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IAGES
Recent Advances in Minimal Access Surgery-2

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CHAPTER

Long-term Outcomes Following Robotic Surgery for Rectal Carcinoma: A Systematic Review

2

YM Goh, S Enoch, CR Selvasekar

ABSTRACT

Introduction

The gold standard surgical management of rectal adenocarcinoma is total mesorectal excision. Technically, there are challenges in performing this procedure either open or laparoscopically. Robotic surgery is increasingly performed as it provides superior view and visualization of the autonomic nerves in the pelvis and has demonstrated promising short-term outcomes for rectal adenocarcinoma. There is, however, a paucity of literature assessing long-term outcomes following robotic surgery in rectal cancer. Hence, this systematic review aims to assess long-term outcomes of robotic surgery for resection of rectal adenocarcinoma.

Methods

A systematic review was conducted to identify all studies that assessed long-term outcomes following robotic-assisted or robotic surgery for resection of rectal adenocarcinoma. End-points included were pathological outcomes such as circumferential resection margin (CRM), number of lymph nodes harvested and long-term outcomes such as local recurrence, systemic recurrence, disease-free survival (DFS) and overall survival (OS).

Results

Four studies reported assessment of outcomes identified at > 3-year follow-up. A total of 413 patients were included in this review, of which 49.2% underwent neoadjuvant chemoradiotherapy. One study reported positive CRM rate of 5% whilst all other studies did not report any positive CRM. Mean number of lymph nodes harvested was similar (range 15–20.1) which was reported to be significantly higher in two included studies when compared to laparoscopic surgery. Overall 3-year and 5-year local recurrence, systemic recurrence, DFS and OS were similar to that reported in the literature and comparable to laparoscopic surgery outcomes at those time points.

Conclusion

Long-term outcomes following robotic rectal adenocarcinoma resection are comparable to current laparoscopic techniques. However, further assessment

of its cost-effectiveness and quality of life will need to be considered in more detail before making this the standard treatment for rectal carcinoma.

INTRODUCTION

Background

The introduction of robotic surgery has been driving the progression from the conventional open and laparoscopic techniques for rectal carcinoma toward minimally invasive surgery. Evolution of surgical techniques and advancements in technology has resulted in improvements in short-term outcomes recovery time, reduction in length of hospital stay, postoperative pain, and postoperative cosmesis. The standard management of mid and low rectal cancers is total mesorectal excision (TME) with low anterior resection (LAR) or abdominoperineal resection (APR). Currently this procedure can be performed by open, laparoscopic or robotic approach.

- Several recent randomized control trials (RCTs) have reported laparoscopic TME to be associated with improved short-term outcomes compared to open TME.[1,2] Despite the increase in uptake of TME amongst surgeons worldwide, this is still widely regarded as a technically challenging procedure, especially when performed in patients with technically difficult anatomy, for example, a low rectal tumor, narrow pelvis or patients who have undergone previous abdominal or pelvic surgery.[3,4] The four major randomized controlled trials comparing open versus laparoscopic rectal cancer surgery ACOSOG Z6051, COLOR 2, ALACART, and the COREAN trials show no oncological benefit apart from short-term benefit. Hence, with improved technology with the robot, we are assessing if there is evidence that long-term outcomes are better. In this regard, robotic-assisted surgery may be advantageous as it provides three-dimensional stereoscopic view as well as fixed traction and counter-traction intraoperatively with articulated instruments enabling precision surgery. In addition to this, improved visualization of the autonomic plexus in the pelvis has shown to aid recovery of urinary voiding and sexual function.[5,6]

Multiple studies and reviews have been published demonstrating safe and acceptable short-term oncologic outcomes and function following robotic surgery for rectal adenocarcinoma.[7,8] However, there is a paucity of studies assessing the long-term outcomes of robotic surgery for resection of rectal carcinoma. This systematic review aims to assess the long-term oncological outcomes of robotic surgery for resection of rectal adenocarcinoma.

METHODS

Criteria for Considering Studies for This Review

All published studies that assessed long-term outcomes following robotic-assisted (hybrid) where the extrapelvic part is performed laparoscopically or totally robotic surgery (single and double docking) resection for rectal adenocarcinoma were considered. Studies included are those that identified patients undergoing robotic-, robotic-assisted or hybrid robotic surgery for rectal adenocarcinoma with or without adjuvant chemotherapy or

neoadjuvant radiotherapy. Long-term outcomes were defined as studies with mean or median follow-up of > 3 years. Articles excluded were: (1) articles that reported short-term outcomes of < 3 years; (2) studies that did not report on robotic surgery; (3) review articles; (4) overlap between authors or centers in the published literature; and (5) articles limited to human subjects and the English language.

Literature Search

The following databases were searched: (1) MEDLINE from 2001 to end of 2017 via OvidSP, (2) MEDLINE Epub ahead of print, in-process and other non-indexed citations (latest issue) via OvidSP, last search 17th August 2017; (3) Ovid Embase (2001 till 28th July 2017). Additionally, all references of included articles were manually reviewed to identify additional studies. Search terms used were robot-assisted surgery or robotic surg*.mp., rectal.mp or rect*.mp., cancer.mp or carcinoma.mp or malignancy.mo or neoplasm.mp and long term outcome*.mp or outcome*.mp.

Trial Selection and Data Extraction

Two independent reviewers screened all titles and abstracts manually for inclusion. A third reviewer was consulted in the case of disagreement. Relevant data was entered into Review Manager 5.4 (Cochrane Collaboration, Oxford, United Kingdom). The following data items were extracted: year of publication, country of origin, study design, number of participants (only for robotic surgery), pathological diagnosis, patient demographics, e.g., gender, mean age, body mass index (BMI), American Society of Anesthesiologists (ASA) class, operation type and robotic system utilized, duration of study, use of neoadjuvant and adjuvant chemotherapy or radiotherapy, mean operating time, tumor location, circumferential resection margin, number of retrieved lymph nodes, mean follow-up, local recurrence, systemic recurrence, DFS, and OS.

RESULTS

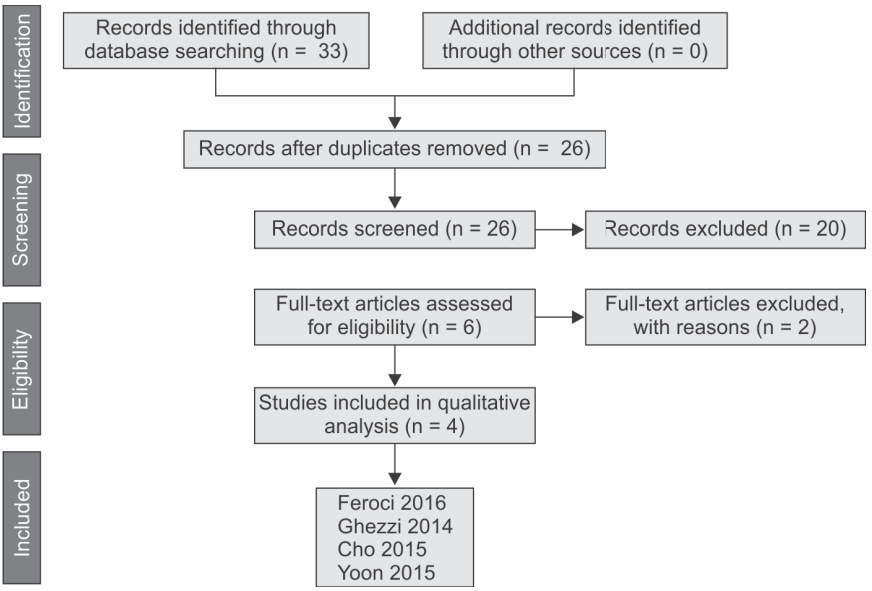
Description of Studies

Initial search of these databases revealed a total of 33 results. Of these, seven duplicates were removed. Of the remaining 26, 20 articles were excluded after review of the title and abstract. After a full text review of the remaining six articles, two were excluded. This left a total of four articles that met the inclusion criteria and hence included in this systematic review **(Flowchart 1)**.

Study Characteristics (Table 1)

All articles included in this review were published within the last 2 years with studies conducted between January 2007 and December 2014. Two of these studies are prospective case series[9,10] and the other two are retrospectively[11,12] conducted case series. Of the four articles included in this review, one was performed in Italy, one in Italy and Brazil, and two in South Korea. Follow-up time for all these studies ranged from a mean of 37.4 months to 58.2 months.

Flowchart 1: PRISMA diagram.



Patient Characteristics (Table 1)

A total of 413 patients who had undergone robotic surgery for a diagnosis of rectal adenocarcinoma were included in this study. There were a total of 250 men and 146 women with a mean age of 59.1 years. Mean BMI for all patients were 23.84 kg/m^2. 358 (90.4%) patients had ASA grade 1 or 2 and 38 (9.6%) of patients had ASA grades of 3 or 4.

Operation Type and Use of Adjuvant Therapy (Table 2)

Operation type differed in these studies. One author performed robotic-assisted TME in their study.[10] Two authors performed low anterior resection (LAR) in a total of 269 patients.[11] Meanwhile Ghezzi et al. reports performing ultra-low anterior resection (ULAR) and coloanal anastomosis (CA) in a total of 11 patients, abdominoperineal resection (APR) in nine patients and posterior pelvic exenteration (PPE) in 1 patient.[11] 53 patients were reported by Cho and colleagues to have undergone CA[9] and robotic-assisted resection was used in all cases reported by Yoon et al.[12] Two authors used the Da Vinci Surgical System for all cases.[9,11] Only Da Vinci is currently available for use. A total of 27 (6.81%) patients had undergone adjuvant chemotherapy. 195 (49.2%) patients were reported to have undergone adjuvant chemoradiotherapy (45–50.4 Gy external beam radiation and systemic 5-fluorouracil). Mean operating time was between 299 and 361.1 minutes.

Oncological Characteristics and Resection (Table 2)

Three articles included in this study measured the distance of the tumor from the anal verge.[9-11] Only one article reported the location of the tumor based on its position in the upper, middle, and lower third of the rectum.[9] Other articles included in this review measured the tumor distance from the anal verge in

Table 1: Study and population characteristics.

Author	*Country*	*Type of study*	*Prospective/ Retrospective*	*Number of patients*	*Diagnosis*	*Mean follow-up (months)*	*Gender (M:F)*	*Mean age (years)*	*Mean BMI(kg/m²)*	*ASA class n (%)*			
										1	2	3	4
Feroci 2016[9]	Italy	Case series	Prospective	53	Mid and low rectal Ca (I-III disease)	37.4	27:26	66 (42–84)	24.6	11 (20.8)	33 (62.3)	9 (16.9)	
Ghezzi 2014[10]	Brazil/Italy	Case series	Prospective	65	Extraperitoneal rectal cancer	46.7 ± 11.5	41:24	61 ± 11.8	24.7 ± 3.6	12 (18.5)	49 (75.4)	4 (6.2)	0(0)
Cho 2015[11]	South Korea	Case series	Retrospective	278	Rectal adenocarcinoma	51 ± 13.1	182: 96	57.4 ± 11.6	23.5 ± 2.9	253 (91.0)		25 (9.0)	
Yoon 2015[12]	South Korea	Case series	Retrospective	17	Rectal adenocarcinoma	58.2	-	-	-	-	-	-	-

Table 2: Operation type, oncological characteristics, and long-term outcomes.

Author	*Type of operation n (%)*		*Operating system*	*Length of study*	*Adjuvant chemotherapy n (%)*	*Adjuvant radiotherapy n (%)*	*Mean operating time (min)*	*Tumor location (from anal verge)*		*+ve CRM (%)*	*No. of retrieved lymph nodes*	*30-day mortality n (%)*	*Mean follow-up (months)*	*Local recurrence (%)*		*Systemic recurrence (%)*		*Disease-free survival (%)*		*Overall survival (%)*	
														3 yrs	*5 yrs*	*3 yrs*	*5 yrs*	*3 yrs*	*5 yrs*	*3 yrs*	*5 yrs*
Feroci 2016[9]	TME		Not relevant (NR)	Jan 2008–Dec 2014	27 (50.9)	NR	342 (249–536)	8 (4–12)		0	18 (4–49)	0	37.4 (2–85)	1.9	NR	17	NR	79.2	NR	90.2	NR
Ghezzi 2016[10]	LAR + CR	44 (67.7)	Da Vinci S surgical system	Dec 2006–Dec 2010	13 (8.32)		299 ± 58.0 nb≥	6.2 ± 2.7		0	20.1 ± 10.3	0	46.7 ± 11.5	2.5	3.2	NR	18.5	80	73.2	90	85.0
	ULAR + CA	11 (16.9)																			
	APR	9 (13.8)																			
	PPE	1 (1.5)																			
Cho 2014[11]	LAR	225 (80.9)	Da Vinci Surgical System	Jan 2007–June 2011	182 (65.5)		361.6± 91.9	Upper n (%)	37 (13.3)	14 (5.0)	15.0 ± 8.1	-	51 ± 13.1	1.8	5.9	12.2	16.3	-	81.8	-	92.2
	CA	53 (18.1)						Middle n (%)	172 (61.9)												
								Lower n (%)	69 (24.8)												
Yoon 2015[12]	Robotic-assisted resection		-	-	-	-	-	-	-	-	-	-	58.2	-	-	-	-	-	79.7	-	94.1

centimeters.[10,11] Most (61.9%) patients included in this case series had tumors located in the middle third of the rectum.[9]

Circumferential resection margin (CRM) was reported the study by Cho et al. who demonstrated a positive CRM rate of 5%.[9] Other studies did not report CRM[10,11] apart from Yoon et al. who did not assess the proportion of positive CRM in their case series.[12] Cho et al. reported no significant difference in the number of lymph nodes harvested during robotic surgery when compared to laparoscopic surgery (p = 0.069).[9] Meanwhile, Feroci et al. and Ghezzi et al. report a significantly larger number of lymph node harvested following robotic surgery when compared to laparoscopic surgery (p = <0.001).[10,11]

Recurrence and Survival Rates (Table 2)

Three authors reported 3-year local recurrence rates (range 1.8–2.5%).[9,10] 5-year local recurrence were reported by two authors (range 3.2–5.9%).[9,11] At 3 and 5-year follow-up, systemic recurrence rates were higher than the reported local recurrence (12.2–18.5%).[9-11] Ghezzi et al. reported a statistically lower local recurrence rate in their cohort of patients who had undergone robotic surgery when compared to open surgery (p = 0.024).[11] He reported a 3-year local recurrence rate of 2.5%, which was higher than the other two articles included in this review.[9-11]

Disease-free survival at 3 years is 79.2–80%[10,11] and at 5 years is 73.2–81.8%.[9,10,12] OS rates at 3 years are > 90% and at 5 years >85%.[9-12] 5-year DFS and OS rates in the robotic surgery group compared to open surgery was reported although no significant difference was identified in this small cohort of patients.[11] Feroci et al. also reported a similar finding and these results are comparable to previously reported short- and long-term outcomes.[10] Meanwhile, Cho and colleagues demonstrated no significant differences in the 5-year OD and DFS rates in their case matched retrospective study with a larger cohort of patients. This study noted a significantly lower incidence of late voiding dysfunction in the robotic surgery group when compared to the laparoscopic surgery group.[9]

DISCUSSION

Current literature reports satisfactory short-term outcomes and improvement in function following robotic or robotic-assisted surgery for rectal carcinoma.[13] There is, however, a dearth of literature reporting satisfactory long-term outcomes of robotic surgery. This is reflected by the short duration, 7 years, over which data is collected.

Our systematic review demonstrates a comparatively large cohort of patients who had mid-rectal tumors (total of 172 patients, 61.9%)[9] which would influence the operation performed and outcomes. This is reflected by a greater proportion of patients (80.9%) included in this study who underwent LAR compared to 18.1% who underwent CA.[9] All studies report low positive CRM rates (0–5%) in patients who underwent robotic-/robot-assisted procedures. This is lower than positive CRM rates in reported literature following open surgery (16.7%)[2] and comparable to rates reported following laparoscopic surgery 0.8%[14] and 1.69%.[15]

The proportion of patients who have received neoadjuvant chemoradiotherapy, positive CRM or number of retrieved lymph nodes do not seem to influence local and systemic recurrence rates, DFS, and OS. In total, 56.1% of patients in this review received neoadjuvant chemoradiotherapy. Cho et al. report the greatest proportion of patients who received neoadjuvant chemoradiotherapy in their study. This study reported positive CRM rates of 5.0%, which is not shown to be statistically significant when case matched to positive CRM rates, reported in the laparoscopic surgery case-matched cohort of patients ($p = 1.000$).[9] Both Feroci et al. and Ghezzi et al. report significantly larger number of lymph nodes harvested during robotic surgery when compared to laparoscopic surgery ($p = <0.001$).[10,11] Cho and colleagues, however, report no significant difference in the number of reported lymph nodes harvested which is comparable to published literature.[9,15,16] It is likely that a type I error has occurred due to the small population sample sizes in these groups.

3-year and 5-year local recurrence rates following robotic surgery in our review article is comparable to a systematic review by Indar et al. who reported 4% at 3-year and 6.8% at 5-year follow-up.[17] Our results show overall lower systemic recurrence rates compared to other prospectively collected studies at 22.5%.[18] DFS and OS rates following robotic surgery is comparable to patients who have undergone laparoscopic surgery, as demonstrated in a prospective case series reporting 5-year DFS of 74.5%[18] and another review reporting overall 5-year survival of 68.4%.[8] Nevertheless, DFS and OS is dependent on tumor stage at time of operation, which has not been assessed in our review due to the small total number of patients who have undergone robotic surgery.

Advancements in minimally invasive surgery and the development of robotic surgery for rectal carcinoma have demonstrated improved preservation of autonomic nerves and genitourinary function. These implications suggest an overall improvement in patient outcomes especially when performed in patients requiring complex procedures and dissection intraoperatively. Studies have demonstrated that robotic surgery is associated with increased performance and safety compared to laparoscopic surgery.[19] Nevertheless, robotic surgery is still considered a new technique and longer-term outcomes of robotic surgery are lesser known. Whilst current data seems to support the use of robotic surgery for treatment of rectal cancer, other factors such as learning curves and cost implications need to be considered before it can be the new gold standard access for rectal resections. Odermatt et al. suggests that the formal learning process for robotic TME in experienced laparoscopic surgeons could be reduced[20] whilst Jimenez-Rodriguez et al. suggest that the mean number of cases required for a surgeon to be classed as an expert in robotic surgery to be 39 patients.[21] It is likely that with current training in laparoscopic surgery that these numbers will continue to decrease, shortening the learning curve. At present robotic surgery costs significantly more than laparoscopic surgery despite having similar short-term outcomes in both patient groups. Nevertheless, the cost-effectiveness of robotic surgery is unclear due to the paucity of long-term outcomes at present. These initial high costs may be compensated by improvements in quality-adjusted life years and postoperative morbidity.[22]

LIMITATIONS

The limitations of this systematic review, firstly, is its size, due to a limited number of studies reporting long-term outcomes in the published literature to date. Secondly, all studies and data extracted in this review article are case series. Thirdly, there was variation between different units with regards to the technical steps, operation type, and considerations of hybrid versus robotic surgery. This could influence outcomes in different units. Finally, the follow-up time identified between different units varied significantly and an incomplete report on follow-up between units may lead to performance bias. Other studies in this review measured the distance of the tumors from the anal verge; however, the proportion of patients who had tumors in each third of the rectum were not identified which made meaningful interpretation of comparative results difficult. It looks like there is some preliminary data on the benefit of robot in low rectal cancer to preserve the sphincters by allowing a coloanal anastomosis. Nevertheless, this systematic review attempts to establish the long-term outcomes of performing robotic surgery given the paucity of literature available. Further analysis of long-term effects of robotic surgery on functional outcomes and quality of life should be assessed.

CONCLUSION

In conclusion, despite limitations in this study due to paucity of data, the authors of this article allude to favorable long-term outcomes in the use of robotic surgery for rectal adenocarcinoma Assessment of its cost-effectiveness and quality of life following robotic surgery for rectal carcinomas will need to be considered in further detail before making this the standard treatment for rectal carcinoma.

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IAGES Recent Advances in Minimal Access Surgery-2

Recent Advances in Minimal Access Surgery-2 is a continuation of the series dedicated to the emerging trends in Minimal Access Surgery. It is compilation of topics covering all the developments in this branch of surgery. The first volume of the book had covered a variety of topics and the second volume exclusively focused on Luminal Laparoscopic Surgery contributed by many eminent experts from across the world.

There have been various recent technological developments and refinements in luminal laparoscopic surgery of the foregut, colon, rectum and bowel. Such surgery has now become routine practice. This volume is expected to be a useful update for the readers to keep them abreast with the recent developments in this subject.

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