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Research Article

Abdominoperineal Resection is Associated with a Poor Outcome Compared with Anterior Resection for Rectal Cancer: A Meta-Analysis

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Abstract

Background: It's controversies whether Anterior Resection (AR) is superior to Abdominoperineal Resection (APR) for rectal cancer. To solve this question, a meta-analysis was performed.

Methods: Studies published from 1990 to May 2014 evaluating outcomes after AR and APR for rectal cancer were identified by an electronic literature search. A meta-analysis was performed to compute Hazard Ratio (HR) along with 95% Confidence Intervals (CI). We extracted HRs of Disease-Free Survival (DFS) and Overall-Survival (OS) compared these two methods using a random-effects model.

Results: Twenty four studies met the inclusion criteria, yielding a total of 21,221 patients. Pooled adjusted HRs were 1.276 (95% CI, 1.266 -1.287) for DFS and 1.130 (95% CI, 1.126-1.133) for OS that compared APR with AR. Sensitivity analyses were performed and APR was still associated with poor prognosis.

Conclusion: APR has been associated with poor prognosis compared with AR. While possible, a more radical operation, extralevator abdominoperineal resection should be considered.

Keywords: Rectal cancer; Meta-Analysis; Abdominoperineal resection; Disease free survival

Introduction

Colorectal cancer is the third most commonly diagnosed cancer in males and second in females [1]. It is also one of the leading causes of cancer mortality worldwide, and rectal cancer accounts for 30 to 35% of these cases [1].

Miles, who introduced Abdominoperineal Resection (APR) in 1908, based his work on that the spread of tumors of the lower rectum occurred through the lymph nodes outside the levator ani muscles. APR was thought to address this problem. Anterior Resection (AR) was later introduced for proximal rectal cancers. Improvements in stapling technology over the following decades have resulted in an increase in the number of sphincter-saving operations [2]. The more important recent advance in rectal cancer surgery has been the Total Mesorectal Excision (TME). TME is defined as sharp pelvic dissection between the parietal and visceral planes of the pelvic fascia and it has been introduced since 1982 by Heald [3]. TME and precise perimesorectal plane dissection were introduced in all the major countries of Europe in 1995 [4]. Local recurrence rate can decrease to less than 10% for middle and lower rectal carcinomas with this procedure [5]. Following several workshops and operative demonstrations around the world, TME is now generally accepted as the standard procedure for rectal cancer [6].

Previously APR was thought to be able to eradicate border field than AR and achieve better outcomes in disease free survival or even overall survival. Others suggest otherwise [7-10]. It's not clear if the worse outcome associated with APR is a result of surgical procedure or patient- and tumor-related factors. Many studies have tried to explicate these relationships. Possible reasons for high local recurrence of APR compared with AR include the higher incidence of inadequate margin [11] or lymph node involvement that may follow a different pattern in low rectal carcinomas. Very low cancers have a dual lymphatic drainage [12]. Tumor or rectal perforation are other important factors that might contribute to poorer outcomes in APR.

However, due to tumor nature and anatomic reason, further randomized-controlled trials would not be feasible to compare these two methods. This question has been further complicated by different neoadjuvant, adjuvant, and chemotherapy agents. Since prospective randomized studies comparing APR with AR are ethically unavailable, we try to answer this question from previous studies through meta-analysis. This is the first meta-analysis that attempts to answer this question.

Method

Search strategy and Selection criteria

We systematically searched Pub Med and Medlines for relevant articles published up to May12, 2014, with the following search terms, "anterior" and "rectal cancer, "abdominoperineal" and "rectal cancer" without language restriction. Additional search methods included manual review of the reference lists of relevant

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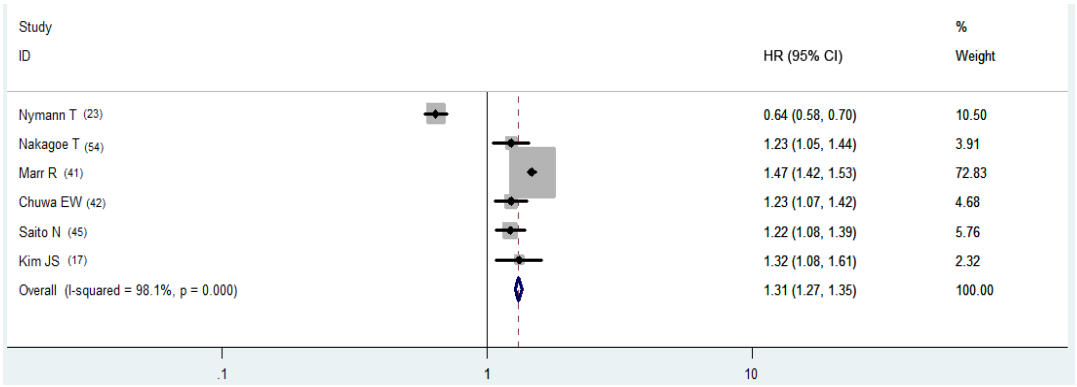

Figure 1a: Univariate HR of DFS.

studies. Studies were included if the following were true: (1) they were published with extractable information on disease free survival (DFS) or overall survival (OS); (2) they were primary rectal cancer. Chemotherapy was not used in patients with rectal cancer during the late 1990s. Whether adjuvant was used or not are included as well. Studies before 1990 were excluded. Kaplan-Meier DFS or OS graph with three or fewer outcome events was considered as inadequate and was excluded. Only original articles were included; posters, abstracts, and conference reports were excluded.

Information on age and stage were extracted when available and taken into account in the analysis. Abdominoperineal excision was often involved positive circumferential resection margins [13] which has been associated with a poor prognosis [14]. Due to variable factors adjustments in each studies, if any one of stage, age or margin were included in original studies for adjustment, the HR were considered as multivariate analysis.

We assessed the methodologic quality of included studies using the Newcastle-Ottawa Scale [15] for determining the quality of individual cohort studies included in the meta-analysis.

Statistical analysis

We extracted HR by direct or indirect methods [16] based on the available information provided in the selected articles. If information for applying these methods was not available, a graph methods, which stratifies the published survival curve into nonoverlapping intervals to estimate the log HR, was used to extract the HR [16]. Summary HRs were obtained using the random-effect model. Forest plots were used to display the study-specific HRs and the summary estimates. Heretorgenetiy among the studies was tested with Q statistics. Analyses were conducted with Stata version 12.0 (Stata Corp, College Station, TX). Two-sided p values <0.05 were regarded as statistically significant.

Results

Literature search

The steps of our literature search are shown in (Figure 1). After reviewing titles and abstracts, 104 potential papers were extracted to review in full. Two papers [17,18] were from two different but overlap periods of the same hospital. Due to one paper provided information to overall survival and the other to disease-free survival without double weighting. Both of the papers were included.

Four articles were excluded due to language problem [19-22]. Four other articles were excluded due to unavailable in our setting [23-26]. Two of the four were from the same Chinese journal. As for the rest, one is excluded due to a short report [27]. One is excluded due to abdominosacral resection instead of abdominoperineal resection [28]. One is excluded due to use chi-square test for survival data [29]. Some paper with hazard ratio of local recurrence only [30]. Two paper is excluded due to less or equal to 3 events and was unable to extract hazard ratio from survival curve [31, 32]. Two were excluded due to more than 3 survival curve and unable to extract [33,34]. Others were excluded due to no extractable hazard ratio (HR) of DFS or OS.

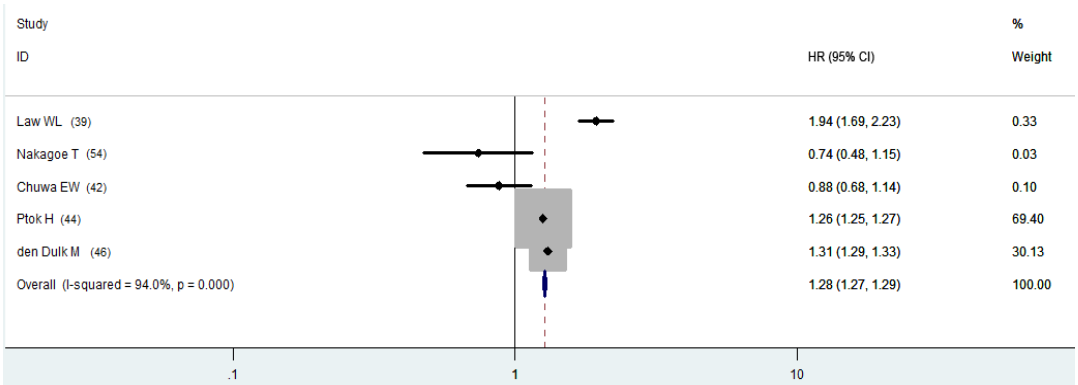

Figure 1b: Multivariate HR of DFS.

Table 1: Methodologic quality of studies, based on the Newcastle-Ottawa scale (N = 24).

Studies	Representative-ness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure: APR *vs.* LAR	Demonstration that outcome of interest not present at start	Study controls for initial staging and/ or for an additional factor	Assessment of outcome	Was median follow-up 2.5 years or more?	Adequacy of follow-up (80%)	Total
Tuscano D [37]	—a	★	★	★	—	—	—	★	4
Holm T [36]	★b	★	★	★	★★	★	—	—	7
Nymann T [53]	★	★	★	★	—	—	—	★	5
Bozzetti F [38]	★	★	★	★	★★	★	★	—	8
Zaheer S[35]	★	★	★	★	★★	★	★	★	9
Wibe A [8]	★	★	★	★	★★	—	★	—	7
Law WL [39]	★	★	★	★	★★	★	★	—	8
Harling H [40]	★	★	★	★	★★	★	—	★	8
Nakagoe T [54]	★	★	★	★	★★	★	★	★	9
Marr R [41]	★	★	★	★	—	★	—	—	6
Haward RA [7]	★	★	★	★	★c	★	—	—	6
Chuwa EW [42]	★	★	★	★	★★	★	★	—	8
Kim NK [43]	★	★	★	★	★★	—	★	★	8
Ptok H [44]	★	★	★	★	★★	★	—	★	8
Saito N [45]	★	★	★	★	—	★	★	★	7
den Dulk M [46]	★	★	★	★	★★	★	★	★	9
Ferenschild FT [47]	★	★	★	★	★★	★	★	—	8
Kim JS [17]	★	★	★	★	★★	—	★	—	7
Anderin C [48]	★	★	★	★	★★	★	★	—	8
Silberfein EJ [49]	★	★	★	★	★★	★	★	—	8
Chambers W [50]	★	★	★	★	—	—	★	—	5
Lange MM [51]	★	★	★	★	★★	—	★	★	8
Omidvari S [52]	★	★	★	★	★★	★	★	—	8
Kim JC [18]	★	★	★	★	★★	—	★	—	7

The first score, "*representativeness of the exposed cohort*", was scored as positive where the study was considered truly or somewhat representative of the general population in the location of the study. Studies on selected groups or where there was no description if the cohort were scored as negative. The second score, "*selection of the non-exposed cohort*", was scored as positive if the population was selected and then each subject was identified as either exposed or non-exposed, so that the non-exposed cohort was drawn from the same community as the exposed cohort. The third score, "*ascertainment of exposure*", related to operation methods in our analysis. The fourth score, "*demonstration that the outcome of interest was not present at start of the study*", was scored as positive as operation outcome was not presented initially. The fifth score, "*comparability of the cohorts on the basis of design or analysis*", was scored according to whether the analysis controlled for initial staging and/or for an additional factor (e.g. marginal status, age, or others). The sixth score, "*assessment of outcome*", was scored positively if one of outcomes or start time were defined clearly initially. The seventh score was "*was follow-up long enough for outcomes to occur*". It was decided that a median follow-up of greater than 2.5 years would be adequate as most colon cancer recurred within 2 years [9]. The eighth and final score, "*adequacy of follow up of cohorts*" was scored positively if the follow-up was complete or the subjects lost to follow up were less than 20%. The highest possible total score was 9. The distribution of total scores for the 24 studies were as follows: 4 (1 study), 5 (2 studies), 6 (2 studies), 7 (4 studies), 8 (12 studies) and 9 (3 studies). A) Tuscano D didn't specify whether these 34 patients represent all these group of patients or not. B) This study combined two different time periods of study groups. C) This study didn't adjust for stage information but adjust for other factors.

Methodological quality scores ranged from 4 to 9 on a scale of 10 (Table 1). With regard to the quality of the studies, 21 trials (87.5%) showed a high-quality score (6 points). The distribution of total scores for the 24 studies were as follows: 4 (1 study), 5 (2 studies), 6 (2 studies), 7 (4 studies), 8 (12 studies) and 9 (3 studies). Because most of the studies received a score of 6 or above and the standard criteria have not been established, we considered the studies to be of adequate quality for the analysis.

Study characteristics

We identified 24 eligible studies [7,8,17,18,35-54] published from 1990 to 2014 (Table 2a). There were 21,221 patients included in these studies (Table 2b). All were retrospective cohort studies except one matched retrospective cohort study. [18] Fifteen studies were from Europe, two studies from United States and seven studies from Asia. Patients received variable radiation and chemotherapies. The predominant chemo radiation therapy regimens and adjuvant

Table 2a: Studies of compared low anterior resection with abdominoperineal resection.

Study	Year	country	Design	No. of institutes	Male (%)	location	Radiation	Chemoradiation regimen	Adjuvant chemotherapy
Tuscano D [37]	1992	Italy	Retrospective	Single	67	≦7.5cm	No	No	No
Holm T[36]	1995	Sweden	Retrospective	Multiple	59	≦25cm	47.7 *vs.* 49.6%	No	No
Nymann T [53]	1995	Denmark	Retrospective	single	63	≦18cm	No	No	No
Bozzetti F [38]	1996	Italy	Retrospective	Single	59	≦8cm	NA	NA	NA
Zaheer S [35]	1998	US	Retrospective	Single	61	NA	No	No	No
Wibe A [8]	2004	Norway	Retrospective	47	58	≦12cm	6 *vs.* 16%	No	No
Law WL [39]	2004	Hong Kong	Retrospective	Single	61	≦12cm	7.1 *vs.* 45	5FU	44.4 *vs.* 41 II, III
Harling H [40]	2004	Denmark	Retrospective	Multiple	NA	≦15cm	34%	NA	NA
Nakagoe T [54]	2004	Japan	Retrospective	Single	64	NA	No	No	III, 5FU
Marr R [41]	2005	UK	Retrospective	Single	56	NA	No	No	11.9%
Haward RA [7]	2005	UK	Retrospective	Multiple	61	NA	NA	NA	NA
Chuwa EW [42]	2006	Singapor	Retrospective	Single	58	≦10cm	No	No	No
Kim NK [43]	2006	Korea	Retrospective	single	70	NA	all	5FU_LV	All, 5FU_LV
Ptok H [44]	2007	German	Retrospective	75	61	≦8 cm	NA	NA	49.7 vs. 53.4
Saito N [45]	2009	Japan	Retrospective	Single	70	≦5 cm	No	T3 (36.4%)	III 5FU_LV, UFUR, others
den Dulk M [46]	2009	Europe	Retrospective	Multiple	66	NA	Variable	5FU_LV	5FU_LV
Ferenschild FT [47]	2009	Netherlands	Retrospective	Single	54	≦15cm	Variable	Variable	No
Kim JS [17]	2009	Korea	Retrospective	Single	72	≦6cm	Yes	5FU_LV	NA
Anderin C [48]	2010	Sweden	Retrospective	8	57	≦6cm	73 vs71%	NA	NA
Silberfein EJ [49]	2010	US	Retrospective	Single	57	NA	88%	5FU, capecitabine	II or III, 5FU_LV
Chambers W [50]	2010	UK	Retrospective	Single	68	NA	63 *vs.* 59.5%	NA	3.7 vs 26.2%
Lange MM [51]	2013	Netherlands	Retrospective	2	61	≦12cm	Yes	5FU_LV	5FU_LV, levamisole, or capecitabine
Omidvari S [52]	2013	Iran	Retrospective	Single	58	≦12cm	84.4 *vs.* 71.4%	5FU_LV, capecitabine, oxaliplatin	5FU_LV, capecitabine, oxaliplatin, irinotecan 57.9 vs 42.1%
Kim JC [18]	2013	Korea	Retrospective, matched	Single	59	≦6cm	39 vs 13%	5FU-LV or capecitabine	III, II with poor prognostic factor

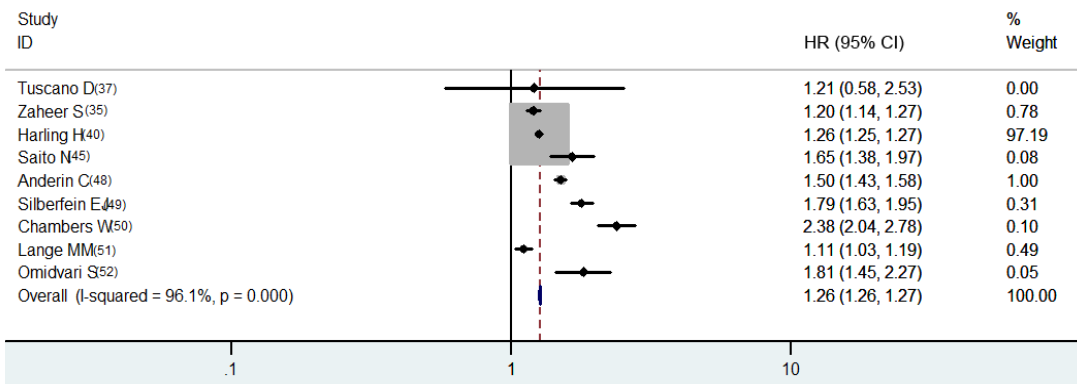

Figure 2a: Univariate HR of OS.

chemotherapies were 5-fluorouracil-based.

HRs of data from one article was calculated by the direct methods, 16 by the indirect methods, and seven by the graph method. The median age of the patients was around 60 years, and the majority of the patients were men. Most studies calculated the start points from the date of primary treatment (surgery) except one [7] that started from the diagnosis date (Table 3). Eight out of the 24 studies did not provide information on HRs of disease-free survival or overall survival.

Disease free survival and overall survival

As univariate analysis (Table 2b), six out of 24 had information of disease-free survival, the pooled HR compared APR with AR was

Table 2b: Patient characteristics of studies.

Source	Median follow up (mo.)	Median age	stage	Methods	TME	AR	APR	DFS_ HR_U	DFS_ HR_M	OS_ HR_U	OS_ HR_M	Adjuvstage[a]	Adjuage[a]	Adju margin[a]
Tuscano D	25[b]	60	≦III	Direct	Yes	13	11	NA	NA	1.21	NA	-	-	-
Holm T	NA	68 *vs.* 69[c]	≦III	Indirect	NA	470	664	NA	NA	NA	1.14	Yes	Yes	Yes
Nymann T	NA	68.7 *vs.* 64.9[c]	≦III	Graph	NA	74	101	0.64	NA	NA	NA	-	-	-
Bozzetti F	77	64	≦III	Indirect	Yes	93	257	NA	NA	NA	0.72	Yes	Yes[d]	Yes
Zaheer S	5.6y	67	all	Graph	Yes	272	169	NA	NA	1.20	NA-	-	-	-
Wibe A	44	69	≦III	Indirect	Yes	1315	821	NA	NA	1.86	1.3	Yes	Yes	Yes
Law WL	35.4	67	all	Indirect	Yes	419	69	NA	1.94	NA	NA	Yes	Yes	Yes
Harling H	NA	NA	≦III	Indirect	V	2199	1263	NA	NA	1.26	NA	-	-	-
Nakagoe T	47.4	66	≦III	Indirect	Yes	116	91	1.23	0.74	NA	NA	Yes	Yes	Yes
Marr R	NA	NA	NA	Graph	Yes	355	181	1.47	NA	NA	NA	-	-	-
Haward RA	NA	NA	NA	Indirect	NA	1535	1986	NA	NA	NA	1.10	No	Yes	No
Chuwa EW	38	65	≦III	Indirect	Yes	547	93	1.23	0.88	NA	NA	Yes	Yes	NA
Kim NK	39.4	55	≦III	Indirect	Yes	41	56	NA	NA	NA	2.86	yes	No	Yes
Ptok H	NA	66	≦III	Indirect	Yes	601	956	NA	1.26	NA	NA	Yes	No	Yes
Saito N	40 *vs.* 58[c]	57 *vs.*59[c]	≦III	Graph	Yes	132	70	1.65	NA	1.22	NA	-	-	-
den Dulk M	5.4y	NA	≦III	Indirect	V	2280	1353	NA	1.31	NA	1.17	Yes[e]	Yes[f]	Yes
Ferenschild FT	3.6y	69[g]	≦III[h]	Indirect	Yes	145	65	NA	NA	NA	0.74	Yes[e]	Yes	Yes
Kim JS	47.7	NA	≦III	Graph	Yes	72	50	1.32	NA	NA	NA	-	-	-
Anderin C	6.4y	67*vs.* 72[c]	≦III	Indirect	Yes	113	438	NA	NA	1.50	1.19	Yes	Yes	Yes
Silberfein EJ	95	57	≦III	Indirect	Yes	176	128	NA	NA	1.79	1.75	Yes	Yes	No
Chambers W	4.8y	64	≦III	Graph	NA	81	42	2.38	NA	NA	NA	-	-	-
Lange MM	92	71[g]	≦III	Indirect	Yes	259	107	NA	NA	1.11	1.45	Yes	Yes	No
Omidvari S	37	57[h]	All[i]	Graph[j]	Yes	96	42	NA	NA	1.81	NA	-	-	-
Kim JC	76 *vs.* 84[c]	54[g]	≦III	Indirect	Yes	402	402	NA	NA	NA	0.994	Yes	Yes	NA

Abbreviation: NA, not available; TME, total mesorectal excision; DFS_HR_U, univariate of hazard ratio for disease-free survival, APR/AR; DFS_HR_M, multivariate of hazard ratio for disease-free survival, APR/AR; OS_HR_U, univariate of hazard ratio for overall-survival, APR/AR; OS_HR_M, multivariate of hazard ratio for overall-survival, APR/AR; V, variable.

[a]DFS_HR_M or OS_HR_M adjusted for stage, age or margin; [b]Mean follow up; [b]AR vs. APR; [c]age is excluded while p-value less than 0.2 during univariate analysis and then not included in Cox model; [d]only adjusted for lymph node status; [e]propensity score; [f]Mean age; [g]4.8% liver metastasis not found initially but found during operation; [h]15% of stage IV; [i]12% laparoscopic and 88% open approach.

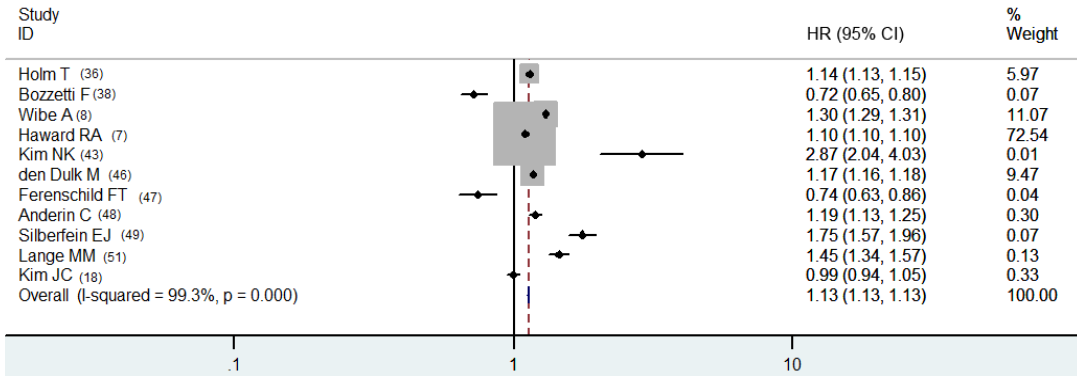

Figure 2b: Multivariate HR of OS.

1.311 (95% CI, 1.272-1.352). There was significant heterogeneity (p<0.001, Figure 1a). HRs from nine studies on OS was 1.264 (95% CI, 1.257-1.270), also with significant heterogeneity (p<0.001, Figure 2a).

Table 3: Methodologic definitions.

Studies	Start time	Disease-free survival	Overall survival
Tuscano D [37]	NA	NA	NA
Holm T [36]	NA	Recurrence within the radiation target area defined as local and outside this area as distant metastasis	NA
Nymann T [53]	NA	NA	NA
Bozzetti F [38]	Surgery date	Pelvic recurrence, distant metastases, or second primary	Occurrence of death, or to the last follow-up assessment available for living patients
Zaheer S [35]	Primary treatment	Date of first recurrence	Death
Wibe A [8]	NA	NA	NA
Law WL [39]	Surgery date	Histologically proven or radiologically evident disease with subsequent clinical progression	NA
Harling H [40]	Surgery date	NA	Death or when censored
Nakagoe T [54]	Surgery date	Date of first recurrence	NA
Marr R [41]	NA	Cancer-specific survival, died of noncancer-related illness were censored from further analysis from the time of death	NA
Haward RA [7]	Diagnosis date	NA	Death or when censored
Chuwa EW [42]	Date of primary treatment	Date of first recurrence-local, systemic, or both	Date of death
Kim NK [43]	NA	NA	NA
Ptok H [44]	Surgery date	A local and/or systemic recurrence A new tumor , either histologically or an imaging	Death of the patients, irrespective of its cause
Saito N [45]	Surgery date	NA	NA
den Dulk M [46]	Surgery date	Death due to rectal cancer	NA
Ferenschild FT [47]	Surgery date	NA	NA
Kim JS [17]	NA	NA	NA
Anderin C [48]	Surgery date	NA	Time of death or the end of follow-up
Silberfein EJ [49]	Surgery date	NA	NA
Chambers W [50]	NA	NA	NA
Lange MM [51]	NA	NA	NA
Omidvari S [52]	Date of initial treatment	Any type of treatment failure	Death from any reason or the last follow-up
Kim JC [18]	NA	NA	NA

Abbreviation: NA, not available.

As for multivariate HR of DFS, studies were adjusted different for stage, age and margin (Table 2b). Combining five papers HRs on DFS adjusting variable for stage, ages and margin, [39, 42, 44, 46, 54] the pooled HR comparing APR with AR was 1.276 (95% CI, 1.266-1.287), again with significant heterogeneity ($p<0.001$, Figure 1b). Multivariate HRs of OS [7,8,17,18,36,38,43,47-49,51] adjusted variable for stage (eight studies), age (eight studies) and margin (five studies) was 1.130 (95% CI, 1.126-1.133) (Table 2b). There was a statistically significant heterogeneity among studies ($p<0.001$, Figure 2b).

Sensitivity analyses

Potential sources of heterogeneity include tumor location of the rectal cancer, geographical region where the study was conducted and year of the treatment. Also, age was adjusted for with different methods. To assess if any of these factors causing heterogeneity, subgroup analysis were performed within stratum of the relevant study features. Subgroup analyses were performed for tumor located within 12cm of anal verge. Subgroups for different regions of Europe and Asia were analysis and for those received operation within 10 years (2004) as well.

Heterogeneity was equally evident in all strata except DFS in studies conducted in Asia and for tumor within 12cm anal verge (data not shown). However, the studies numbers were small. Nonetheless, APR continues to show a poor prognosis as compared with AR in different subgroups.

Discussion

Cancers of the lower rectum have a less favorable oncologic outcome compared with those situated at upper locations [8, 55-57]. Lower rectal carcinomas had a twice chance of circumferential margin involvement compared to tumors situated over 5 cm from anal verge (26.5% v 12.6%). After chemo radiation therapy, AR might be performed as well. In lower rectal carcinoma, three times more positive margins were present in patients operated by APR than AR (30.4% v 10.7%) [58]. In the late nineteenth century, APR was the standard operation for lower rectal cancer. Due to the development of stapler technique, AR was later more widely adopted. Previously APR was thought to have better survival due to the wider dissection [37]. However, later studies showed that APR was associated with poor survival due to involvement of more positive margins [13,48] or perforation, [48] higher local recurrence rates, and poorer

survival of low rectal cancer [58]. Even after adjusting for margins and perforation, APR was still associated with a poor prognosis [44]. Among the studies included in our analysis, most of the HRs for OS were adjusted for stage, age and margin and APR was still associated with a poor prognosis. The median tumor level located from anal verge also lower in the APR group than in the AR group [48]. In early 1990s, TME was not widely adopted but now it was current standard of treatment. TME cannot always be performed [9] because of the presence of a large tumor around this lower level. Visualization and access at the floor of the pelvis are limited. Nevertheless 18 out of 24 (75%) studies stated that they had performed TME on all study patients with 2 studies of variable performing TME.

In our analysis, we showed that APR was associated with poor disease free and overall survival even after adjusted for age, margin and stage. Though we found a significant heterogeneity in the pooled disease free survival or overall survival of APR compared with AR, all the analysis and most of the subgroup analyses showed the poor prognosis associated with APR while compared with AR. The heterogeneity might due to patient racial composition or difference in age adjustment. Holm T et al., [36] indicated that they had adjusted for age without a detailed description. Some studies adjusted for age with variable cut points [38] or with propensity score [8]. One study adjusted for age at cut point of 65 year-old [42] while others at 80 year-old [47] or 72 year-old [48]. Also, variable definitions of clear margin were used. The proximal, distal, and circumferential resection margins free from tumor instead of tumor involvement within 1 mm of the circumferential resection margin (CRM positive) were used by Anderin C et al., [48] while others did not provide a clear definition.[36] Radiation therapy has been a standard care for T3 rectal cancer [59]. Since the introduction of radiotherapy, local recurrence has been reduced from 11.4% to 6.1% [60]. Radiotherapy has been considered as standard therapy for stage II and III rectal cancer. However, radiation therapy has only shown a marginal effect in improvement. Due to the lack of strong evidence specifically for rectal cancer, support for the use of adjuvant chemotherapy in patients with rectal cancer is generally extrapolated from the data available for colon cancer [61].

P. How et al., [10] has published a review article of "a systematic review of cancer related patient outcomes after anterior resection and abdominoperineal excision for rectal cancer in the total mesorectal excision era" in 2011. They suggested that tumours treated by APR were lower and more locally advanced. They suggested that surgical technique itself for the tradition APR was also inadequate and resulted in poor outcomes. The results of our meta-analysis support their conclusion as well.

In recent years, a more extended approach, later called the extralevator abdominoperineal resection, has been propose by T. Holm [62]. Review article suggested that extended APR such as cylindrical resection was associated with a lower rate of radial margin involvement and improved local control rate compared to conventional APR [63]. A meta-analysis has confirmed this finding [64].

Up to 90% of patients undergo sphincter-preserving surgery will subsequently have a change in bowel habit, ranging from increased bowel frequency to fecal incontinence or evacuatory dysfunction. These have been called anterior resection syndrome [65]. An uncertain preference for one or the other surgical procedure cannot be discerned, particularly a prospective study [66] and a meta-analysis [67] on the quality of life following APR vs. AR had failed to show a superiority of AR.

Some might argue that the surgical indications for APR were different from anterior resection. Decision was based on the location of the tumor. Difference in tumor locations could also reflect a difference in tumor biology in term of spread. To answer this theory, one should compare APR vs anterior resection in upper 2/3 rectal cancer which might seem impossible due to unethical. However, as we could see that 7 out of 24 inclusions studies were from lower rectum (8cm) (Table 2A). Among them 3 papers were available for univariate OS analysis. It still showed that APR were worse than LAR (HR 1.509, 95% CI, 1.439-1.582) but non-significant after adjusted for age or margin (HR 0.954, 95% CI, 0.761-1.193) (data not shown).

Rectal cancer treatment was a rather complex issue. Surgical options including LAR or APR were performed by tumor location and the extent of tumor invasion. Despite of several trials have been done to compare the long term outcome of this two surgical options, there was still no consensus nor guideline to follow. The major reasons may be small size in each trial or dispersed distribution of rectal cancer in different patients or even each surgeon's personal favor in certain surgical procedure. In order to solve these problems, meta-analysis could provide a more robust evidence to this important clinical issue.

Further study might be needed whether the poor prognosis is due to rupture during the operation. Due to the poor prognosis of APR compared with AR, extralevator abdominoperineal resection [64] might be another choice while APR were deem unsuitable.

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