Systematic review

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Possible benefits of robot-assisted rectal cancer surgery regarding urological and sexual dysfunction: a systematic review and meta-analysis

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Abstract

Aim Robot-assisted surgery for rectal cancer may result in lower rates of urogenital dysfunction compared with laparoscopic surgery. A systematic review was conducted of studies reporting urogenital dysfunction after robot-assisted rectal cancer surgery.

Method PubMed, Embase and the Cochrane Library were systematically searched in February 2014. All studies investigating urogenital function after robot-assisted rectal cancer surgery were identified. The inclusion criteria for meta-analysis studies required comparison of robot-assisted with laparoscopic surgery and the evaluation of urological and sexual function by validated questionnaire. The outcome was evaluated using the International Prostate Symptom Score (IPSS), the International Index of Erectile Function (IIEF) and the Female Sexual Function Index.

Results Ten studies including 689 patients were included. For the meta-analysis this fell to four including 152 patients in the robotic group and 161 in the laparoscopic group, without heterogeneity. The IPSS score at 3 and 12 months favoured robot-assisted surgery [mean difference (MD) −1.58; 95% CI (−3.1, −0.0), [$P = 0.04$; and MD −0.90 (−1.81, −0.02), $P = 0.05$]. IIEF scores at 3 months' follow-up [MD −2.59 (−4.25, −0.94),] $P = 0.002$] and 6 months' follow-up [MD −3.06 (−4.53, −1.59), $P = 0.0001$] were better after robot-assisted than laparoscopic surgery.

Conclusion Although there were few data and no randomized controlled trials the results of the review suggested that robot-assisted surgery resulted in improved urogenital function than after laparoscopy.

Keywords Robotic surgery, sexual dysfunction, urinary dysfunction

Introduction

The main aim of rectal cancer surgery is to avoid local recurrence and pelvic autonomic nerve damage [1–3]. Total mesorectal excision in rectal cancer surgery results in increased survival and a reduction in local recurrence [4–7]. It is also possible that urogenital dysfunction after pelvic surgery has decreased. Despite the advantages of laparoscopic surgery [8] including shorter postoperative recovery time, reduced postoperative pain, reduced blood loss, shorter hospital stay and better cosmesis [9,10], a large randomized controlled trial showed no advantage regarding male sexual function preservation after laparoscopic compared with conventional open rectal surgery [11].

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In addition to the benefits associated with laparoscopy, robot-assisted surgery may add further improvements including a stable three-dimensional view, reduction of tremor of the surgeon, an increased seven degrees of freedom of movement and improved comfort for the surgeon [12]. Robot-assisted surgery may also be superior to laparoscopic surgery with regard to conversion, blood loss and hospital stay [13]. Whether urogenital function is better is not known. For this reason a systematic review was carried out to investigate urogenital function after robot-assisted surgery and to compare it with laparoscopic surgery.

Method

Search strategy

A systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines [14].

The search strategy was based on the PICO model and was developed in collaboration with a biomedical librarian as follows: P (population), patients with rectal cancer; I (intervention), robot-assisted surgery; C (comparison), laparoscopic surgery; O (outcome), sexual and urological dysfunction. The PubMed, Cochrane Library and Embase databases were searched systematically in February 2014 for relevant articles published before this date investigating urogenital function after robot-assisted surgery. We used the following search terms: rectum OR rectal OR colorectal AND robot OR robotic OR robotics OR da Vinci OR computer AND sexual OR urologic OR urological OR urinary OR erectile OR erection OR impotence OR impotent OR incontinence. There were no language restrictions or other limits to the search. We also manually searched reference lists of all retrieved articles for additional studies. The authors of included studies in the meta-analysis were contacted for supplementary data material.

Eligibility criteria

To be included in the qualitative analysis studies had to be reported in English and had to investigate urogenital function after robot-assisted rectal cancer surgery. To be included in the quantitative analysis (meta-analysis), studies had to investigate urogenital function on the basis of validated scoring systems [International Prostate Symptom Score (IPSS), International Index of Erectile Function (IIEF) or Female Sexual Function Index (FSFI)], with a control group of patients treated by laparoscopic surgery.

Outcome measures

Studies using the IPSS were included. This is a subjective scoring system based on a 0–5 scale in seven categories (incomplete emptying, frequency, intermittency, urgency, weak stream, straining, nocturia), with a maximum score of 35 points and with high scores corresponding with greater dysfunction [15]. To assess male sexual function, we included studies using IIEF. This is a validated and reliable self-administered scoring system and includes a 15-item questionnaire focusing on erectile function, orgasmic function, sexual desire and satisfaction of intercourse. Only erectile function was assessed in the meta-analysis due to data being available. A higher score with a maximum of 30 was related to better erectile function [16]. Female sexual function was investigated on the basis of FSFI, a 19-item self-reported measure of desire, arousal, lubrication, orgasm and pain. Again, higher score was related to better sexual function [17].

Bias and quality assessment

For detecting risk of bias at a study level, the Newcastle–Ottawa scale (NOS) was used as recommended by the Cochrane Collaboration [18]. This is a rating system scoring studies 0–9, where 0 indicates the highest and nine indicates the lowest risk of bias. To assess the outcome of the meta-analysis, quality of evidence was evaluated on the basis of Grading of Recommendations Assessment, Development and Evaluation (GRADE). The GRADE approach divides the outcome into four categories: high, moderate, low and very low. A specific outcome of the meta-analysis may be downgraded based on the following factors: risk of bias, imprecision and inconsistency. Conversely, outcome may be upgraded based on strong association (large magnitude of effect), confounders reducing or increasing any demonstrated effect and dose–response relation [19].

Statistical analysis

All end-points were qualitatively summarized and we also aimed to perform a meta-analysis on each outcome variable, when studies reported comparable data. For the meta-analysis, we used review manager (Revman version 5.1, Nordic Cochrane Center, Cochrane Collaboration, 2011). For typing data, the 'continuous' method was used, in which pooled estimates showed the mean difference between the two groups (robotic *vs* laparoscopic). If little heterogeneity among the studies was found, we aimed to use the fixed effect model. If heterogeneity was significant we used the random effect model to take this into account. For IPSS and IIEF, the means with standard deviation and the number of patients from each included study were extracted. Results of the pooled estimates were presented as forest plots and the degree of heterogeneity was expressed as I^2. According to the Cochrane Collaboration, heterogeneity was classified as low, moderate or high based on a value of the I^2 statistic of 25%, 50% or 75%, respectively.

Results

Ten articles were included in the systematic review comprising 689 patients. Four of these comprising 313 patients were eligible for meta-analysis. All included studies were cohort studies of which seven were prospective and three retrospective. Of the included studies, eight were rated with six stars using NOS and two [20,21] with five stars. The study selection process is shown in Fig. 1.

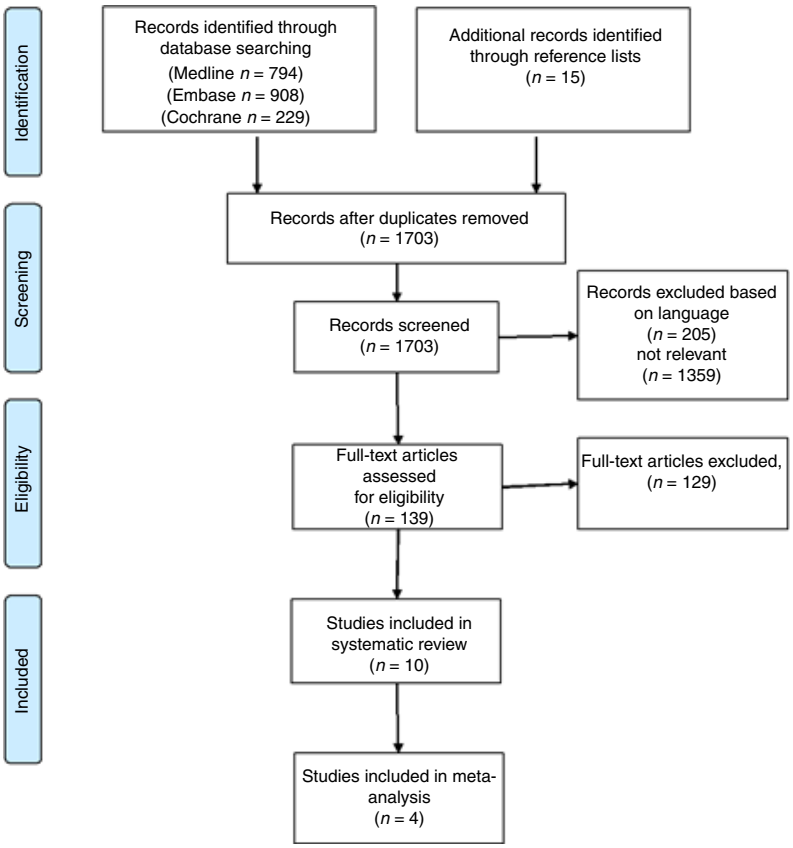

Figure 1 PRISMA flow diagram.

Two of the included articles with the same authorship enrolled patients in overlapping time frames [22,23]. When the corresponding author was contacted, we were informed that there was only a minor overlap in the populations and therefore we chose to include both studies. Article characteristics are summarized in Table 1.

IPSS scores

Of the 10 included articles, nine reported the urological outcome. Four of these were eligible for meta-analysis, with a NOS score of 6 in all studies [22–25]. A total of 162 patients were included in the meta-analysis at 3 and 6 months' follow-up. At 12 months' follow-up, 193 patients were included.

Over 3 months' follow-up the pooled estimates showed a significant difference of IPSS scores in favour of robotic surgery [mean difference (MD) −1.58, 95% confidence interval (CI) (−3.1, −0.05), $P = 0.04$] with little heterogeneity ($P = 0.33$; $I^2 = 9\%$) (Fig. 2). At 6 months' follow-up, the pooled estimates did not differ significantly [MD −0.59, 95% CI (−2.00, 0.82), $P = 0.41$) with no heterogeneity ($P = 0.78$; $I^2 = 0\%$) (Fig. 3). Finally there was a significant improvement after robotic surgery at 12 months' follow-up [MD −0.90, 95% CI (−1.81, 0.02), $P = 0.05$] again with no heterogeneity ($P = 0.78$; $I^2 = 0\%$) (Fig. 4). Based on the GRADE approach, the quality of evidence was very low. The outcome was downgraded based on study design, high risk of bias and imprecision.

Of the nine studies reporting urological outcome, five were not suitable for meta-analysis. A retrospective study [26] investigated 100 patients who underwent robot-assisted rectal surgery, but only 78 completed the IPSS questionnaire. At follow-up IPSS scores were comparable with those measured preoperatively. A prospective study [27] evaluated 74 (38 male) patients after robot-assisted surgery at 1, 6 and 12 months' follow-up. During the whole period of the study, there was no significant deterioration in voiding and continence in the men. Among the 36 women in the same study continence and bladder filling were significantly worse after 1 month, but they then improved to become comparable with the preoperative state at 12 months' follow-up. Another prospective study [28] investigated urogenital

Table 1 Characteristics of included studies

Author	Year	Country	Design	Comparison	Sample size			Gender M/F		IPSS	IIEF	FSFI
					Rob	Lap	Total	Rob	Lap			
Park *et al.* [22]	2014	Korea	PCS	*	32	32	64	32/0	32/0	*	*	NR
Park *et al.* [23]	2013	Korea	RCS	*	40	40	80	28/12	25/15	*	*	NR
Kim *et al.* [24]	2012	Korea	PCS	*	30	39	69	18/12	20/19	*	*	NR
D'Annibale *et al.* [25]	2013	Italy	RCS	*	50	50	100	30/20	30/20	*	*	NR
Staniculea *et al.* [26]	2013	Romania	RCS		100	NR	100	66/34	NR	*	*	*
Luca *et al.* [27]	2013	Italy	PCS		74	NR	74	38/36	NR	*	*	*
Leung *et al.* [28]	2012	Hong Kong	PCS		33	NR	33	33/0	NR	*	*	NR
Patriti *et al.* [29]	2009	Italy	PCS	*	29	37	66	11/18	12/25	NR	NR	NR
Erguner *et al.* [21]	2013	Turkey	PCS	*	27	37	74	13/14	17/20	NR	NR	NR
Hellan *et al.* [20]	2007	USA	PCS		39	NR	39	21/18	NR	NR	NR	NR

PCS, Prospective Cohort Study; RCS, Retrospective Cohort Study; Rob, Robot; Lap, Laparoscopy; NR, No Record.

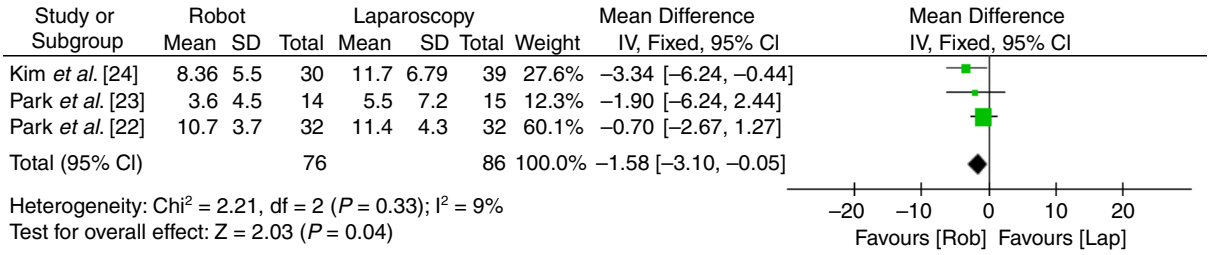

Figure 2 Forest plot showing IPSS score 3 months after surgery.

outcome in 33 men after robot-assisted surgery. At 3 months' follow-up, the IPSS was comparable with preoperative scores. A prospective study [29] including 66 patients investigated urogenital function after robot-assisted and laparoscopic surgery. Although the IPSS was not used, no difference was found in the incidence of urinary retention between the groups (2.7% *vs* 3.4%, $P > 0.05$). Finally a study [20] which followed 39 patients prospectively after robot-assisted surgery reported a urinary disorder in only one patient.

IIEF score

Of the 10 included studies, nine reported sexual function, of which three were suitable for meta-analysis with 128 patients at 3 and 125 patients at 6 months' follow-up [22–24]. The studies all had an NOS score of 6. Patients included in the meta-analysis were all sexually active before surgery. Any patient who was not sexually active was excluded from the analysis.

At 3 months' follow-up, the pooled estimates showed better erectile function after robot-assisted than laparoscopic surgery [MD −2.59, 95% CI (−4.25, −0.94), $P = 0.002$] with no heterogeneity ($P = 0.41$; $I^2 = 0\%$) (Fig. 5). At 6 months the pooled estimates again showed a significant improvement of erectile function after robotic compared with laparoscopic surgery [MD −3.06, 95% CI (−4.53, −1.59), $P = 0.0001$) again with no heterogeneity ($P = 0.36$, $I^2 = 1\%$) (Fig. 6). Using the GRADE approach the quality of the evidence was rated as very low due to study design, high risk of bias and imprecision.

Seven studies were not suitable for meta-analysis of IIEF. The three which were included a prospective study [25] in which erectile function was restored completely in the robotic group ($n = 30$) but only partially in the laparoscopic group ($n = 30$) 1 year after rectal cancer surgery ($P = 0.045$). The other two studies [26,27] ($n = 69$) found that IIEF score initially decreased significantly after robot-assisted rectal surgery but then increased up to 12 months of follow-up at which point it was comparable with the preoperative score. In one study [28] 33 male patients prospectively assessed for urinary and sexual function after robot-assisted surgery showed no difference in the IIEF at 3 months from preoperative values. A prospective study comparing robot-assisted with laparoscopic surgery [29] investigated erectile function not using IIEF. Overall

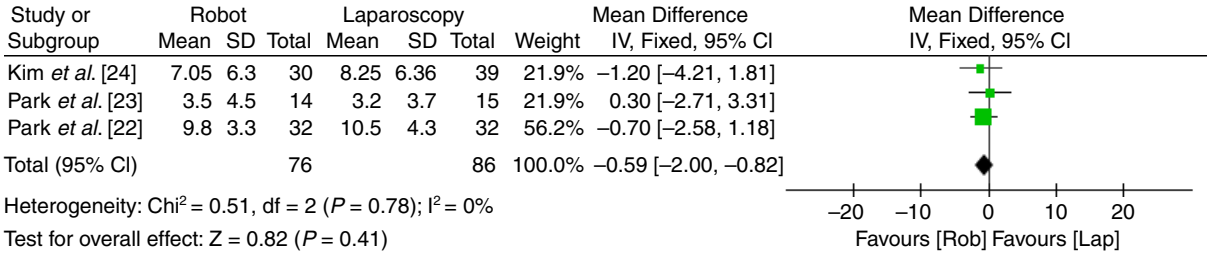

Figure 3 Forest plot showing IPSS score 6 months after surgery.

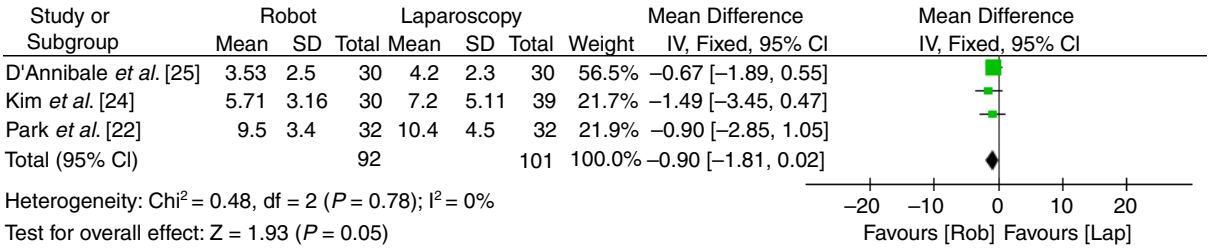

Figure 4 Forest plot showing IPSS score 12 months after surgery.

erectile dysfunction was measured without defining the criteria. No difference of erectile dysfunction after laparoscopic (16.6%) and robotic (5.5%) surgery was found ($P > 0.05$). Another prospective study [21] of 64 patients reported no significant difference in sexual dysfunction after laparoscopic (2.7%) and robotic (0%) surgery (0.58).

FSFI score

Two studies [26,27] investigated 49 women for sexual function after robotic-assisted rectal surgery. The FSFI score had fallen at 1 and 6 months' follow-up, whereafter it increased and became comparable with preoperative values at 12 months.

Discussion

Robot-assisted rectal cancer surgery is gaining popularity, but it is still not clear whether the technological advantages translate into less risk of urogenital dysfunction. The current study found the IPSS score 3 and 12 months after robot-assisted surgery to be better than after laparoscopic surgery, but any difference was small and at 6 months the difference was not statistically significant. These inconsistent results are likely to be due to small sample size and the high risk of bias, and it is not possible to conclude that there is a difference. Based on the GRADE approach, we found that quality of evidence was very low for all the end-points largely due to high risk of bias within studies and imprecision. Imprecision was primarily due to the small study populations. The qualitative synthesis found that urogenital function was almost the same at 1 year after robot-assisted surgery as it was before the operation. These results supported the findings of the present meta-analysis.

This systematic review and meta-analysis included the best available evidence and was conducted according to accepted guidelines. To evaluate risk of bias within studies and the outcome of meta-analysis, we only used tools recommended by the Cochrane Collaboration [18]. Nevertheless the results should be interpreted with caution as all studies were non-randomized and included small numbers of patients. Based on the NOS, all studies were rated with six stars, which translated into a high risk of bias. Although there was no heterogeneity in the meta-analyses and the significantly positive effect of the robot technique was constant in all but one of the analyses, none of the studies made any adjustment for possible confounding factors, which may result in a high risk of selection bias. The limitations of these existing studies could be minimized with larger randomized controlled trials.

Urogenital dysfunction is seemingly caused by injury during surgery to the hypogastric nerves, sacral splanchnic nerves or both [30]. Because of this, it is accepted that careful dissection aimed to achieve nerve preserva-

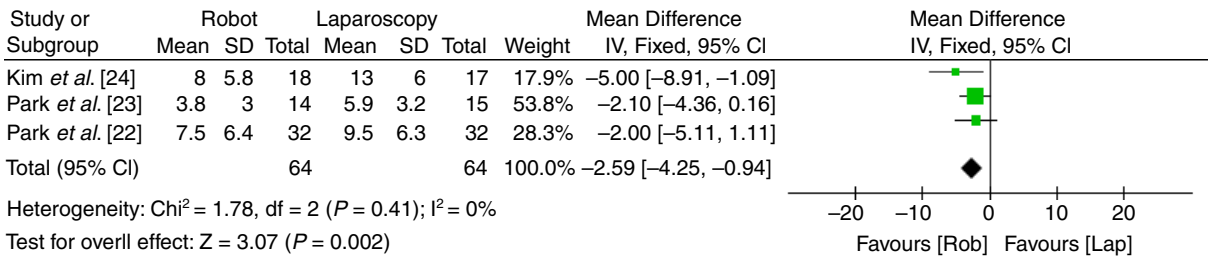

Figure 5 Forest plot showing IIEF change from baseline to 3 months after surgery.

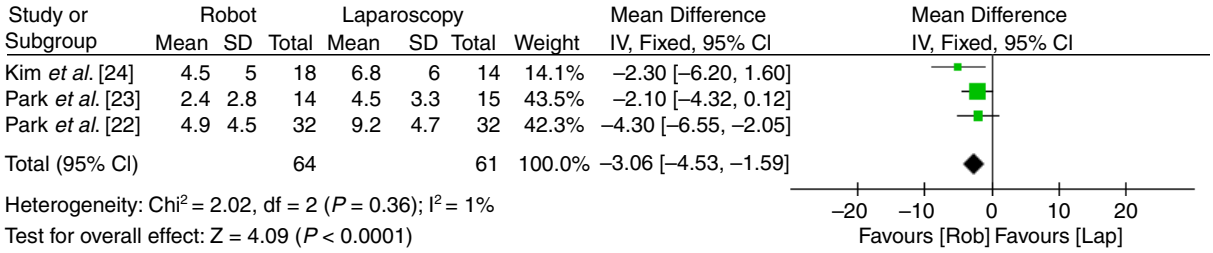

Figure 6 IIEF change from baseline 6 months after surgery.

tion is crucial to maintain sexual and urological function. The standard laparoscopic approach in pelvic surgery is very difficult to perform in the pelvis and requires high levels of competence [31,32]. This may be due to poor dexterity, rigidity of the instruments and a two-dimensional rather than a three-dimensional view [33]. The instrumentation and more stable three-dimensional view of the robotic system may permit an easier identification of the nerves [34].

In conclusion, robotic rectal cancer surgery may improve sexual function and there is a tendency towards improved urinary function, but these results were not consistent. A decrease of urogenital complications might be seen if robotic surgery becomes more widely accepted [23]. At the moment, however, the results of this meta-analysis must be interpreted with caution due to risk of bias and imprecision. We believe this is an important matter of sufficient clinical relevance that any randomized controlled trial comparing robotic and laparoscopic surgery should include detailed recording of urogenital function.

Conflict of interest

No disclaimers, funding or conflicts of interest.

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Author contributions

M. Broholm: contributions to conception and design; acquisition of data; analysis and interpretation of data; drafting the article; revising the article for intellectual content; final approval of the article. H.-C. Pommergaard: contributions to conception and design; acquisition of data; analysis and interpretation of data; revising the article for intellectual content; final approval of the article. I. Gögenur: contributions to conception and design; revising the article for intellectual content; final approval of the article.

References

1 Maurer CA, Z'Graggen K, Renzulli P *et al.* Total mesorectal excision preserves male genital function compared with conventional rectal cancer surgery. *Br J Surg* 2001; **88:** 1501–5.
2 Ho VP, Lee Y, Stein SL *et al.* Sexual function after treatment for rectal cancer: a review. *Dis Colon Rectum* 2011; **54:** 113–25.
3 Cunsolo A, Bragaglia RB, Manara G *et al.* Urogenital dysfunction after abdominoperineal resection for carcinoma of the rectum. *Dis Colon Rectum* 1990; **33:** 918–22.
4 Heald RJ, Moran BJ, Ryall RD *et al.* Rectal cancer: the Basingstoke experience of total mesorectal excision, 1978–1997. *Arch Surg* 1998; **33:** 894–9.
5 MacFarlane JK, Ryall RD, Heald RJ. Mesorectal excision for rectal cancer. *Lancet* 1993; **341:** 457–60.
6 Clausen N, Wolloscheck T, Konerding MA. How to optimize autonomic nerve preservation in total mesorectal exci-

sion: clinical topography and morphology of pelvic nerves and fasciae. *World J Surg* 2008; **32:** 1768–75.
7 Kim NK, Aahn TW, Park JK *et al.* Assessment of sexual and voiding function after total mesorectal excision with pelvic autonomic nerve preservation in males with rectal cancer. *Dis Colon Rectum* 2002; **45:** 1178–85.
8 Jacobs M, Verdeja JC, Goldstein HS. Minimally invasive colon resection (laparoscopic colectomy). *Surg Laparosc Endosc* 1991; **1:** 144–50.
9 Baek JH, Pastor C, Pigazzi A. Robotic and laparoscopic total mesorectal excision for rectal cancer: a case-matched study. *Surg Endosc* 2011; **25:** 521–5.
10 Trastulli S, Cirocchi R, Listorti C *et al.* Laparoscopic *vs* open resection for rectal cancer: a meta-analysis of randomized controlled trials. *Colorectal Dis* 2012; **14:** 277–-296.
11 Jayne DG, Brown JM, Thorpe H *et al.* Bladder and sexual function following resection for rectal cancer in a randomized clinical trial of laparoscopic versus open technique. *Br J Surg* 2005; **92:** 1124–32.
12 Lanfranco AR, Castellanos AE, Desai JP *et al.* Robotic surgery: a current perspective. *Ann Surg* 2004; **239:** 14–21.
13 Xiong B, Ma L, Zhang C *et al.* Robotic versus laparoscopic total mesorectal excision for rectal cancer: a meta-analysis. *J Surg Res* 2014; **188:** 404–14.
14 Moher D, Liberati A, Tetzlaff J *et al.* Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Open Med* 2009; **3:** 123–30.
15 Park YW, Lee JH. Correlation between the visual prostate symptom score and international prostate symptom score in patients with lower urinary tract symptoms. *Int Neurourol J* 2014; **18:** 37–41.
16 Rosen RC, Riley A, Wagner G *et al.* The International Index of Erectile Function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology* 1997; **49:** 822–30.
17 Rosen R, Brown C, Heiman J *et al.* The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. *J Sex Marital Ther* 2000; **26:** 191–208.
18 Reeves BCDJ, Higgins JPT, Wells GA. Including non-randomized studies. In: *Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0* (updated March 2011) (eds Higgins JPT, Green S). The Cochrane Collaboration, 2011. Chapter 13. Available from www.cochrane-handbook.org.
19 Balshem H, Helfand M, Schunemann HJ *et al.* GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol* 2011; **64:** 401–6.
20 Hellan M, Anderson C, Ellenhorn JD *et al.* Short-term outcomes after robotic-assisted total mesorectal excision for rectal cancer. *Ann Surg Oncol* 2007; **14:** 3168–73.
21 Erguner I, Aytac E, Boler DE *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:** 316–9.
22 Park SY, Choi GS, Park JS *et al.* Urinary and erectile function in men after total mesorectal excision by laparoscopic or robot-assisted methods for the treatment of rectal cancer: a case-matched comparison. *World J Surg* 2014; **38:** 1834–42.
23 Park SY, Choi GS, Park JS *et al.* Short-term clinical outcome of robot-assisted intersphincteric resection for low rectal cancer: a retrospective comparison with conventional laparoscopy. *Surg Endosc* 2013; **27:** 48–55.
24 Kim JY, Kim NK, Lee KY *et al.* A comparative study of voiding and sexual function after total mesorectal excision with autonomic nerve preservation for rectal cancer: laparoscopic versus robotic surgery. *Ann Surg Oncol* 2012; **19:** 2485–93.
25 D'Annibale A, Pernazza G, Monsellato I *et al.* Total mesorectal excision: a comparison of oncological and functional outcomes between robotic and laparoscopic surgery for rectal cancer. *Surg Endosc* 2013; **27:** 1887–95.
26 Stanciulea O, Eftimie M, David L *et al.* Robotic surgery for rectal cancer: a single center experience of 100 consecutive cases. *Chirurgia (Bucur)* 2013; **108:** 143–51.
27 Luca F, Valvo M, Ghezzi TL *et al.* Impact of robotic surgery on sexual and urinary functions after fully robotic nerve-sparing total mesorectal excision for rectal cancer. *Ann Surg* 2013; **257:** 672–8.
28 Leung AL, Chan WH, Cheung HY *et al.* Initial experience on the urogenital outcomes after robotic rectal cancer surgery. *Surg Pract* 2013; **17:** 13–7.
29 Patriti A, Ceccarelli G, Bartoli A *et al.* Short- and medium-term outcome of robot-assisted and traditional laparoscopic rectal resection. *JSLS* 2009; **13:** 176–83.
30 Masui H, Ike H, Yamaguchi S *et al.* Male sexual function after autonomic nerve-preserving operation for rectal cancer. *Dis Colon Rectum* 1996; **39:** 1140–5.
31 Ito M, Sugito M, Kobayashi A *et al.* Influence of learning curve on short-term results after laparoscopic resection for rectal cancer. *Surg Endosc* 2009; **23:** 403–8.
32 Bege T, Lelong B, Esterni B *et al.* The learning curve for the laparoscopic approach to conservative mesorectal excision for rectal cancer: lessons drawn from a single institution's experience. *Ann Surg* 2010; **251:** 249–53.
33 Berguer R, Rab GT, Abu-Ghaida H *et al.* A comparison of surgeons' posture during laparoscopic and open surgical procedures. *Surg Endosc* 1997; **11:** 139–42.
34 Luca F, Cenciarelli S, Valvo M *et al.* Full robotic left colon and rectal cancer resection: technique and early outcome. *Ann Surg Oncol* 2009; **16:** 1274–8.