

Comparison of Laparoscopic Intersphincteric Resection and Abdominoperineal Resection for Ultra-Low Rectal Cancer Patients - a Retrospective Analysis, and a Meta-analysis of Oncology Outcome

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Abstract

Purpose

The aim of the study is to evaluate the surgical and oncology outcomes between laparoscopic Intersphincteric Resection (LISR) and laparoscopic-assisted Abdominoperineal Resection (LARC) for ultra-low rectal cancer patients by using a retrospective analysis, and a meta-analysis of the literature was carried out to further validate the oncology outcome.

Patients and methods:

Between April 2014 and December 2015, a total of 38 rectal cancer patients who underwent LISR and 41 LARC patients were enrolled in this study. The comparison between the groups was based on clinicopathological characteristics and surgical outcomes. Meta-analysis of published studies, exploring oncology outcome of between LISR and LARC, was carried out using STATA 12.0 software.

Results

Operating time, blood loss, length of hospital stay, and postoperative complication rates was similar between LISR group and LARC group; Patients undergoing LISR also had a similarly 5-year local recurrence and overall survival rate with LAPR. Meta-analysis showed that five studies, which included a total of 791 patients were final involved for this analysis. Comparing APR, ISR patients obtain similarly 5-years recurrence rate and 5-years survival rate.

Conclusion

This study suggests that LISR is as technically feasible, safe, and effective as LARC for treating patients with low rectal cancer. Additional high-powered randomized trials are needed to determine whether LISR truly offers any advantages.

Introduction

Rectal cancer accounts for approximately 30% of colorectal cancers and is a leading cause of cancer death worldwide [1]. The introduction of total mesorectal excision (TME) and preoperative chemoradiotherapy (CRT) has dramatically decreased the local recurrence rates and improved survival in rectal cancer patients [2]. However, these improvements have been relatively modest for patients with very low rectal cancer, compared with those with mid-to-upper rectal cancer.

In China, most of the rectal cancer was low-lying [3], traditionally, most rectal carcinomas lying less than 5 cm from the anal verge or less than 2 cm from the dentate line are treated by laparoscopic abdominoperineal resection (LAPR) [4]. Intersphincteric resection (ISR) is a procedure that is performed to avoid permanent colostomy in patients with very low rectal cancer [5]. It enables preservation of the sphincter in patients who would have undergone abdominoperineal resection in the past. However, with ISR, there is a potential risk of increased recurrence[6], because preservation of the anal canal, external sphincter, and levator ani muscles for such low tumors may compromise distal margins[7]. Thus, the oncologic outcomes may vary greatly depending on the skills of the surgeons. There have been only limited studies on the oncologic outcomes after ISR compared with APR.

Totally laparoscopic intersphincteric resection (LISR) is not yet an established technique and its safety and feasibility are unclear. Our aim was to clarify the safety and feasibility of LISR for clinical stage I-III rectal cancer comparing to LAPR.

Materials And Methods

Study design

Patients who received LISR or LAPR for ultra-low rectal cancer located below the peritoneal reflection at the Guangxi Cancer Hospital, between Between April 2014 and December 2015 were assessed retrospectively. Our methodology conformed to the principals outlined in the Declaration of Helsinki[8]. The patients were fully informed about the operation and a detailed inform consent form reporting the operation details were signed by the patients. In addition to routine investigations, computed tomography (CT) of chest, abdomen and pelvis, positron emission tomography-computed tomography (PET-CT), and colonoscopy was performed in all patients as part of preoperative work-up.

Patient demographics, preoperative and operative data, and outcomes were included in the analysis. Key variables of interest included age, sex, body mass index (BMI), preoperative diagnosis, duration of surgery, duration of ileocolic anastomosis, intraoperative blood loss, total length of hospital stay, postoperative duration of intestinal function recovery, postoperative pain, and incidence of postoperative in-hospital complications (infection, obstruction, and bleeding). Pathological data, including tumor-node-metastasis (TNM) stage and the number of nodes dissected, were also reviewed. All pathological data fell into the category of T1–4NxM0.

Inclusion Criteria For ISR

ISR was offered to patients with preoperative T1–4 tumors that were circumferential resection margin (CRM) negative according to the TNM classification (seventh edition) and showed no evidence of extension into the external anal sphincter or the levator ani muscle and to those in whom resection could be performed with a distal margin of at least 2 cm for T₂ or T₃ tumors or 1 cm for T₁ tumors. Patients with prior history of abdominal surgery, previous malignancy or those who had psychiatric disorders or severe organ dysfunction such as severe cardiopulmonary disorders were excluded.

Neoadjuvant chemoradiotherapy (NAC) was performed for patients with tumors that invaded the other organs or structures (T4)[9]. Patients with stage III tumor who provided their informed consent for adjuvant chemotherapy were given postoperative systemic chemotherapy with a 5-fluorouracilbased regimen.

Surgical Procedure For LISR And LAPR

A circular incision of the rectal mucosa and of the internal muscular layer was made at least 1 cm below the lower margin of the tumor via a transanal dissection. LISR was basically performed according to the methods described by Schiessel and colleagues. In the abdominal approach, ligation and dissection were performed at the root of the inferior mesenteric artery with mobilization of the splenic flexure. The rectum was mobilized to the level of the puborectalis muscle using the technique of total mesorectal excision (TME). Autonomic nerve preservation was routinely performed for patients without tumors invading the nerves. Dissection of the intersphincteric space between the internal anal sphincter and the external anal sphincter was advanced as low as possible from the abdomen to facilitate the transanal approach. After the operator moved to a transanal approach, the rectum and anal canal were

irrigated with povidone iodine and saline to prevent scatter of cancer cells. Following closure of the anal orifice at the distal cut end, the internal sphincter was circumferentially incised, and the intersphincteric plane was dissected. After specimen removal and irrigation of the pelvic cavity, lateral pelvic lymph node dissection was performed for advanced.

The surgical procedure for LAPR was as previous described [10].

Follow-up And Oncologic Outcomes

All patients were followed on an outpatient basis. Patients were examined with chest and abdominopelvic CT and carcinoembryonic antigen measurement every 3 months for 1 years and then yearly for at least 3 years. The date and first site of recurrence were recorded for each patient. Local recurrence was defined as intrapelvic recurrence, recurrence at the pelvic floor or anastomotic site, or recurrence at lateral pelvic lymph nodes. Other recurrences were defined as distant metastases.

Meta-analysis

Search strategy: The Pubmed, Embase, Cochrane Library electronic databases, and Wanfang Data and DNKI (China National Knowledge Infrastructure) were searched for comparative studies published up to January 2020. The following medical subject heading (MeSH) terms and words were used for the search in all possible combinations: "Intersphincteric Resection," "ISR," "Abdominoperineal Resection," "ARC," "laparoscopic," and "laparoscopy."

A manual search of the reference lists of relevant articles was also performed. No language or time restriction was used. Data were extracted from each study by two independent reviewers (Xianwei Mo and Hao Lai). Disagreements were resolved by consensus.

Eligibility criteria: Inclusion criteria were described as follows: (1) The study design was a case-match design (randomized, controlled trials (RCTs) or controlled clinical trials (CCTs)) that compared LISR to LARC; (2) LISR or LARC can be performed using any type of laparoscopic or endoscopic instruments; (3) studies that were included contained information on at least one of the following outcome measures: disease free survival rate (DFS), and 5-years overall survival rate (OS). Exclusion criteria were as follows: (1) case reports, reviews, and quasi-randomized trials; and (2) over-lapping data.

Results

Patient and tumor characteristics

The characteristics of the patients who underwent LISR or LAPR are listed in Table 1. Histologically curative resection was performed for all patients. No significant differences were observed between the two groups in age, gender, BMI, ASA Score, T stage, N stage, histology, and distance from anus. However, tumor size was differed significantly.

Table 1
Patients' characteristics and operation details

Variables	LISR (N = 38)	LAPR (N = 41)	P
Age (yeas)	57.21 ± 13.45	59.54 ± 12.89	0.435
Gender			
Male	30	27	0.864
Female	8	14	
BMI	21.31 ± 3.64	22.44 ± 2.85	0.128
ASA Score			
I	7	5	0.735
II	29	34	
III	2	2	
Tumor size (CM)	4.24 ± 1.74	3.25 ± 1.37	0.006
T stage (T ₁ /T ₂ /T ₃ /T ₄)	0/9/8/21	1/3/8/26	0.115
N stage (N ₀ /N ₁ /N ₂)	20/12/5	18/17/6	0.652
Histology			
Well	4	2	0.540
Moderate	28	30	
poor, and others	6	9	
Operative time (min)	259.47 ± 80.25	279.90 ± 82.32	0.268
Blood loss (ml)	166.58 ± 120.97	139.63 ± 114.98	0.313
Time to first exhaust (day)	3.18 ± 1.97	2.46 ± 1.00	0.042
Length of hospital stay (day)	15.97 ± 15.54	11.27 ± 8.35	0.095
Postoperative complication			
ileus	2	1	0.196
bleeding	3	1	
5-years recurrence rate	14/38	12/41	
5-years survival rate	26/38	30/41	

Table 2
Characteristics. of Included Studies

Study	Study design	Study period	Country	Group	N	T stage	NAC	Surgery	Inclusion Criteria
Xianwei Mo <i>et al.</i>	CCT	2019	China	ISR	38	T ₁ = 0; T ₂ = 9; T ₃ = 8; T ₄ = 21	21	Laparoscopy	ISR was offered to patients with preoperative T1–4 tumors that were circumferential resection margin (CRM) negative according to the TNM classification (seventh edition) and showed no evidence of extension into the external anal sphincter or the levator ani muscle and to those in whom resection could be performed with a distal margin of at least 2 cm for T2 or T3 tumors or 1 cm for T1 tumors.
				APR	41	T1 = 1; T2 = 3; T3 = 8; T4 = 26	26	Laparoscopy	
Shunsuke Tsukamoto <i>et al.</i>	CCT	2018	Japan	ISR	112	T ₁ /T ₂ = 39; T ₃ /T ₄ = 73;	NA	Laparotomy	Patients at age 20 years or older who were diagnosed with stage I to III colorectal adenocarcinoma.
				APR	173	T ₁ /T ₂ = 26; T ₃ /T ₄ = 147;	NA	Laparotomy	
Chang Hyun Kim. <i>et al.</i>	CCT	2015	Korea	ISR	162	T ₀ = 4, T ₁ = 4, T ₂ = 11, T ₃ = 20, T ₄ = 1.	162	Laparotomy	Consecutive patients who underwent APR or ISR after receiving neoadjuvant CRT for locally advanced (radiological T3-4 and/or Np) rectal cancer were enrolled in this study.

Note: ISR, Intersphincteric Resection; APR, Abdominoperineal Resection; CCT, controlled clinical trials; RCT, randomized controlled trials; NA, not available; MVR, Multivisceral Resections.

Study	Study design	Study period	Country	Group	N	T stage	NAC	Surgery	Inclusion Criteria
				APR	40	T ₀ = 5, T ₁ = 1, T ₂ = 11, T ₃ = 21, T ₄ = 2.	40	Laparotomy	
Jin Soo Kim <i>et al.</i>	CCT	2009	Korea	ISR	72	T ₀ = 6; T _{1/2} = 14; T _{3/4} = 30	72	Laparotomy	Investigation was undertaken on patients meeting the following eligibility criteria: (1) histologically proven primary rectal adenocarcinoma, (2) tumor distance from anal verge less than 6 cm, and (3) preoperative CRT.
				APR	50	T ₀ = 9; T _{1/2} = 15; T _{3/4} = 48	50	Laparotomy	
Note: ISR, Intersphincteric Resection; APR, Abdominoperineal Resection; CCT, controlled clinical trials; RCT, randomized controlled trials; NA, not available; MVR, Multivisceral Resections.									

Operative and Postoperative Outcomes and Pathological Data

Patients in the LISR group had a similarly operative time (259.47 ± 80.25 vs 279.90 ± 82.32 minutes, $p = 0.268$), blood loss (166.58 ± 120.97 vs 139.63 ± 114.98 ml, $p = 0.313$), length of hospital stay (15.97 ± 15.54 vs 11.27 ± 8.35 days, $p = 0.095$), and postoperative complication with LAPR group; however, time to first exhaust was shorter in LAPR group than in LISR group (3.18 ± 1.97 vs 2.46 ± 1.00 days, $p = 0.042$).

Survival And Patterns Of Recurrence

The actuarial distant metastases-free survival rate was 63.16% in LISR group and 70.73% in LAPR group, respectively (Table 1). Patients undergoing LISR had a similarly 5-year local recurrence and overall survival rate with LAPR. The most common seen recurrence place was pelvic cavity. In addition, patients with advanced tumors, as assessed by restaging MRI and luminal circumferential involvement, suffered local recurrence significantly more frequently if they had been treated using APR rather than ISR.

Meta-analysis

The whole process of study selection is abided to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) and PRISMA-Protocol guidelines[11]. Its results will be presented in a PRISMA flow chart with clearly reasons of exclusion and inclusion at each stage. A total of 352 articles that mentioned LISR

and LAPR from the database was carefully screen. We screened the full texts, titles, abstracts, and so on, or a combination of these, and removed the duplicate results. At last, four studies were eligible for this final meta-analysis [12–15].

Outcome Measurements

5-years recurrence rate

The available data for the 5-years recurrence rate was provided by four studies [12–14], which included 688 patients. No significant difference was noted for the 5-years recurrence rate between the ISR and APR subgroups (Fig. 1), without heterogeneity across the trials, and without publication bias ($P = 0.59$).

5-years Survival Rate

Three studies, which included 304 patients, provided available data regarding 5-years survival rate[12, 14, 15], and showed no statistically significant difference between the ISR and APR subgroups (Fig. 2), without heterogeneity across trials, and without publication bias ($P = 0.76$).

Discussion

In the past 20 years, ISR has been performed as an anus-preserving alternative to avoid the need for permanent colostomy in patients with invasive low rectal cancer located near the anal canal[16, 17]. Only a small number of reports have compared the long-term outcomes of ISR with those of APR[14], and very few report describe the LISR. We compared surgical outcomes of patients with ultra-low rectal cancer who underwent either LISR or LAPR. The main findings were as follows: short-term surgical outcomes, including operating times, blood loss during surgery, postoperative pain, and postoperative morbidities, were similar in both groups. Our findings also generally agree with previous studies, in which patients undergoing ISR had similarly oncology outcomes compared with patients undergoing restorative surgery.

Previous studies have shown that LAR and especially ISR often lead to severe functional problems both in short and long term and may result in a poor defecatory function. Patients with very low anastomoses are especially prone to develop a condition termed “low anterior resection syndrome”[18], which incorporates a number of unpleasant symptoms such as frequent defecation, urgency, and stool incontinence, and severely impairs QoL. These commonly occurring problems after deep sphincter-preserving surgery are probably the reason why recent studies have shown that QoL after ISR and LAR, contrary to former beliefs, is not better than QoL after APR. This is in accordance with the results of our study which show an equivalent global health status for all three groups. There were no significant differences in most of the QoL items. However, diarrhea and constipation were significantly worse in ISR and LAR compared to APR patients. Patients with ISR showed significantly more symptoms in the gastrointestinal tract and more defecation problems, which is consistent with current literature and well explicable as the operation impairs anorectal function the most.

Fecal incontinence was common in patients after ISR[19]. This is well explicable as patients undergoing ISR generally have direct impairment of anal sphincter function as the cranial part of the internal sphincter is removed. Moreover, most of or the entire transition zone are also removed resulting in an impairment of sensibility and hence also to more

incontinence. Finally, radiation therapy may have to involve the anal sphincter more in very low tumors in need for intersphincteric resection.

Our findings also generally agree with previous studies, in which patients undergoing ISR had similarly oncology outcomes compared with patients undergoing restorative surgery. It has also been suggested that inadequate excision, resulting in a greater CRM involvement and a less intact TME plane, is a major determinate of outcome. Nagtegaal et al reported that local recurrence rates were higher among patients with positive CRMs, regardless of the surgical technique used, and a more positive margin was present in patients undergoing APR (30.4%) compared with anterior resection (AR) (10.7%, $P=0.01$)[20].

This study has a number of limitations. First, the exact indication of APR is not included. As discussed above, invasion of the external sphincter was rare, and some of the factors that may have influenced the choice of surgical method could not always be determined. Second, it can be argued this study includes too few patients, and in fact, although tumor perforation is regarded as an important predictive factor for local recurrence following resection of low rectal cancer, we could not fully assess its impact in our study due to its rarity. Finally, more refined MRI predictors, such as CRM involvement, were not used. In a future study, a more detailed and informative analysis based on preoperative MRI may provide more individualized treatment guidelines.

Conclusion

This study suggests that LISR is as technically feasible, safe, and effective as LARC for treating patients with low rectal cancer. Additional high-powered randomized trials are needed to determine whether LISR truly offers any advantages.

Abbreviations

LISR: Laparoscopic intersphincteric resection; LARC: Laparoscopic-assisted abdominoperineal resection; LAPR: Laparoscopic abdominoperineal resection; ISR: Intersphincteric resection; TME: Total mesorectal excision; CRT: Preoperative chemoradiotherapy; NAC: Neoadjuvant chemoradiotherapy; RCTs: Controlled trials; CCTs: Controlled clinical trials; DFS: Disease free survival rate; OS: 5-years overall survival rate.

Declarations

Availability of data and materials

The data came from our hospital's data system.

Ethics approval and consent to participate

The name of the ethics committee: Ethics Committee of Affiliated Cancer Hospital of Guangxi Medical University. Ethics References No: LW2020037.

Consent for publication

We simply extracted data and did not involve the private information of patients.

Conflict of interest

The authors declared that we have no conflict of interest.

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Authors' contributions

Article topic design was contributed by XM and HQ. Data processing was performed by WW, HL, ZH, JL, HZ and YL. XM and WT are the corresponding authors. All authors read and approved the final manuscript.

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Figures

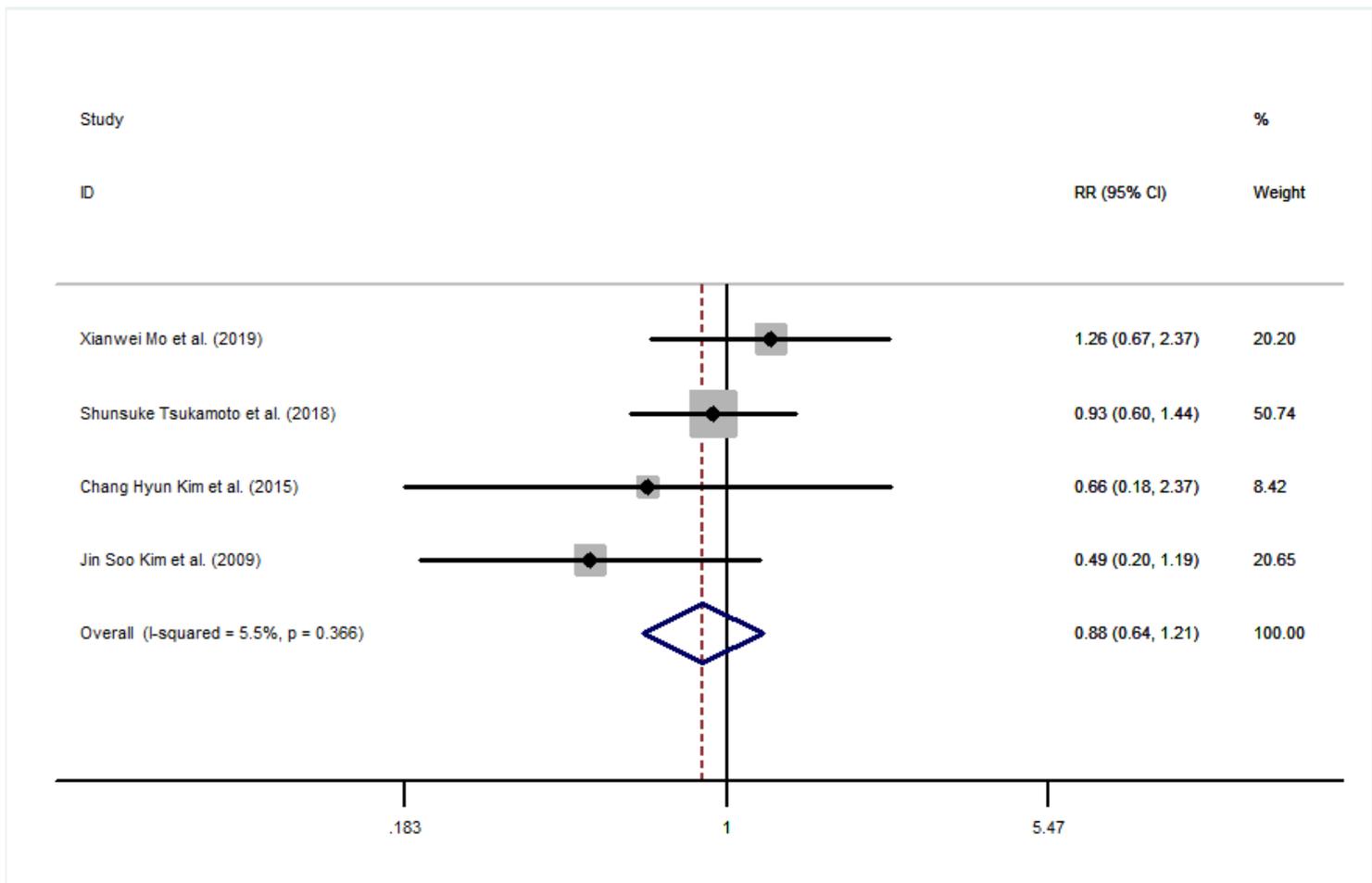


Figure 1

5-years recurrence rate between the ISR and APR subgroups.

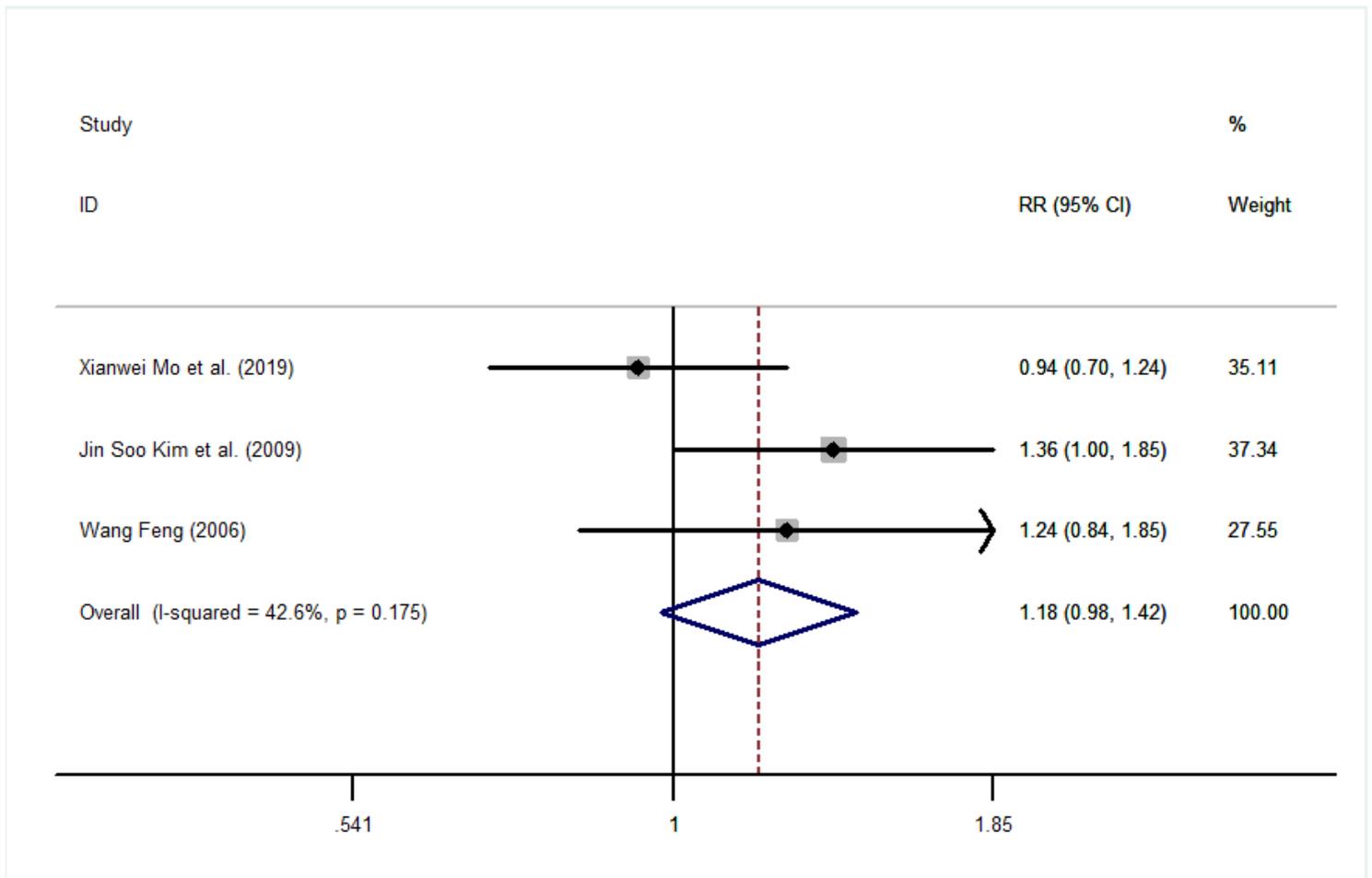


Figure 2

5-years overall survival rate between the ISR and APR subgroups.

Supplementary Files

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