

Region Västra Götaland, HTA-centrum

Health Technology Assessment

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Robotically assisted laparoscopic surgery for rectal cancer

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Robotically assisted laparoscopic surgery for rectal cancer

[Robotassisterad laparoskopisk operation av rektalcancer]

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HTA-centrum

Summary from HTA-centrum, Region Västra Götaland

Robotically assisted laparoscopic surgery for rectal cancer

Question at issue, PICO:

In adult patients with rectal cancer, is robotically assisted laparoscopic surgery better than laparoscopic or open surgery concerning long time survival, health related quality of life and local recurrence?

P= Patients, I= Intervention, C= Comparison, O=Outcome

P= Adult patients with rectal cancer, who are about to undergo surgical treatment with curative intention

I= Robotically assisted laparoscopic rectal resection or amputation

C1= Laparoscopic rectal resection or amputation

C2= Open rectal resection or amputation

O= Critical*: Long term survival. Long term health related quality of life, measured with validated instruments. Local recurrence.

Important:* Pathological resection margin. Complications. Postoperative rehabilitation.

Not important:* Operating time. Length of hospital stay.

** Imply critical, important or not important outcomes for decision-making.*

Summary of the health technology assessment:

Method and patient category:

Rectal cancer is diagnosed in approximately 400 patients annually in Region Västra Götaland. Surgery is the only curative option for patients with rectal cancer and is undertaken in 90% of these patients. Open or laparoscopic rectal resection or amputation is marred with a high frequency of postoperative morbidity. Robotically assisted laparoscopic surgery is used for other cancer operations and it has recently been suggested that this technique might be better for both rectal cancer patients and surgeons' ergonomics.

Results and quality of evidence

Thirteen relevant articles were identified in the systematic literature search: one systematic review (SR), nine cohort studies and three case series. The SR had high methodological quality, but included only cohort studies with high risk of bias. The quality of evidence according to GRADE was based on the SR and the nine cohort studies. Due to the high risk of bias in the cohort studies, it was decided not to perform a meta-analysis.

Long term survival

One cohort study reported disease-free two-year survival: 83.5 %, 81.9% and 79.7% in the robotically assisted laparoscopic, laparoscopic and open groups respectively.

Conclusion: It is uncertain whether there is any difference in disease-free survival after robotically assisted laparoscopic, compared to laparoscopic or open surgery, for rectal cancer. Very low quality of evidence (GRADE⊕○○○).

Long term quality of life and Local recurrence

No studies reported these outcomes.

Pathological resection margin

Most studies reported CRM (Circumferential resection margin) and DRM (Distal resection margin) as surrogate variables for oncological result. One SR and four cohort studies compared robotically assisted laparoscopic with laparoscopic surgery, while five cohort studies compared robotically assisted laparoscopic with open surgery. CRM is considered to be the most important variable. For robotically assisted laparoscopic surgery versus laparoscopic surgery positive CRM ranged 0 -7.5% and 2.5 – 12% respectively in the different studies and for robotically assisted laparoscopic surgery versus open surgery 0 – 4.2% and 1 – 10% respectively.

Conclusion: It is uncertain whether there is any difference regarding surrogate variables for oncological result after robotically assisted laparoscopic versus laparoscopic and open surgery for rectal cancer respectively. Very low quality of evidence (GRADE⊕○○○).

Complications

One SR, eight cohort studies and three case series reported complications comparing robotically assisted laparoscopic with either laparoscopic or open surgery and one cohort study reported complications after all three methods. No differences were observed between the three techniques, e.g. for anastomotic leakage frequencies were: 5 – 12% for robotically assisted laparoscopic, 5 – 14% for laparoscopic and 2 – 9% for open surgery.

Conclusion: It is uncertain whether there is any difference in the frequency of complications associated with robotically assisted laparoscopic surgery, compared to laparoscopic or open surgery, for rectal cancer.

Postoperative bowel function recovery

One SR and four cohort studies compared robotically assisted laparoscopic with laparoscopic surgery and four cohort studies compared with open surgery. The only parameter reported in all studies was time to first flatus. In robotically assisted laparoscopic versus laparoscopic surgery time to first flatus ranged 2.1 – 2.4 and 2.2 – 2.5 days respectively and for robotically assisted laparoscopic versus open surgery 2.0 – 2.2 and 3.0 – 3.1 in the different studies.

Conclusions: It is uncertain whether robotically assisted laparoscopic surgery for rectal cancer, compared to laparoscopic or open surgery, results in any difference regarding the time to first flatus after surgery. Very low quality of evidence (GRADE⊕○○○).

Operative time

One SR and four cohort studies compared robotically assisted laparoscopic with laparoscopic surgery with operative time ranging 236 – 310 and 185 – 278 minutes respectively in the different studies. Four cohort studies compared robotically assisted laparoscopic with open surgery showing shorter operating time with open surgery (operative time ranging from 188 – 338 and 103 – 274 respectively in the different studies).

Conclusions: It is uncertain whether robotically assisted laparoscopic surgery for rectal cancer is more time consuming than laparoscopic or open surgery.

Very low quality of evidence (GRADE⊕○○○).

Length of hospital stay

One SR and four cohort studies compared robotically assisted laparoscopic with laparoscopic surgery with length of stay ranging 8 – 11.1 and 10 – 13.5 days respectively in the studies. Five cohort studies reported length of stay ranging 5 – 10.8 and 6 – 16 days in the studies for robotically assisted laparoscopic versus open surgery.

Conclusions: It is uncertain whether the length of hospital stay is shorter after robotically assisted laparoscopic, compared to laparoscopic or open surgery for rectal cancer.

Very low quality of evidence (GRADE⊕○○○).

Ethical aspects:

It is ethically questionable to use a significantly more expensive surgical technique in the absence of documented patient benefits. Robotically assisted laparoscopic surgery for rectal cancer needs further evaluation and should be used only in randomized controlled trials.

Economical aspects:

The use of robotically assisted laparoscopic surgery is approximately 59000 SEK more expensive per patient than laparoscopic and open surgery if 100 patients undergo surgery with this technique annually. For 100 rectal cancer operations the increased cost would be approximately 5.9 million SEK annually.

Concluding remarks:

Rectal cancer is frequently diagnosed and surgery is the only curative option. Robotically assisted laparoscopic surgery has recently been suggested to be better than open or conventional laparoscopic surgery for both rectal cancer patients and surgeons' ergonomics. The identified literature comprised only non-randomized cohort studies and case series. No patient benefits with robotically assisted laparoscopic surgery were documented and the quality of evidence was very low (GRADE⊕○○○) for all studied outcomes. The use of robotically assisted laparoscopic surgery is associated with an added cost of approximately 59000 SEK per patient if 100 patients are operated annually using this technique. This technique needs further evaluation.

An updated search in January 2014 identified four additional cohort studies and two case series fulfilling the PICO criteria. These studies did not influence any of the conclusions or the quality of evidence.

Robotassisterad laparoskopisk operation av rektalcancer

Frågeställning: Hos vuxna patienter med rektalcancer, är robotassisterad laparoskopisk kirurgi bättre än laparoskopisk eller öppen kirurgi avseende långtidsöverlevnad, hälsorelaterad livskvalitet och lokalrecidiv?

PICO: P= Patienter, I= Intervention, C= Comparison, O=Outcome (utfall)

P= Vuxna patienter med rektalcancer som ska genomgå kurativt syftande kirurgi

I= Robotassisterad laparoskopisk resektion eller amputation av rektum

C1= Laparoskopisk resektion eller amputation av rektum

C2= Öppen kirurgisk resektion eller amputation av rektum

O= *Kritiska**: Långtids överlevnad och hälsorelaterad livskvalitet (med validerade instrument). Lokalrecidiv.

*Viktiga**: Patologisk resektionsmarginal. Komplikationer. Postoperativ återhämtning.

*Mindre viktiga**: Operationstid, Vårdtid.

*för beslutsfattande

Sammanfattning av HTA-rapporten

Metod och målgrupp:

Rektalcancer drabbar årligen ungefär 400 individer i Västra Götaland. Kirurgi är den enda kurativt syftande behandlingsformen och cirka 90% av rektalcancerpatienter genomgår kirurgi. Öppen kirurgisk eller laparoskopisk resektion eller amputation av rektum är förenade med avsevärd sjuklighet och ibland även dödlighet. Robotassisterad laparoskopisk operation har börjat användas vid andra cancerformer och det har nyligen föreslagits att denna teknik kan vara bättre både för rektalcancerpatienter och ergonomiskt för behandlande kirurg.

Kunskapsläge och evidensstyrka:

Tretton relevanta artiklar identifierades i den systematiska litteratursökningen: en systematisk översikt (SR), nio icke-randomiserade kohortstudier och tre fallserier. Den systematiska översikten höll hög metodologisk kvalitet men inkluderade enbart kohortstudier med nedsatt intern validitet. De nio kohortstudierna granskades kritiskt. Bedömningen av evidensstyrka (GRADE) baserades på en SR och nio kohortstudier. På grund av den bristande interna validiteten i kohortstudierna beslutades att ej göra en meta-analys.

Långtidsöverlevnad:

En kohortstudie rapporterade sjukdomsfri tvåårsöverlevnad: 83,5 %, 81,9% och 79,7% vid robotassisterad laparoskopisk, laparoskopisk respektive öppen kirurgi.

Slutsats: Det är osäkert huruvida det är någon skillnad i sjukdomsfri tvåårsöverlevnad efter robotassisterad laparoskopisk, laparoskopisk och öppen kirurgi för rektalcancer.

Otillräckligt vetenskapligt underlag (GRADE ⊕○○○).

Långtids hälsorelaterad livskvalitet samt lokalrecidiv:

Inga studier.

Patologisk resektionsmarginal

De flesta studierna redovisade CRM (Circumferentiell resektionsmarginal) och DRM (Distal resektionsmarginal). CRM bedöms vara den viktigaste surrogatvariabeln. En SR och fyra kohortstudier jämförde robotassisterad laparoskopisk med laparoskopisk och fem kohortstudier jämförde robotassisterad laparoskopisk med öppen kirurgi. För robotassisterad laparoskopisk versus laparoskopisk kirurgi varierade positiv CRM mellan 0 -7,5% respektive 2,5 – 12% och för robotassisterad laparoskopisk kirurgi versus öppen kirurgi mellan 0 – 4,2% respektive 1 – 10% i de olika studierna.

Slutsats: Det är osäkert huruvida det är någon skillnad vad gäller surrogatvariabler för onkologiskt resultat vid robotassisterad laparoskopisk jämfört med laparoskopisk eller öppen kirurgi för rektalcancer.

Otillräckligt vetenskapligt underlag (GRADE ⊕○○○).

Komplikationer

En SR, åtta kohortstudier och tre fallserier redovisade komplikationer efter robotassisterad laparoskopisk jämfört med laparoskopisk eller öppen kirurgi och en kohortstudie redovisade komplikationer för alla tre teknikerna. Inga skillnader sågs mellan teknikerna: exempelvis var frekvensen anastomosläckage 5 – 12%, 5 – 14% och 2 – 9% efter robotassisterad laparoskopisk, laparoskopisk respektive öppen kirurgi.

Slutsats: Det är osäkert huruvida det är någon skillnad i komplikationsfrekvens efter robotassisterad laparoskopisk jämfört med laparoskopisk eller öppen kirurgi för rektalcancer.

Otillräckligt vetenskapligt underlag (GRADE ⊕○○○).

Postoperativ återhämtning av tarmfunktion

En SR och fyra kohortstudier jämförde robotassisterad laparoskopisk med laparoskopisk och fyra kohortstudier jämförde med öppen kirurgi. Den enda parameter som redovisades i alla studierna var tid till första gasavgång, vilket redovisas här. För jämförelsen robotassisterad laparoskopisk versus laparoskopisk kirurgi varierade tiden till första gasavgång mellan 2,1 – 2,4 respektive 2,2 – 2,5 och för jämförelsen robotassisterade laparoskopisk versus öppen kirurgi mellan 2,0 – 2,2 respektive 3,0 – 3,1 i de olika studierna.

Slutsats: Det är osäkert huruvida robotassisterad laparoskopisk jämfört med laparoskopisk eller öppen kirurgi för rektalcancer påverkar tid till första postoperativa gasavgång.

Otillräckligt vetenskapligt underlag (GRADE ⊕○○○).

Operationstid

En SR och fyra kohortstudier jämförde operationstid för robotassisterad laparoskopisk och laparoskopisk kirurgi; range för operationstiden var 236 – 310 respektive 185 – 278 minuter i de olika studierna. Fyra kohortstudier jämförde robotassisterad laparoskopisk med öppen kirurgi; range var 188 – 338 respektive 103 – 274 minuter i de olika studierna.

Slutsats: Det är osäkert huruvida operationstiden är längre för robotassisterad laparoskopisk jämfört med laparoskopisk eller öppen kirurgi.

Otillräckligt vetenskapligt underlag (GRADE ⊕○○○).

Vårdtid

En SR och fyra kohortstudier jämförde robotassisterad laparoskopisk med laparoskopisk kirurgi; range för vårdtiden var 8 – 11,1 respektive 10 – 13,5 dagar i de olika studierna. Fem kohortstudier rapporterade vårdtider med range 5 – 10,8 respektive 6 – 16 dagar för robotassisterad laparoskopisk och öppen kirurgi i de olika studierna.

Slutsats: Det är osäkert huruvida vårdtiden är kortare efter robotassisterad laparoskopisk jämfört med laparoskopisk eller öppen kirurgi för rektalcancer.

Otillräckligt vetenskapligt underlag (GRADE ⊕○○○).

Etiska aspekter:

Det är etiskt tveksamt att i rutinsjukvård använda en avsevärt dyrare operationsteknik för vilken förbättrad patientnytta ej är visad. Robotassisterad laparoskopisk kirurgi behöver utvärderas i stora, helst randomiserade, kliniska studier.

Ekonomiska aspekter:

Robotassisterad laparoskopisk kirurgi medför cirka 59000 SEK i ökad kostnad per patient jämfört med laparoskopisk och öppen kirurgi vid 100 operationer årligen. Om metoden skulle användas på 100 rektalcancerpatienter årligen i Västra Götaland blir årlig kostnadsstegring cirka 5,9 miljoner SEK.

Slutsatser:

Rektalcancer är en relativt vanlig cancersjukdom och kirurgi är enda behandlingsform med kurativ potential. Robotassisterad laparoskopisk kirurgi har nyligen föreslagits medföra både bättre patientnytta samt underlätta för opererande kirurg. Den identifierade litteraturen innefattade enbart icke-randomiserade kohortstudier, en översikt över sådana studier samt fallserier. Ingen dokumenterad patientnytta kunde identifieras och det vetenskapliga underlaget var otillräckligt för alla studerade utfall (GRADE ⊕○○○). Robotassisterad laparoskopisk kirurgi är förenat med avsevärt högre kostnad (59000 SEK per operation vid 100 operationer årligen) än laparoskopisk eller öppen kirurgi. Tekniken behöver utvärderas i stora kliniska studier.

En uppdatering av sökningen genomfördes i januari 2014. Ytterligare fyra kohortstudier och två fallserier identifierades. Dessa studier påverkade ej slutsatser eller evidensstyrka.

HTA-kvalitetssäkringsgruppen har ett uppdrag att yttra sig över genomförda HTA i Västra Götalandsregionen. Yttrandet skall innefatta sammanfattning av frågeställning, samlat kunskapsläge och evidensgradering för patientnytta och risker samt ekonomiska och etiska aspekter för den studerade teknologin.

Projektet har pågått under perioden 2013-03-13 –2014-01-29.
Sista uppdatering av artikelsökning: Januari 2014

För HTA-kvalitetssäkringsgruppen 2014-01-29

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Which health technology or method will be assessed?

1a The question was posed by

Karl Kodeda, MD, PhD, Department of Surgery, Sahlgrenska University Hospital/Östra, Göteborg, Sweden.

Eva Haglind, MD, PhD, Professor, Department of Surgery, Sahlgrenska University Hospital/Östra, Göteborg, Sweden.

1b Participants, in the project

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1c Participants, from the HTA centre and external reviewers

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1d Conflicts of interest for the proposer or any of the participants in the work group

No conflicts of interest reported.

Disease/disorder of Interest and Present Treatment

2a Disease/disorder of interest and its degree of severity

Rectal neoplasm

- Risk of premature death
- Risk of permanent illness or damage, or reduced quality of life
- Risk of disability and health-related quality of life

2b

Prevalence and incidence of rectal cancer

The Swedish rectal cancer incidences 2012 were 1242 men and 857 women. Of these, 903 men and 626 women underwent surgery. In Region Västra Götaland, 411 cases of rectal cancer were diagnosed in 2012. During the same year, 363 had surgery (including local excision).

2c Present treatment of the rectalcancer.

Laparoscopic or open rectal resection or laparoscopic or abdominoperineal excision.

2d Number of patients per year who undergo current treatment regimen?

See 2b.

2e The normal pathway of a patient through the health care system

The patient is referred from a primary care physician, from other hospital departments, or admitted as an emergency case. The normal pathway includes that all patients are discussed on a multidisciplinary board after completed work-up and prior to surgery. The treatment plan, including decision of the need for neoadjuvant treatment (radio/chemotherapy), is discussed. At discharge from the hospital, a follow-up consultation is booked to convey the result from the pathology examination; this has implications for decisions regarding adjuvant chemotherapy treatment. Local routines for long-term follow-up will then be applied.

2f Actual wait time in days for medical assessment /treatment

In the case of a colorectal cancer (in the non-emergency setting), surgery is usually performed within four weeks. If neoadjuvant treatment is needed, surgery may be performed later, but treatment starts within four weeks.

3a Name/description of the health technology at issue

The health technology at issue is robotically assisted laparoscopic surgery for rectal cancer. In all reviewed studies, the da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA) was used. Today, this is the only surgical robotic system on the market. Different surgical techniques were used in the studies. The following steps are regularly included in robotically assisted laparoscopic surgery for rectal cancer:

- Colonic mobilization with ligation of the inferior mesenteric vessels.
- Total or partial mesorectal excision (TME/PME) or abdominoperineal excision
- Specimen retrieval
- Depending on the type of procedure, bowel continuity is restored or a colostomy is constructed. A temporary diverting ileostomy is performed in many cases with distal rectal cancer excision and a low colorectal anastomosis.

3b The work group's understanding of the potential value of the health technology

The hypotheses of improved patient outcomes by the use of robotically assisted laparoscopic surgery for rectal cancer are based on presumed enhancement of the improvements found when using laparoscopic as compared to open surgical technique, i.e. less perioperative blood loss, shorter time to resume bowel movements and oral intake, shorter hospital stay and shorter time to recovery. Furthermore, the improved visualization of the operating field could hypothetically result in shorter operating times and less nerve damage. In addition, the working condition for the operating surgeon is suggested to be improved. Finally, the learning curve for laparoscopic rectal cancer surgery is in our and others' experience fairly long, and it is possible that the addition of the 3D visual field, by the robot device, might shorten that learning curve.

If future properly designed and conducted studies confirm these hypotheses, it could imply improved patient outcomes regarding postoperative recovery and quality of life and decreased overall costs for rectal cancer treatment.

The proposed way forward should be at large colorectal units, with routine use of laparoscopic technique for rectal cancer surgery and within the framework of well-designed prospective, controlled and preferably randomized trials.

Diagnosis: Rectal cancer; C20.9

Treatment: Surgery for rectal cancer; JBG00, JBG10, JBG30, JBG01, JBG11 and JBG31

3c The central question for the current HTA project in one sentence

In adult patients with rectal cancer, is robotically assisted laparoscopic surgery better than laparoscopic or open surgery concerning primarily long time survival, health related quality of life and local recurrence?

3d PICO

P= Patients, I= Intervention, C= Comparison, O=Outcome

P= Adult patients with rectal cancer, who are about to undergo surgical treatment with curative intention

I= Robotically assisted laparoscopic rectal resection or amputation

C1= Laparoscopic rectal resection or amputation

C2= Open rectal resection or amputation

O= Critical*:

Long term survival

Long term health related quality of life, measured with validated instruments

Local recurrence

Important:*

Pathological resection margin

(e.g. measured with CRM - circumferential resection margin and/or DRM – distal resection margin)

Complications

Postoperative rehabilitation

Not important:*

Operating time

Length of hospital stay

*Imply critical, important or not important for decision making.

4 Search strategy, study selection and references – Appendix 3

During March 2013 two librarians (TS, ME) performed systematic searches in PubMed, Embase, the Cochrane Library, and a number of HTA-databases. Reference lists of relevant articles were scrutinized for additional references. Search strategies, eligibility criteria and a graphic presentation of the selection process are accounted for in Appendix 3. The librarians conducted the literature searches, selected studies and independently assessed the obtained abstracts and a first selection of full-text articles for inclusion or exclusion. Any disagreements were resolved in consensus. The remaining articles were sent to the participants, who read the articles independently and then decided in a consensus meeting which articles that should be included.

The literature search identified a total of 343 articles (after removal of duplicates). The librarians then excluded 308 articles after reading their abstracts. Another five articles were excluded by the librarians after reading the articles in full text. The remaining 30 articles were sent to the participants, and 13 of them were finally included in the report. One systematic review (SR) was evaluated with the AMSTAR-protocol, nine cohort studies were critically appraised using checklists from SBU (Swedish Council on Health Technology Assessment) for cohort studies, and finally three case series, were used for only reporting complications.

An update of the search in January 2014 identified seven relevant articles published after March 2013. One duplicate was excluded. The remaining six articles included four cohort studies and two case series.

5a Describe briefly the present knowledge of the health technology

Thirteen relevant articles were identified in March 2013: one systematic review (SR), nine cohort studies and three case series. No randomized controlled trials were found. The SR had high methodological quality, but included studies with high risk of bias. The nine cohort studies were critically appraised. The quality of evidence according to GRADE was based on the SR and the cohort studies. Due to the high risk of bias in the cohort studies, it was decided not to perform a meta-analysis.

Long term survival

One cohort study reported long term survival data. Disease-free two-year survival was similar in the three groups (83.5 %, 81.9% and 79.7% in the robotically assisted laparoscopic, laparoscopic and open groups respectively).

Conclusion: It is uncertain whether there is any difference in disease-free survival after robotically assisted laparoscopic surgery, compared to laparoscopic or open surgery, for rectal cancer. Very low quality of evidence (GRADE ⊕○○○)

Long term quality of life, measured with validated methods

No studies reported this outcome.

Local recurrence

No studies reported this outcome.

Pathological resection margin

Some information regarding the oncological result of surgery can be retrieved from studying surrogate variables, e.g. circumferential resection margin (CRM) and distal resection margin (DRM).

One SR and four cohort studies reported surrogate variables for oncological results, comparing robotically assisted laparoscopic surgery with laparoscopic surgery, while five cohort studies compared robotically assisted laparoscopic surgery with open surgery. Most studies reported CRM, DRM and harvested lymph nodes, as surrogate variables for oncological result. We consider CRM as the most clinically important surrogate variable and the further analyses are based on CRM. In Swedish pathology reports the standard cut off for positive CRM is <1mm. In the included cohort studies, different cut offs for positive CRM are used and in some studies the cut off is not reported.

For comparison of robotically assisted laparoscopic surgery to laparoscopic surgery, one study (D'Annibale, 2013) showed a significant difference (CRM, defined as positive if < 2 mm) to the advantage of robotically assisted laparoscopic surgery (0 vs. 12%, p=0.022). The remaining studies showed no differences.

For the comparison of robotically assisted laparoscopic surgery to open surgery, one study (Kang J, 2013) showed a statistically significant difference (CRM positive not defined), again to the advantage of robotically assisted laparoscopic surgery (7(4.2%) vs. 17(10.3%), p=0.034). The remaining studies showed no differences.

Conclusion: It is uncertain whether there is any difference regarding surrogate variables for oncological result after robotically assisted laparoscopic compared to laparoscopic surgery, as well as compared to open surgery for rectal cancer.

Very low quality of evidence (GRADE ⊕○○○).

Complications

Nine cohort studies reported complications comparing robotically assisted laparoscopic surgery with either laparoscopic or open surgery and one cohort study reported complications after robotically assisted laparoscopic surgery compared to both methods. Three case series reported complications. The reported frequencies of complications are within the range of what has previously been reported for rectal surgery. No significant differences in the frequency of complications were observed between the three different surgical technique groups (exemplified by the most common serious complication, anastomotic leakage: 5 – 12% for robotically assisted laparoscopic surgery, 5 – 14% for laparoscopic surgery and 2 – 9% for open surgery).

Conclusion: It is uncertain whether there is any difference in the frequency of complications associated with robotically assisted laparoscopic surgery, compared to laparoscopic or open surgery, for rectal cancer.

Very low quality of evidence (GRADE ⊕○○○).

Postoperative bowel function recovery

One SR and four cohort studies reported results for postoperative rehabilitation comparing robotically assisted laparoscopic surgery with laparoscopic surgery. Four cohort studies reported results for postoperative bowel function recovery comparing robotically assisted laparoscopic surgery with open surgery. The only parameter that was reported in all of the studies was time to first flatus and this parameter was chosen for comparison. In the studies comparing robotically assisted laparoscopic and laparoscopic surgery one of the studies reported slightly but significantly shorter time to first flatus in the robotically assisted laparoscopic surgery group (2.2 vs. 2.4, $p < 0.01$). In the studies comparing robotically assisted laparoscopic and open surgery two of the studies reported that time to first flatus was significantly shorter in the robotic surgery group but the mean difference was small (less than one day (2 vs. 3 $p < 0.03$ and 2.2 vs. 3, $p < 0.01$).

Conclusions: It is uncertain whether robotically assisted laparoscopic surgery for rectal cancer, compared to laparoscopic or open surgery, results in any difference regarding the time to first flatus after surgery.

Very low quality of evidence (GRADE ⊕○○○).

Operating time

One SR and four cohort studies reported operating time comparing robotically assisted laparoscopic surgery with laparoscopic surgery. Operating time was significantly longer for robotically assisted laparoscopic surgery as compared to laparoscopic surgery in three of the studies (mean operating time for the robotically assisted procedures varied between 235 – 310 minutes and the corresponding figures for the standard laparoscopic procedures were 185 – 280 minutes). Four cohort studies reported results for operating time comparing robotic surgery with open surgery. All four studies showed that open surgery was less time consuming (mean operating time for the robotically assisted procedures were 188– 338 minutes and the corresponding figures for the open procedures were 103 – 274 minutes). It was not described in the studies whether the learning curve regarding the new technique for the surgical team had leveled out or not.

Conclusions: It is uncertain whether robotically assisted laparoscopic surgery for rectal cancer is more time consuming than laparoscopic surgery or open surgery.

Very low quality of evidence (GRADE ⊕○○○).

Length of hospital stay

One SR and four cohort studies reported length of hospital stay comparing robotically assisted laparoscopic surgery with laparoscopic surgery. Two of these cohort studies reported shorter hospital stay in the robotically assisted group (e.g. Kang J, 2013, 10.8 ± 5.5 days vs. 13.5 ± 9.2 days, $p < 0.01$). Five cohort studies reported results for length of hospital stay comparing robotically assisted laparoscopic surgery with open surgery. Two of these studies reported shorter hospital stay in the robotic group (e.g. Kang J, 2013, 10.8 ± 5.5 days vs. 16.0 ± 8.6 days, $p < 0.01$). One study showed insignificantly longer and two insignificantly shorter hospital stay in the robotic group.

Conclusions: It is uncertain whether the length of hospital stay is shorter after robotically assisted laparoscopic, compared to laparoscopic or open surgery for rectal cancer (range 5 – 11.1, 10 – 13.5 and 6 – 16.0 days respectively).

Very low quality of evidence (GRADE ⊕○○○).

Results of updated search

An update of the search in January 2014 identified seven articles published after March 2013, fulfilling the PICO criteria. One duplicate was excluded. The remaining included four cohort studies and two case series.

One of the cohort studies (Halabi, 2013) was a large registry study comparing 1425 robotically assisted laparoscopic operations with 9075 laparoscopic operations for rectal cancer. Reported outcomes corresponding to our PICO included length of stay, mortality and complications. There were no significant differences between the groups for any of these outcomes. Specifically, in the robotically assisted and laparoscopic groups the length of stay (median (range) was 6 (4 – 7) and 7 (4 – 8) days. Anastomotic complications occurred in 8.6% and 10.3% and early mortality in 0% and 0.7% of the patients in the two groups respectively.

Another cohort study (Saklani, 2013) included 74 robotically assisted and 64 laparoscopic operations and reported the outcome local recurrence which was not reported in the previous studies. With a mean follow up of 30.1 ± 9.9 months there were two (2.7%) and four (6.3%) local recurrences respectively ($p= 0.420$).

The remaining two cohort studies were small and with a high risk of bias. The two case series did not affect the conclusions regarding complications. In summary, the six articles published after March 2013 neither influenced any of the conclusions nor changed the quality of evidence.

5b Outcome tables – Appendix 1

5c Excluded articles – Appendix 2

5d Ongoing research?

A search in clinicaltrials.gov (2013-08-09) using the search terms ((*rectal OR rectum*) AND (*robot OR robotic OR robot-assisted OR davinci OR da vinci OR zeus*)) identified 15 trials. Four RCT's were relevant for our question.

NCT01423214

A Trial to Assess Robot-assisted Surgery and Laparoscopy-assisted Surgery in Patients With Mid or Low Rectal Cancer

Kyungpook National University, Korea

Started Jun 2013. Expected to be completed Dec 2018. Planned enrollment: 540 patients.

Primary endpoint: quality of rectal cancer surgery, especially in total mesorectal excision quality and a circumferential margin positivity rate.

Secondary endpoint: 3- and 5-year disease-free survival. Pelvic autonomic nerve preservation, short-term morbidity, pathological quality (i.e. number of harvested lymph node), local recurrence, and blood loss during surgery.

NCT01736072

RObotic Versus LAParoscopic Resection for Rectal Cancer (ROLARR)

University of California, Irvine USA

University of Leeds, Great Britain

Started Dec 2011. Expected to be completed Jan 2016. Planned enrollment: 400 patients.

Primary end point: rate of conversion to open surgery (as an indicator of surgical technical difficulty).

Secondary outcome: oncological efficacy (pathological CRM positivity rates)
Other outcome measures: intra-operative and post-operative complications
30-day post-operative mortality. Three-year disease-free and overall survival.
Sexual Dysfunction Assessment.

NCT01591798

Efficacy Study of Robotic Surgery for Rectal Cancer

National Cancer Center, Korea

Started Mar 2012. Expected to be completed Dec 2017. Planned enrollment: 146 patients.

Primary outcome: Quality of mesorectal excision

Secondary outcome: Short-term postoperative outcome. Sexual and urinary function, Quality of life, Anorectal function

Long-term outcome: 3 year disease-free survival.

NCT01130233

Randomized Trial on Robotic Assisted Resection for Rectal Cancer

The University of Hong Kong, China

Started Jun 2009. Expected to be completed Dec 2014. Planned enrollment: 98 patients.

Primary outcome: Bladder function

Secondary outcome: tumor status, recurrence and survival. Quality of life.

6 Which medical societies or health authorities recommend the new health technology?

None at present. The National Board of Health and Welfare are presently rewriting the recommendations for the care of patients with rectal cancer.

Ethical aspects

7 Ethical consequences

It is ethically problematic to introduce robotically assisted laparoscopic surgery for the treatment of rectal cancer into routine clinical practice since the technique is associated with high costs and the hypotheses on patient benefits are not documented.

8a When can this new health technology be put into practice?

In Region Västra Götaland a protocol for a feasibility study has been approved by the Local Ethical Board and negotiations are under way to find operating time at the local da Vinci robot system.

8b Is this technology used in other hospitals in Region Västra Götaland?

No, but in several hospitals in Sweden; Linköping University Hospital, Skåne University Hospital/Malmö, Örebro University Hospital, possibly shortly joined by the Departments of Surgery at Hallands Hospital and Karlstad Hospital.

8c According to the work group, will there be any consequences of the new health technology for personnel?

Training for the entire surgical team. Better working conditions in the operating theatre for the surgeon in the robotic console, unchanged for the rest of the team.

8d Will there be any consequences for other clinics or supporting functions at the hospital or in the whole Region Västra Götaland, Sweden?

Impossible to tell at present time. If the technology is introduced the referrals to a center performing robotically assisted laparoscopic surgery for rectal cancer would probably increase.

9a Present costs of currently used technologies

The average cost, over the last three years (2011-2013), regarding open rectal resection at Sahlgrenska University Hospital/Östra, Göteborg, Sweden is 179 234 SEK. The corresponding cost for a laparoscopic rectal resection is 168 407 SEK, for an open abdominoperineal excision 202 017 SEK and for a laparoscopic abdominoperineal excision 203 789 SEK.

9b Expected costs of the new health technology?

A da Vinci robot (the only available device) costs around 20 – 25 million SEK. The Intuitive Surgical Inc., selling the da Vinci robot, offers training at a European center for 3-5 days. Published data suggests that only one robotically assisted laparoscopic procedure for rectal cancer can be performed per day, i.e. approximately 200 procedures per year. In addition to the investment cost of the machinery comes a yearly cost for the soft-ware, approximately 1-1.5 million SEK and costs for the necessary device-specific disposable instruments. The amount per procedure is at least around 20 000 SEK. This cost does not include staplers.

9c Total change of cost

In our calculation the cost for a da Vinci robot was set at 20 million SEK, the annual license fee at 1 million SEK and the added cost (compared to open surgery) for disposable instruments at 20 000 SEK/operation (see below). The depreciation time was set to 7 years, in accordance with local routine. An assumption on the number of procedures was made, starting at 40 robotically assisted laparoscopic cases the first year and increasing to 60/year the second year and 100/year thereafter. The case-load in our hospital is such that more than 100 cases per year was considered unlikely.

Robot 20 000 000

Depreciation time (years) 7

Annual license fee 1 000 000

Instrument cost /operation 20 000

Year	Operations	Instrument	Robot	Annual fee	Total cost	Cost per operation
1	40	800 000	2 857 143	1 000 000	4 657 143	116 429
2	60	1 200 000	2 857 143	1 000 000	5 057 143	84 286
3	100	2 000 000	2 857 143	1 000 000	5 857 143	58 571
4	100	2 000 000	2 857 143	1 000 000	5 857 143	58 571
5	100	2 000 000	2 857 143	1 000 000	5 857 143	58 571
6	100	2 000 000	2 857 143	1 000 000	5 857 143	58 571
7	100	2 000 000	2 857 143	1 000 000	5 857 143	58 571
Total:	600	12 000 000	20 000 000	7 000 000	39 000 000	493 571

With these calculations, the added cost for a robotically assisted laparoscopic operation for rectal cancer, not counting longer operating times, would be from 116 000 SEK to 59 000 SEK per operation.

9d Can the new technology be adopted and used within the present budget (clinic budget/hospital budget)?

No.

9e Are there any available analyses of health economy? Cost advantages or disadvantages?

One of the studies included in this HTA report is primarily a health economy analysis (Baek SJ, 2012), however the design of the study was not optimal and no efforts were made to make the analysis more generally applicable, such as a sensitivity test. The study concluded that robotically assisted laparoscopic surgery for rectal cancer was more costly, than laparoscopic surgery. Total hospital charges in U.S. dollars (\$14,647 vs. \$9,978; $p = 0.001$).

Unanswered Questions

10a Important gaps in scientific knowledge?

It is unknown if there are any advantages for the robotically assisted laparoscopic surgery regarding:

Long term survival, quality of life, local recurrence, short term outcomes, pathological resection margin, operating time, hospital stay, postoperative recovery and complications (major and minor).

10b Is there any interest in your own clinic/research group/organisation to start studies/trials within the research field at issue?

Yes, a protocol for a feasibility study has been approved by the Local Ethical Board and negotiations are under way to find operating time at the local da Vinci robot system for the 20 cases in that study. The long term plan is to join a randomised trial, depending on time, possibly the ROLARR (c.f. 5d above: NCT01736072). An alternative could be to host a multicenter randomized trial with long-term survival as primary outcome.

Project: Robotically assisted laparoscopic surgery for rectal cancer
 Appendix 1:1 Outcome variable: Disease-free survival

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Intervention: Robot assisted laparoscopic surgery	Control				
Kang J, 2013	Korea	Cohort	165/165 165/165	#	83.5% (n.s.)	Laparoscopic surgery 81.9% Open surgery 79.7%	2 year disease-free survival Follow-up: 22.4 months (range, 1–48 months) #”None of the patients were lost to follow-up according to the text.”	?	+	?

Project: Robotically assisted laparoscopic surgery for rectal cancer
 Appendix 1:2:1 Robot assisted vs. laparoscopic surgery
 Outcome variable: Pathological resection margin

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Robot assisted laparoscopic surgery	Laparoscopic surgery				
Trastulli S, 2012	Italy	Meta-analysis of six non-randomized cohort studies	274/346		CRM positive 2.9% p=0.62 DRM WMD laparoscopic vs. robot-assisted 0.09 (CI -0.14 – 0.32) p=0.46	3.0%	CRM, Circumferential resection margin DRM, Distal resection margin WMD= Weighted mean difference #The Trastulli et al authors' overall quality score (modified Newcastle-Ottawa scale) of the included studies: Median, (range): 6.5 (5 – 9)	#	#	#
D'Annibale A, 2013	Italy	cohort	50/50	-	CRM positive, N 0 (p= 0.022) DRM, cm. Mean (SD) 3 (1.1) (range 2–7) (p= 0.908)	6 (12%) 3 (1.6) (range 1–6)	CRM: < 2 mm DRM: cm 6 conversions in Laparoscopic group first 50 laparoscopic operations	-	-	-
Kim JY, 2012	Korea	cohort	30/39	-	CRM positive: N(%): 2 (6%), p= 0.407 DRM Mean (SD): 2.79 (1.02) p= 0.816	1 (2.5) 2.86 (1.36)	CRM positive: ≤ 1mm	-	-	-
Park SY, 2013	Korea	cohort	40/40	-	CRM positive: n (%) 3 (7.5) p= 1 DRM, cm Mean (SD) 1.4 (0.9), p= 0.619	2 (5.0) 1.3 (0.9)	CRM positive: ≤1 mm	-	-	-
Kang J, 2013	Korea	cohort	165/165	-	CRM positive: (%): (4.2%) n.s. DRM: Mean (SD), cm 1.9 (1.4)	11 (6.7) 2.0 (1.7)	CRM positive not defined	?	+	?

Project: Robotically assisted laparoscopic surgery for rectal cancer
 Appendix 1:2:2 Robot assisted laparoscopic vs. open surgery
 Outcome variable: Pathological resection margin

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Robot assisted laparoscopic surgery	Open surgery				
Bertani E, 2011	Italy	cohort	52/34	-	CRM positive n (%) 2 (4%) DRM, mm. Median (range) 26 (1-70)	2 (6) 26 (1-80)	CRM= Circumferential resection margin; positive not defined DRM= Distal resection margin	-	-	-
Biffi R, 2011	Italy	cohort	49/105	-	CRM positive, n (%): 0, (p=1) DRM, cm Mean (SD) 2.9 (1.6) (p= <0.001)	2 (1.9) 1.9 (1.2),	CRM positive not defined	?	?	-
deSouza AL , 2011	US	cohort	36/46(51)	0/5	CRM positive n, (%): 0, n.s. DRM positive n (%): 1 (2.8)	3 (6.5) 0	CRM or DRM positive not defined	-	-	-
Kim JC, 2012	Korea	cohort	100/100	-	CRM positive, n 1, (p=1) DRM,cm Mean (SD) 2.7 (1.7) (p=0.001)	1 1.9 (1.3)	DRM positive = ≤ 1mm	-	-	-
Kang J, 2013	Korea	cohort	165/165	-	CRM positive: n (%) 7 (4.2%) , p = 0.034 DRM, cm Mean (SD) 1.9 (1.4)	17 (10.3) 2.2 (1.7)	CRM positive not defined	?	+	?

Project: Robotically assisted laparoscopic surgery for rectal cancer
 Appendix 1:3:1 Robot assisted vs. laparoscopic surgery
 Outcome variable: Postoperative bowel function

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Robot assisted laparoscopic surgery	Laparoscopic				
Trastulli S, 2012	Italy	Meta-analysis of four studies	246/364	#	Time to regular diet, days WMD robotic minus laparoscopic: -0.43 CI -1.06 to 0.20 p=0.18		WMD= Weighted mean difference #The Trastulli et al authors' overall quality score (modified Newcastle-Ottawa scale) of the included studies: Median, (range): 6.5 (5 – 9)	#	#	#
Baek SJ, 2012	Korea	cohort	154/150	-	Time, days. Mean (SD) to: -flatus passage 2.1 (1.0) (range 0–8) p=0.656 -defecation 2.5 (1.2) (range 0–7), p=0.208 -oral feeding 3.0 (2.2) (range 1–17), p=0.781	2.2 (1.0) (range 0–7) 2.7 (1.3) (range 0–8) 2.9 (2.4) (range 1–21)		-	-	?
D'Annibale A, 2013	Italy	cohort	50/50	-	Time to: oral feeding (days) Median, interquartile range 3 (3–5), p=0.005	5 (4–6)		-	-	+
Park SY, 2013	Korea	cohort	40/40	-	Time, days. Mean (SD) to: -flatus passage 2.4 (1.6), p=0.572 -oral feeding 7.5 (3.5), p=0.359	2.5 (1.3) 7.7 (2.3)		-	-	-
Kang J, 2013	Korea	cohort	165/165	-	Time, days. Mean (SD) to: -flatus passage 2.2 (1.1), p<0.001 -oral feeding 4.5 (1.9), p<0.001	2.4 (1.2) 5.2 (2.4)		?	+	+

Project: Robotically assisted laparoscopic surgery for rectal cancer
 Appendix 1:3:2 Robot assisted laparoscopic vs. open surgery
 Outcome variable: Postoperative bowel function

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Robot assisted laparoscopic surgery	Open surgery				
Bertani E, 2011	Italy	cohort	52/34	-	Time, days. Median (range) -flatus passage 2 (1-5), p= 0.003 -oral intake 2 (1-13), p= 0.001	3 (1-9) 3 (2-12)		?	-	+
Kim JC, 2012	Korea	cohort	100/100	-	Time to flatus passage, days. Mean (SD) 2.1 (0.9)	3.1 (1)		?	-	-
Kang J, 2013	Korea	cohort	165/165	-	Time, days Median (SD) to: -flatus passage: 2.2 (1.1), p= <0.001 -resumed soft diet: 4.5 (1.9), p= <0.001	3.0 (1.4) 6.4 (2.5)		?	+	+

Project: Robotically assisted laparoscopic surgery for rectal cancer
 Appendix 1:4:1 Robot assisted laparoscopic vs. laparoscopic surgery
 Outcome variable: Operative time in minutes

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Robot assisted laparoscopic surgery	Laparoscopic surgery				
Trastulli S, 2012	Italy	Meta-analysis of seven cohort studies	341/461	-	WMD robot assisted minus laparoscopic: 21 minutes (CI -11 to 54) P= 0.20		WMD= Weighted mean difference #The Trastulli et al authors' overall quality score (modified Newcastle-Ottawa scale) of the included studies: Median, (range): 6.5 (5 – 9)	#	#	#
Baek SJ, 2012	Korea	cohort	154/150	-	Mean (SD) 285.2 (69.1) (range 130–475), p=0.018	219.7 (71.2) (range 95–465)	"additional time in robotic surgery for docking, but trends show that docking time decreased as the surgical teams gained experienced." "difference in tumor characteristics led to an increase in operative time"	-	-	?
D'Annibale A, 2013	Italy	cohort	50/50	-	Median (range) 270 (240–315) p=0.863	280 (240–350)	The laparoscopic operations were the first 50 to be performed in this clinic. It is unclear if the robot assisted surgery were the first?	-	-	-
Park SY, 2013	Korea	cohort	40/40	-	Mean (SD) 235.5 (57.5), p= 0.001	185.4 (72.8)	A comparison of intersphincteric resection for low RC "operation time of the last five cases was around 180 min, which is similar to the mean operation time of the L-ISR group. Therefore, the final comparison of operation times of R-ISR and L-ISR can be achieved after additional stabilization of R-ISR "	-	-	?
Kang J, 2013	Korea	cohort	165/165	-	Mean (SD) 309.7 (115.2), p = 0.012	277.8 (81.9)		?	+	?

Project: Robot assisted laparoscopic surgery for rectal cancer
 Appendix 1:4:2 Robot assisted laparoscopic vs. open surgery
 Outcome variable: Operative time in minutes

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Robot assisted laparoscopic surgery	Open surgery				
Bertani E, 2011	Italy	cohort	52/34	-	Median (range) 260 (190–570) p= 0.001	164 (100–350)		?	-	+
deSouza AL, 2011	US	cohort	36/51	0/5	Mean (SD) 337.9 (81.8) p=0.003	273.8 (100.8)	Open procedure via hand port ”the initial few cases in the robotic group were used to standardize the technique for robotic TME. These early cases, together with the initial learning curves of the 2 surgeons and the additional time to dock and undock the robot, contributed to the increased operative time”	-	-	+
Kim JC, 2012	Korea	cohort	100/100	-	Mean (SD) 188 (45), p<0.001	103 (23)	Substantially shorter op time, in both groups compared to the other included studies	+	-	+
Kang J, 2013	Korea	cohort	165/165	-	Mean (SD) 309.7 (115.2) p< 0.001	252.6 (88.1)		?	+	+

Project: Robotically assisted laparoscopic surgery for rectal cancer
 Appendix 1:5:1 Robot assisted vs. laparoscopic surgery
 Outcome variable: Length of stay in days

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Robot assisted	Laparoscopic				
Trastulli S, 2012	Italy	Meta-analysis of seven studies	341/461	-	WMD robotic minus laparoscopic :-0.60 days, p=0.66 (CI-1.76 to 0.43)		WMD= Weighted mean difference #The Trastulli et al authors' overall quality score (modified Newcastle-Ottawa scale) of the included studies: Median, (range): 6.5 (5 – 9)	#	#	#
Baek SJ, 2012	Korea	cohort	154/150	-	Mean (SD) 11.1 (7.0) (range 5–50), p=0.819	10.8 (8.6) (range 4–75)	Primarily an economic analysis.	-	-	?
D'Annibale A, 2013	Italy	cohort	50/50	-	Median (interquartile range) 8 (7–11), p=0.034	10 (8–14)	"The shorter hospital LOS may be related to the lower complication rate for R-TME and the shorter time to oral diet compared to that of L-TME"	-	-	?
Park SY, 2013	Korea	cohort	40/40	-	Mean (SD) 10.6 (4.2), p= 0.113	11.3 (3.6)		-	-	-
Kang J, 2013	Korea	cohort	165/165	-	Mean (SD) 10.8 (5.5), p<0.001	13.5 (9.2)		?	+	+

Project: Robotically assisted laparoscopic surgery for rectal cancer
 Appendix 1:5:2 Robot assisted laparoscopic vs. open surgery
 Outcome variable: Length of stay in days

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Robot assisted laparoscopic surgery	Open surgery				
Bertani E, 2011	Italy	cohort	52/34	-	Median (range) 5 (4–17), p=0.153	6 (5–32)		?	-	-
Biffi R, 2011	Italy	cohort	49/105	-	Mean (SD) 8.4 (9.3), p < 0.001	12.4 (3.2)	A consecutive period of six years (three per group). During this study period, <i>the practice of care</i> , perioperative management, was not changed in the institution according to the text. A higher prevalence of the American Society of Anesthesiologists (ASA) class 3 in the open surgery group.	-	?	+
deSouza AL, 2011	US	cohort	36/46(51)	0/5	Mean (SD) 7.0 (5.8), p = 0.16	7.3 (4.1)		-	-	-
Kim JC, 2012	Korea	cohort	100/100	-	Mean (SD) 7.1 (2.1), p = 0.308	6.9 (1.5)		?	-	-
Kang J, 2013	Korea	cohort	165/165	-	Mean (SD) 10.8 (5.5), p <0.001	16.0 (8.6)		?	+	+

Project: Robotically assisted laparoscopic surgery for rectal cancer
 Appendix 1:6:1 Robot assisted vs. laparoscopic surgery
 Outcome variable: Complications

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Robot assisted laparoscopic surgery	Laparoscopic surgery				
Trastulli S, 2012	Italy	Meta-analysis of seven cohort studies	316/424		Anastomotic leakage 6.9%, p= 0.83	7.5%	# The Trastulli et al authors' overall quality score (modified Newcastle-Ottawa scale) of the included cohort studies: Median, (range): 6.5 (5 – 9)	#	#	#
			278/358		Prolonged postoperative ileus 3.6%, p= 0.55	2.5%				
			192/246		Wound infection 2.6%, p= 0.72	3.6%				
			152/223		Overall morbidity 19.7%, p= 0.95	18.8%				
			147/226		Overall mortality 0.7%, p= 0.86	0.4%				
Baek SJ, 2012	Korea	cohort	154/150	-	Anastomotic leakage 17 (11.0 %) Anastomotic bleeding 4 (2.6%) Postoperative ileus 19 (12.3%) Other 10 (6.5%)	8 (12.0 %) 2 (1.3 %) 7 (4.7 %) 14 (9.3 %)	Other: Not specified How was leakage detected?	-	-	-
D'Annibale A, 2013	Italy	cohort	50/50	-	Anastomotic leakage: 5 (10%), p=0.998 Other: 0, p=0.104 IPSS Mean (SD) 3.24 (2.7) pre-operative, p=0.012 3.53 (2.5) at 1 year, p=0.06 IIEF: No ED 17, p=0.045	7 (14%) Other: 2 pulm infection 1 wound infection 1 not specified 3.50 (3) 4.2 (2.3) IIEF: No ED 10	International prostate symptom score(IPSS) International index of ED= erectile dysfunction, (IIEF) IPSS and IIEF on 30/30 males	-	-	-

Project: Robotically assisted laparoscopic surgery for rectal cancer
 Appendix 1:6:1 Robot assisted vs. laparoscopic surgery
 Outcome variable: Complications

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Robot assisted laparoscopic surgery	Laparoscopic surgery				
Kim JY, 2012	Korea	cohort	30/39 18/20 (males)	-	“IPSS” n.s. difference after 6 months but faster recovery to preoperative values for the “robot group” IIEF: n.s. differences between the groups faster recovery for robot group	“IPSS” n.s. difference after 6 months	IPSS was the base for the analysis of voiding difficulties AND also used for women! Not validated? The IIEF score value was n.s. different at any time between the two groups	-	-	-
Park SY, 2012	Korea	cohort	40/40	-	Anastomotic leakage 3 Intra-abdominal infection 1 Colon ischemia 1 Urinary retention 1 overall: p= 0.745	2 1 1 1	voiding dysfunction, erectile dysfunction and faecal incontinence also analysed, but for a small male sub group consisting of 14/15 patients	-	-	-
Kang J, 2013	Korea	cohort	165/165/ 165	-	Overall n=34 (20.6%) Anastomotic leakage 12 (7.3) Wound infection 1 (0.6) Intrapelvic abscess 7 (4.2) Voiding problem 4 (2.4) Ileus/obstruction 6 (3.6) Postoperative bleeding 2 (1.2) Ischemic colitis 0 (0) Ureteral injury 0 (0) Trocar site hernia 1 (0.6) Rectovaginal fistula 0 (0) Small bowel perforation 1 (0.6) Respiratory problem 0 (0) Cardiology problem 1 (0.6)	46 (27.9%) 17 (10.8) 2 (1.2) 5 (3.0) 7 (4.2) 9 (5.5) 1 (0.6) 1 (0.6) 1 (0.6) 0 (0) 0 (0) 0 (0) 1 (0.6) 1 (0.6)		?	+	?

Project: Robotically assisted surgery for rectal cancer
 Appendix 1:6:2 Robot assisted vs. open surgery
 Outcome variable: Complications

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Robot assisted surgery	Open				
Bertani E, 2011	Italy	cohort	52/34	-	Wound infections 1 Anastomotic leaks 6 Abdominal abscess 1 Other 6	5 3 2 1	"other complications" not defined	+	-	-
Biffi R, 2011	Italy	cohort	49/105	-	Postoperative transfusions Patients, N (%) 1 (2.0) Units, N 1 Infectious 8 (16.3) Non-infectious 10 (20.4) Both 0 Overall 18 (36.7)	6 (5.7) p=0.432 12 p=0.051 15 (14.3) p=0.189 11 (10.5) 5 (4.5) 31 (29.5) p=0.371		?	-	-
deSouza AL, 2011	US	cohort	36/46(51)	0/5	Anastomotic leak 2 Neuropathy 2 CVA 1 SBO 1 <i>Clostridium difficile</i> colitis 1 DVT 1 Erectile dysfunction/retrograde ejaculation 1 Aspiration pneumonia 2 High-output ileostomy 0 UTI 0 Cardiac complication 0 Mortality 1	1 0 1 8 0 2 1 0 7 1 2 1	CVA <input type="checkbox"/> cerebrovascular accident SBO <input type="checkbox"/> subacute bowel obstruction DVT <input type="checkbox"/> deep venous thrombosis UTI <input type="checkbox"/> urinary tract infection	-	-	-

Project: Robotically assisted surgery for rectal cancer
 Appendix 1:6:2 Robot assisted vs. open surgery
 Outcome variable: Complications

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result		Comments	Directness*	Study limitations *	Precision *
					Robot assisted surgery	Open				
Kang J, 2013	Korea	cohort	165/165/ 165	-	Overall n=34 (20.6%) Anastomotic leakage 12 (7.3) Wound infection 1 (0.6) Intrapelvic abscess 7 (4.2) Voiding problem 4 (2.4) Ileus/obstruction 6 (3.6) Postoperative bleeding 2 (1.2) Ischemic colitis 0 (0) Ureteral injury 0 (0) Trocar site hernia 1 (0.6) Rectovaginal fistula 0 (0) Small bowel perforation 1 (0.6) Respiratory problem 0 (0) Cardiology problem 1 (0.6)	41 (24.8) 5 (3.4) 8 (4.8) 6 (3.6) 14 (8.5) 4 (2.4) 1 (0.6) 0 (0) 0 (0) 0 (0) 1 (0.6) 0 (0) 2 (1.2) 0 (0)		?	+	?
Kim JC, 2012	Korea	cohort	100/100 41/38	-	Ileus: 3 Anastomotic leak: 2 voiding difficulty 6 sexual dysfunction: 15	3 4 7 13	Voiding difficulty = reinsertion of catheter/medication Sexual dysfunction only males. Poorly defined	?	-	-

Project: Robotically assisted surgery for rectal cancer
 Appendix 1:6:3 Case series of robot assisted laparoscopic surgery
 Outcome variable: Complications

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result	Comments	Directness*	Study limitations *	Precision *
					Robot assisted laparoscopic surgery				
Kang J, 2011	Korea	Case series	389		TOTAL: 74(19%) Anastomotic leakage 27(7) Wound infection 2(0.5) Intrapelvic abscess 12(3.1) Voiding difficulty 13(3.3) Ileus/obstruction 12(3.1) Rectovaginal fistula 2(0.5) Postoperative bleeding 3(0.8) Subcutaneous emphysema 1(0.3) Ischemic colitis 1(0.3) Trocar site herniation 1(0.3)	Consecutive patients operated for rectal cancer June 2006 – October 2010			
Pigazzi A, 2010	Italy	Case series	143		Total: 59(41.3%) Ileus 8(12.6) Anastomosis leakage 15(10.5) Abscess 10(7) Urinary retention 5(3.5) Wound dehiscence 4(2.8) Fistula 2(1.4) Neurogenic bladder 2(1.4) Ureteral injury 2(1.4) Fever 2(1.4) DVT 2(1.4) Aspiration pneumonia 1(0.7) ARF 1(0.7) Stenosis 1(0.7) Enteritis 1(0.7) Pleural effusion 1(0.7) Intraoperative bleeding 1(0.7) Mortality 0	(112 with anastomoses)			

Project: Robotically assisted surgery for rectal cancer
 Appendix 1:6:3 Case series of robot assisted laparoscopic surgery
 Outcome variable: Complications

* + No problem
 ? Some problems
 - Major problems

Author, year	Country	Study design	Number of patients n=	With drawals - dropouts	Result	Comments	Directness*	Study limitations *	Precision *
					Robot assisted laparoscopic surgery				
Baik SH 2013	Korea	Case series	370		Mild complications 47 (12.7) Moderate complications 8 (2.2) Severe complications 31 (8.4), whereof: Ischemic colitis 1 (0.3) Rectovaginal fistula 1 (0.3) Intra-abdominal abscess 1 (0.3) Anastomotic leakage (total) 28 (7.7) Deaths 0				

Project: Robotically assisted laparoscopic surgery for rectal cancer
 Appendix 2

Study (author, publication year)	Reason for exclusion
Baek JH 2011 Robotic and laparoscopic	Included in the SR
Baik SH 2008 Robotic tumor-specific	Duplicate publication
Baik SH 2009 Robotic versus	Included in the SR
Bianchi PP 2010	Included in the SR
Kang J 2012 Transanal specimen	Duplicate publication
Kim HJ 2013	Incorrect outcome
Kwak JM 2011	Included in the SR. Also duplicate publication
Lin S 2011	Not the latest SR
Memon S 2012	Not the latest SR
Ortiz-Oshiro 2012	Not the latest SR
Park JS 2010 Robotic-assisted	Included in the SR
Park JS 2011	Included in the SR
Patel CB 2011	Too few patients according to our limitations
Patrioti A 2009	Included in the SR

Project: Robotically assisted laparoscopic surgery for rectal cancer
Appendix 2

Study (author, publication year)	Reason for exclusion
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Popescu I 2011	Included in the SR
Scarpinata R 2013	Systematic review judged to be of inferior quality than the SR included in the report
Yang Y 2012	Systematic review judged to be of inferior quality than the SR included in the report

Appendix 3, Search strategy, study selection and references

Question at issue, PICO:

In adult patients with rectal cancer, is robotically assisted laparoscopic surgery better than laparoscopic or open surgery concerning long time survival, health related quality of life and local recurrence?

P= Patients, I= Intervention, C= Comparison, O=Outcome

P= Adult patients with rectal cancer, who are about to undergo surgical treatment with curative intention

I= Robotically assisted laparoscopic rectal resection or amputation

C1= Laparoscopic rectal resection or amputation

C2= Open rectal resection or amputation

O= Critical*:

Long term survival

Long term health related quality of life, measured with validated instruments

Local recurrence

Important:*

Pathological resection margin

(e.g. measured with CRM - circumferential resection margin and/or DRM – distal resection margin)

Complications

Postoperative rehabilitation

Not important:*

Operating time

Length of hospital stay

*Imply critical, important or not important for decision making.

Eligibility criteria

Study design:

Systematic reviews or meta-analyses

Randomized Controlled Trials, ≥ 15 in each group

Non-randomized controlled studies, ≥ 15 in each group

Case series etc. if ≥ 100 patients

No case reports or review articles

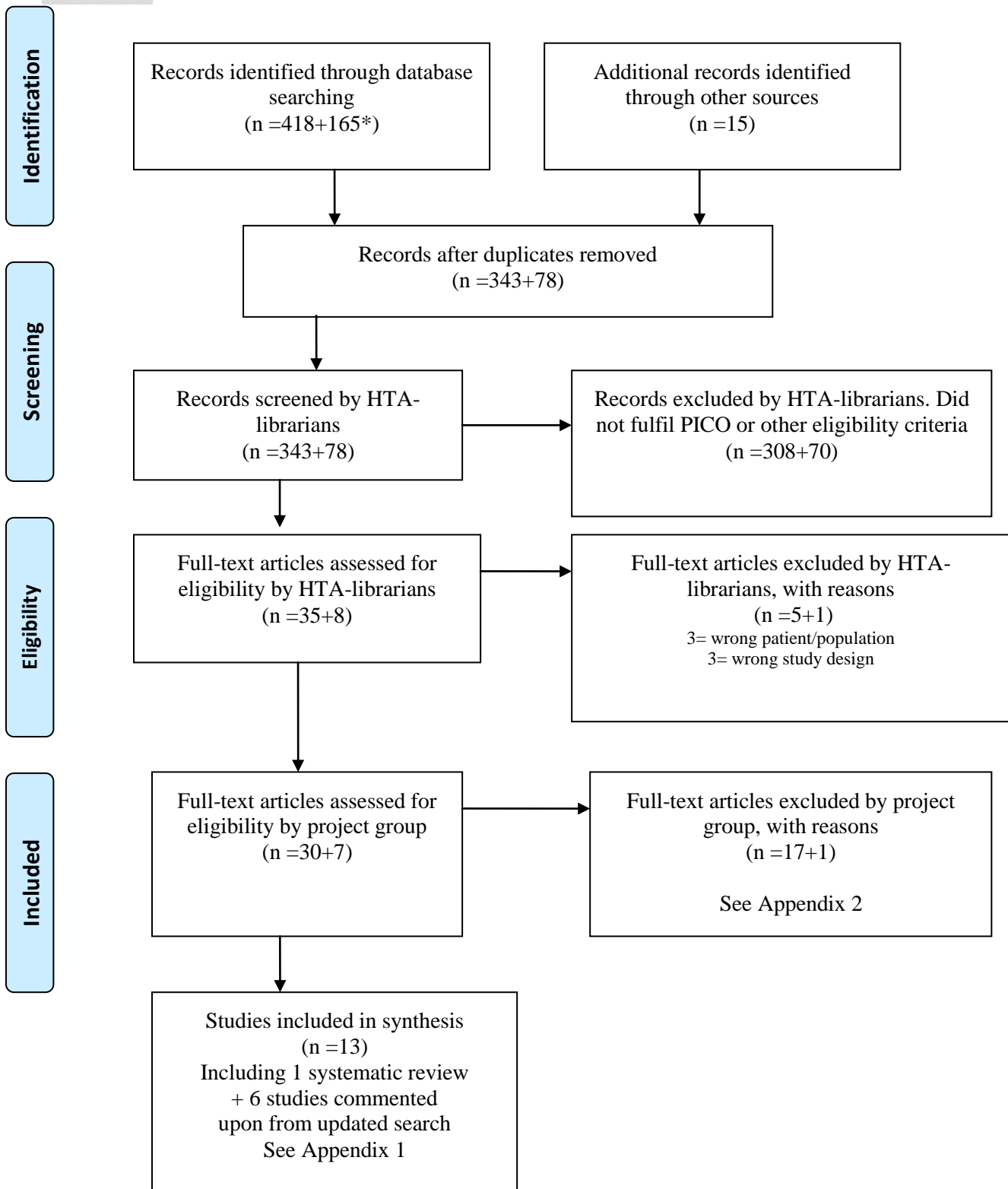
Publication date:

No limit

Language:

Danish, English, French, German, Norwegian, Swedish

Selection process – flow diagram



* Results from the updated search are added with +165 etc.

Search strategies

Database: PubMed

Date: 2013-03-18

No of results: 224

Search updated: 2014-01-29, 62 results

Search	Query	Result
#26	Search #24 NOT #23 Filters: Danish; English; Norwegian; Swedish	224
#25	Search #24 NOT #23	241
#24	Search #21 NOT #22	246
#23	Search ((animals[mh]) NOT (animals[mh] AND humans[mh]))	3762847
#22	Search Editorial[ptyp] OR Letter[ptyp] OR Comment[ptyp] OR case reports[ptyp]	2670078
#21	Search #20 AND #17	284
#20	Search #19 OR #18	43801
#19	Search robot* OR surgery, computer-assisted[mesh] OR computer assist*[tiab] OR da vinci[tiab] OR zeus[tiab] OR telesurgical system*[tiab]	43801
#18	Search robotics[mesh]	11216
#17	Search #16 OR #15	62977
#16	Search #13 AND #14	59857
#15	Search rectal neoplasms[mesh]	35679
#14	Search cancer OR carcinom* OR neoplas* OR tumor OR tumors OR tumour OR tumours OR sarcom* OR adenocarcinom* OR adeno-carcinom* OR adenom* OR lesion* OR malign*	3526996
#13	Search rectal OR rectum	109365

Database: EMBASE (OVID SP)

Date: 2013-03-18

No of results: 166

Search updated: 2014-01-29, 54 results

#	Searches	Results
1	exp rectum tumor/	135801
2	(rectal or rectum).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	134467
3	(cancer or carcinom* or neoplas* or tumor or tumors or tumour or tumours or sarcom* or adenocarcinom* or adeno?carcinom* or adenom* or lesion* or malign*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	3765606
4	((rectal or rectum) adj3 (cancer or carcinom* or neoplas* or tumor or tumors or tumour or tumours or sarcom* or adenocarcinom* or adeno?carcinom* or adenom* or lesion* or malign*)).mp.	47853
5	1 or 4	140466
6	exp robotics/	18481
7	exp computer assisted surgery/	5743
8	(computer assist* adj3 surger*).mp. [mp=title, abstract, subject headings, heading word, drug	13500

	trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	
9	(robot* or da vinci or zeus or telesurgical system*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]	26930
10	6 or 7 or 8 or 9	38837
11	5 and 10	669
12	limit 11 to (embase and (danish or english or norwegian or swedish) and (article or conference paper or "review"))	166

Database: The Cochrane Library

Date: 2013-03-18

No of results: 12

Cochrane reviews 1

Other reviews 5

Clinical trials 5

Economic evaluations 1

Search updated: 2014-01-29, 9 results

ID	Search	Hits
#1	MeSH descriptor: [Rectal Neoplasms] explode all trees	1056
#2	cancer or carcinom* or neoplas* or tumor or tumors or tumour or tumours or sarcom* or adenocarcinom* or adeno?carcinom* or adenom* or lesion* or malign*:ti,ab,kw (Word variations have been searched)	83111
#3	rectal or rectum:ti,ab,kw (Word variations have been searched)	5696
#4	#2 and #3	2425
#5	#1 or #4	2475
#6	MeSH descriptor: [Robotics] explode all trees	337
#7	robot* or da vinci or zeus or telesurgical system*:ti,ab,kw (Word variations have been searched)	522
#8	computer assist* near/3 surger*:ti,ab,kw (Word variations have been searched)	458
#9	#6 or #7 or #8	898
#10	#5 and #9	12

Database: CRD

Date: 2014-02-10*

No of results: 40*

**During the updated search an error was discovered in the original search. The entire search was re-done. Nothing new of relevance was identified when compared to the original search.*

ID	Search	Hits
1	((rectum) OR (rectal))	737
2	((robot*) OR (computer*))	2693
3	((robot*) OR (computer assist*))	807
4	#2 OR #3	2693
5	#1 AND #4	40

The web-sites of **SBU, Kunnskapssenteret** and **Sundhedsstyrelsen** were visited
2011-03-18

Nothing relevant to the question at issue was found

Reference lists

A comprehensive review of reference lists brought 15 new records

Reference lists

Included studies:

Baek SJ, Kim SH, Cho JS, Shin JW, Kim J. Robotic versus conventional laparoscopic surgery for rectal cancer: a cost analysis from a single institute in Korea. *World journal of surgery*. 2012 Nov;36(11):2722-9.

Baik SH, Kim NK, Lim DR, Hur H, Min BS, Lee KY. Oncologic Outcomes and Perioperative Clinicopathologic Results after Robot-assisted Tumor-specific Mesorectal Excision for Rectal Cancer. *Ann Surg Oncol*. 2013 Feb 16. PubMed PMID: 23417433. Epub 2013/02/19.

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Biffi R, Luca F, Pozzi S, Cenciarelli S, Valvo M, Sonzogni A, et al. Operative blood loss and use of blood products after full robotic and conventional low anterior resection with total mesorectal excision for treatment of rectal cancer. *Journal of robotic surgery*. 2011 Jun;5(2):101-7.

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Kang J, Min BS, Park YA, Hur H, Baik SH, Kim NK, et al. Risk factor analysis of postoperative complications after robotic rectal cancer surgery. *World journal of surgery*. 2011;35(11):2555-62.

Kang J, Yoon KJ, Min BS, Hur H, Baik SH, Kim NK, et al. The impact of robotic surgery for mid and low rectal cancer: a case-matched analysis of a 3-arm comparison--open, laparoscopic, and robotic surgery. *Ann Surg*. 2013 Jan;257(1):95-101.

Kim JC, Yang SS, Jang TY, Kwak JY, Yun MJ, Lim SB. Open versus robot-assisted sphincter-saving operations in rectal cancer patients: techniques and comparison of outcomes between groups of 100 matched patients. *The international journal of medical robotics + computer assisted surgery : MRCAS*. 2012 Dec;8(4):468-75.

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Pigazzi A, Luca F, Patrì A, Valvo M, Ceccarelli G, Casciola L, et al. Multicentric study on robotic tumor-specific mesorectal excision for the treatment of rectal cancer. *Ann Surg Oncol*. 2010;17(6):1614-20.

Trastulli S, Farinella E, Cirocchi R, Cavaliere D, Avenia N, Sciannone F, et al. Robotic resection compared with laparoscopic rectal resection for cancer: systematic review and meta-analysis of short-term outcome. *Colorectal Dis*. 2012 Apr;14(4):e134-56.

Articles from updated search, no critical appraisal done:

Erguner I, Aytac E, Boler DE, Atalar B, Baca B, Karahasanoglu T, et al. What have we gained by performing robotic rectal resection? Evaluation of 64 consecutive patients who underwent laparoscopic or robotic low anterior resection for rectal adenocarcinoma. *Surg Laparosc Endosc Percutan Tech*. 2013;23(3):316-9.

Halabi WJ, Kang CY, Jafari MD, Nguyen VQ, Carmichael JC, Mills S, et al. Robotic-assisted colorectal surgery in the United States: a nationwide analysis of trends and outcomes. *World J Surg*. 2013;37(12):2782-90.

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Excluded studies:

Baek JH, Pastor C, Pigazzi A. Robotic and laparoscopic total mesorectal excision for rectal cancer: a case-matched study. *Surg Endosc.* 2011;25(2):521-5.

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Yang Y, Wang F, Zhang P, Shi C, Zou Y, Qin H, et al. Robot-assisted versus conventional laparoscopic surgery for colorectal disease, focusing on rectal cancer: a meta-analysis. *Ann Surg Oncol*. 2012;19(12):3727-36.

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Baek SJ, Al-Asari S, Jeong DH, Hur H, Min BS, Baik SH, et al. Robotic versus laparoscopic coloanal anastomosis with or without intersphincteric resection for rectal cancer. *Surg Endosc*. 2013 Nov;27(11):4157-63.

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Available from:

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Appendix 4

Summary of Findings: Robotically assisted laparoscopic (RAL) versus laparoscopic (LAP) or open (OS) rectal cancer surgery

Outcome variable	Design Number of studies	Study limitations	Consistency	Directness	Precision	Publication bias	Magnitude of effect	Absolute effect	Quality of evidence GRADE
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Disease-free 2-year survival RAL vs LAP	1 Cohort	No serious limitations	No important inconsistency	Some uncertainty (0?)	Serious imprecision (-1)	Unlikely	Not relevant	RAL 83.5% LAP 81.9%	⊕○○○ Very low
Disease-free 2-year survival RAL vs OS	1 Cohort	No serious limitations	No important inconsistency	Some uncertainty (0?)	Serious imprecision (-1)	Unlikely	Not relevant	RAL 83.5% OS 79.7%	⊕○○○ Very low
Positive circumferential resection margin RAL vs LAP	1 SR 4 cohort	Serious limitations (-1)	No important inconsistency	Serious indirectness (-1)	Uncertain precision (0?)	Unlikely	Not relevant	RAL range 0 – 7.5% LAP range 2.5 – 12%	⊕○○○ Very low
Positive circumferential resection margin RAL vs OS	5 Cohort	Serious limitations (-1)	No important inconsistency	Serious indirectness (-1)	Uncertain precision (0?)	Unlikely	Not relevant	RAL range 0 – 4.2% OS range 1 – 10.3%	⊕○○○ Very low
Bowel function recovery – time to first flatus (days) RAL vs LAP	3 Cohort	Serious limitations (-1)	No serious inconsistency	Serious indirectness (-1)	No imprecision	Unlikely	Not relevant	RAL range 2.1 – 2.4 LAP range 2.2 – 2.5	⊕○○○ Very low
Bowel function recovery – time to first flatus (days) RAL vs OS	3 Cohort	Serious limitations (-1)	No serious inconsistency	Serious indirectness (-1)	No imprecision	Unlikely	Not relevant	RAL range 2.0 – 2.2 OS range 3.0 – 3.1	⊕○○○ Very low

Appendix 4

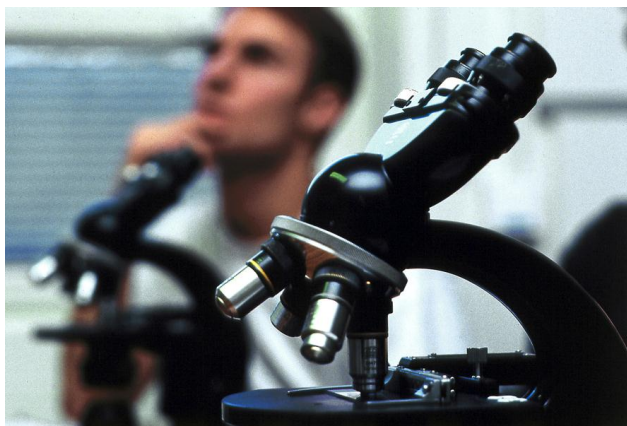
Summary of Findings: Robotically assisted laparoscopic (RAL) versus laparoscopic (LAP) or open (OS) rectal cancer surgery

Outcome variable	Design Number of studies	Study limitations	Consistency	Directness	Precision	Publication bias	Magnitude of effect	Absolute effect	Quality of evidence GRADE
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Operative time (minutes) RAL vs LAP	1 SR 4 cohort	Serious limitations (-1)	No serious inconsistency	Serious indirectness (-1)	No imprecision	Unlikely	Not relevant	RAL range 236 – 310 LAP range 185 – 278	⊕○○○ Very low
Operative time (minutes) RAL vs OS	4 cohort	Serious limitations (-1)	No serious inconsistency	Serious indirectness (-1)	No imprecision	Unlikely	Not relevant	RAL range 188 – 338 OS range 103 - 274	⊕○○○ Very low
Length of stay (days) RAL vs LAP	1 SR 4 cohort	Serious limitations (-1)	No serious inconsistency	Serious indirectness (-1)	No imprecision	Unlikely	Not relevant	RAL range 8 – 11.1 LAP range 10 – 13.5	⊕○○○ Very low
Length of stay (days) RAL vs OS	5 cohort	Serious limitations (-1)	No serious inconsistency	Serious indirectness (-1)	No imprecision	Unlikely	Not relevant	RAL range 5 – 10.8 OS range 6 – 16.0	⊕○○○ Very low

Region Västra Götaland, HTA-centrum

Health Technology Assessment
Regional activity-based HTA



HTA

Health technology assessment (HTA) is the systematic evaluation of properties, effects, and/or impacts of health care technologies, i.e. interventions that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in health care.

To evaluate the quality of evidence the Centre of Health Technology Assessment in Region Västra Götaland is currently using the GRADE system, which has been developed by a widely representative group of international guideline developers. According to GRADE the level of evidence is graded in four categories:

High quality of evidence	= (GRADE ⊕⊕⊕⊕)
Moderate quality of evidence	= (GRADE ⊕⊕⊕○)
Low quality of evidence	= (GRADE ⊕⊕○○)
Very low quality of evidence	= (GRADE ⊕○○○)

In GRADE there is also a system to rate the strength of recommendation of a technology as either “strong” or “weak”. This is presently not used by the Centre of Health Technology Assessment in Region Västra Götaland. However, the assessments still offer some guidance to decision makers in the health care system. If the level of evidence of a positive effect of a technology is of high or moderate quality it most probably qualifies to be used in routine medical care. If the level of evidence is of low quality the use of the technology may be motivated provided there is an acceptable balance between benefits and risks, cost-effectiveness and ethical considerations. Promising technologies, but a very low quality of evidence, motivate further research but should not be used in everyday routine clinical work.

Christina Bergh, Professor, MD.
Head of HTA-centrum

