in February 2012.	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: This information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: This information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: This information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Quote: "An independent observer record the times for the defined periods of patients preparation before the skin incision and after the last skin suture, as well as the actual operation time" Comment: Although operating time was the only outcome reported by the trial and an independent observer used for measuring the operating time, the blinding of observer was not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: This information was not available.
Selective reporting (reporting bias)	High risk	Comment: Some important outcomes which will generally be assessed were not reported
Free of vested interest bias?	Unclear risk	Comment: This information was not available.
Free of expertise bias?	Low risk	Quote: The number of surgeons was limited to three senior residents, all of whom were experienced in the use of AESOP (a type of robot).

White 2003

Methods	Randomised clinical trial.
Participants	Country: USA. Number randomised: 100. Post-randomisation drop-outs: not stated. Revised sample size: 100. Average age: not stated. Females: not stated. Inclusion criteria

	1 Laparoscopic cholecystectomy.
Interventions	Participants were randomly assigned to two groups. Group 1: robotic assistant (n = 50). Group 2: human assistant (n = 50).
Outcomes	The outcomes reported were operating time.
Notes	The only information available was that the operating time was about 30 minutes longer in the robotic assistant group and that there was no requirement for human assistants in the robotic group. Attempts were made to contact the author in February 2012. The author does not work at the hospital anymore, and there were no forwarding contact details available

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: This information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: This information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: This information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: This information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: This information was not available.
Selective reporting (reporting bias)	High risk	Comment: Some important outcomes which are generally expected to be assessed were not reported
Free of vested interest bias?	Unclear risk	Comment: This information was not available.
Free of expertise bias?	Unclear risk	Comment: This information was not available.

Zhou 2006

Methods	Randomised clinical trial.
Participants	Country: China. Number randomised: 40. Post-randomisation drop-outs: not stated. Revised sample size: 40. Average age: not stated. Females: 15 (37.5%). Inclusion criteria 1 Patients undergoing elective laparoscopic cholecystectomy
Interventions	Participants were randomly assigned to two groups. Group 1: robotic assistant (n = 20). Group 2: human assistant (n = 20).
Outcomes	The outcomes reported were mortality, morbidity, operating time, and conversion to open cholecystectomy

Notes	Attempts were made to contact the author in February 2012.	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: This information was not available.
Allocation concealment (selection bias)	Unclear risk	Comment: This information was not available.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Comment: This information was not available.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Comment: This information was not available.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Comment: This information was not available.
Selective reporting (reporting bias)	Low risk	Comment: All important outcomes were reported.
Free of vested interest bias?	Unclear risk	Comment: This information was not available.
Free of expertise bias?	Unclear risk	Comment: This information was not available.

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Heemskerk 2005	Not a randomised clinical trial (provided data for adverse events to be included in discussion)
Hourmont 2003	Not a randomised clinical trial.
Kornprat 2006	Not a randomised clinical trial.
Nio 2004	Not a randomised clinical trial (provided data for adverse events to be included in discussion)
Tanoue 2006	Not a randomised clinical trial (provided data for adverse events to be included in discussion)

DATA AND ANALYSES

Comparison 1 Robot assistant versus human assistant

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Conversion to open cholecystectomy	2	133	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.25, 3.20]
2 Operating time	4	324	Mean Difference (IV, Fixed, 95% CI)	5.00 [-0.55, 10.54]
3 Other data that could not be included in the meta-analysis	Other data	No numeric data		

WHAT'S NEW

Last assessed as up-to-date: 25 July 2012.

Date	Event	Description
27 July 2012	New citation required but conclusions have not changed	A trial, previously excluded from the "Robot assistant for laparoscopic cholecystectomy" review (Gurusamy 2009) is now included in our review due to revised methods related to selective outcome reporting
8 February 2012	New search has been performed	Searches were updated, and the methods were revised according to the latest recommendations of The Cochrane Handbook (Higgins 2011).
7 February 2012	Amended	The title has been changed to increase clarity.

HISTORY

Protocol first published: Issue 3, 2007

Review first published: Issue 1, 2009

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** Indicates the major publication for the study*

PLAIN LANGUAGE SUMMARY

Robot assistant versus human or another robot assistant in patients undergoing laparoscopic cholecystectomy

Patients with symptomatic gallstones generally undergo laparoscopic cholecystectomy (key-hole removal of the gallbladder). During this procedure there is only tunnel vision for the surgeon provided by a camera inserted through one of the key-holes. The surgeon operates using instruments while a nurse or another doctor shows the surgeon the operating field using the camera. Thus, the human assistant acts as the 'surgeons' eyes' during the laparoscopic procedure. Recently, robots have been used to assist the surgeons in performing laparoscopic cholecystectomy. Various types of robots exist. Some just hold the camera and can be controlled by surgeons' voice commands or the surgeons' head movements. Advanced robotic systems can hold the camera and all the instruments, all of which are controlled by the surgeon using a console (like in a gaming device). The role of a robotic assistant in laparoscopic cholecystectomy is not known. We sought this information by undertaking a detailed literature search in a systematic way to obtain all the information available from randomised clinical trials. Such clinical trials, if designed well, provide the best estimate of the true effects of interventions.

A detailed and systematic review of the literature revealed that there were six randomised clinical trials including 560 patients. One trial involving 129 patients did not state the number of patients randomised to the two groups. Of the remaining 431 patients in the remaining five trials, 212 patients underwent laparoscopic cholecystectomy with the help of robot assistant and 219 patients underwent the same procedure with the help of a human assistant. All the trials were at high risk of bias (that is, they were prone to systematic underestimation of harms or overestimation of the benefits of the robotic assistant group or the human assistant group because of the beliefs of the people conducting the trial) and errors due to play of chance. Mortality and surgical complications were reported in only one trial with 40 patients. There were no mortality or surgical complications in either group in this trial. Mortality and morbidity were not reported in the remaining trials. Quality of life or the proportion of patients who were discharged as day-patient laparoscopic cholecystectomy patients were not reported in any trial. There was no significant difference in the proportion of patients who underwent conversion to open cholecystectomy or in the operating time between the two groups. In one trial, about one sixth of the laparoscopic cholecystectomies in which a robot assistant was used required temporary use of a human assistant. In another trial, there was no requirement for human assistants. One trial did not report this information. It appears that there was little or no requirement for human assistants in the other three trials. Robot-assisted laparoscopic cholecystectomy does not seem to offer any significant advantages over human-assisted laparoscopic cholecystectomy. However, our present evidence base is limited by trials that all have high risk of systematic errors (potential to underestimate harms or overestimate benefits of the robot assistant group or the human assistant group) and random errors (that is, play of chance). Therefore, further well-designed randomised trials with low risk of systematic errors and low risk of random errors are needed.

Figure 1. Study flow diagram

Figure 2. Risk of bias graph: review authors' judgments about each methodological quality item presented as percentages across all included studies

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Free of vested interest bias?	Free of expertise bias?
Aiono 2002	?	?	?	?	-	-	+	-
Den Boer 2002	?	?	?	?	?	-	?	-
Gracia 1996	?	?	?	?	?	-	?	-
Kraft 2004	?	?	?	?	?	-	?	+
White 2003	?	?	?	?	?	-	?	?
Zhou 2006	?	?	?	?	?	+	?	?

Figure 3. Methodological quality summary: review authors' judgments about each methodological quality item for each included study