META-ANALYSIS OF THE RECURRENCE AND SURVIVAL RATE REGARDING THE DISTAL RESECTION MARGIN LENGTH IN RECTAL CANCER SURGERY

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Abstract

Background: The optimal distal resection margin (DRM) in rectal cancer surgery required to achieve an adequate oncological outcome remains controversial. The changing trends of the study results showed favorable outcomes of patients receiving as minimal a margin as possible. Therefore, this study aimed to perform a meta-analysis of the recurrence and survival rate regarding the DRM in rectal cancer surgery.

Methods: The study design followed the PRISMA guidelines. The journal was traced and then analyzed with parameters of local recurrence, distant recurrence, disease-free survival, and overall survival rate. Data was analyzed by Review Manager 5.3.

Results: There was a total of 48 studies included in this meta-analysis. There was no difference in recurrence rate by taking 1 cm as the cut-off point for DRM. However, limiting the studies to those measured DRM in a fresh specimen, the local recurrence rate was significantly higher in the group with DRM less than 1 cm to more than 1 cm (OR 1.92; 95%CI 1.21-3.06; p=0.006; I^2 35%). The recurrence rate was significantly higher in the group with DRM less than 5 mm than the group with DRM more than 5 mm (OR 1.52; 95%CI 1.05-2.29; p=0.03; I^2 34%).

Conclusion: This meta-analysis showed that taking 5 mm as a cut-off point was optimal to control the local recurrence rate in rectal cancer. The difference between distant recurrence and survival rate could not be determined due to a lack of data from previous studies.

Keywords: Rectal Cancer, Distal Margin, Safe Margin, Recurrence Survival

Introduction

Rectal cancer is one of the commonly found cancers worldwide (1). The recurrence and survival rate were the main therapeutic goals (2, 3). The introduction of total mesorectal excision, as long as with the presurgical chemotherapy, has allowed the local disease control and increased quality of life (4). Despite these advances, the resection margin status was one of the most important parameters in the prognosis (5).

The goal of achieving safe margins was always challenging, associated with its controversies, clinical judgment, and patient personalization (6). The DRM required to achieve an adequate oncological outcome remains controversial. Changing trends of the study results showing favorable outcomes of patients who received less than 1 cm distal resection margin (DRM) encouraged surgeons to operate with reduced DRM (7). Previously, the standard 5 cm margin was reduced to 2 cm and later with advances in surgical techniques to 2 cm rule or even less (8). From 1983 to 2007, the recommended DRM for rectal cancer has been reduced due to the findings of the rate of microscopic distal spread from studies. William et al. (1983) (9) recommended 5 cm, Shirouzu et al. (1995) (10) recommended 1 cm, Ono et al. (2002) (11) recommended 3 cm, Wang et al. (2006) (12) recommended 4 cm, and Guillem et al. (2007) (7) recommended 1 cm. The Current National Comprehensive Cancer Network guidelines recommended 4–5 cm DRM for partial mesorectal excision and 1-2 cm for total mesorectal excision (TME) (13).

Regardless of many studies have been done, the DRM was still inconclusive. Some even recommended as minimal as one millimetre due to its favorable results. Besides that, those studies were mostly retrospective, lack of length measurement standard, combining all subjects with various tumor sizes and histopathology features. Therefore, the purpose of this study was to perform a meta-analysis regarding the recurrence and survival rate of rectal cancer regarding the distal resection margin's length in rectal cancer surgery.

Materials and Methods

This meta-analysis was performed based on the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement and the Cochrane Handbook for Systematic Reviews of Interventions (Figure 1). All pooled analyses were based on published studies and thus did not require ethical approval and patient consent.

Literature search

Electronic databases were searched for studies published up until June 2021, including Medline, Embase, Web of Science, and Pubmed. The studies included and relevant reviews were also manually searched to include any relevant articles. The references of included studies were also analyzed for further investigation.

Selection criteria

Selection criteria were done based on the PICOS acronym (Population, intervention, comparator, outcomes, and study design), the author defined the inclusion criteria as below: Population (P): all patients that were diagnosed with rectal cancer based on histopathology examination. Intervention (I) and comparator (C): comparing the DRM and circumferential resection margin (CRM) with various cut off point. Outcomes (O): the following measured outcomes were included: local recurrence rate, distant

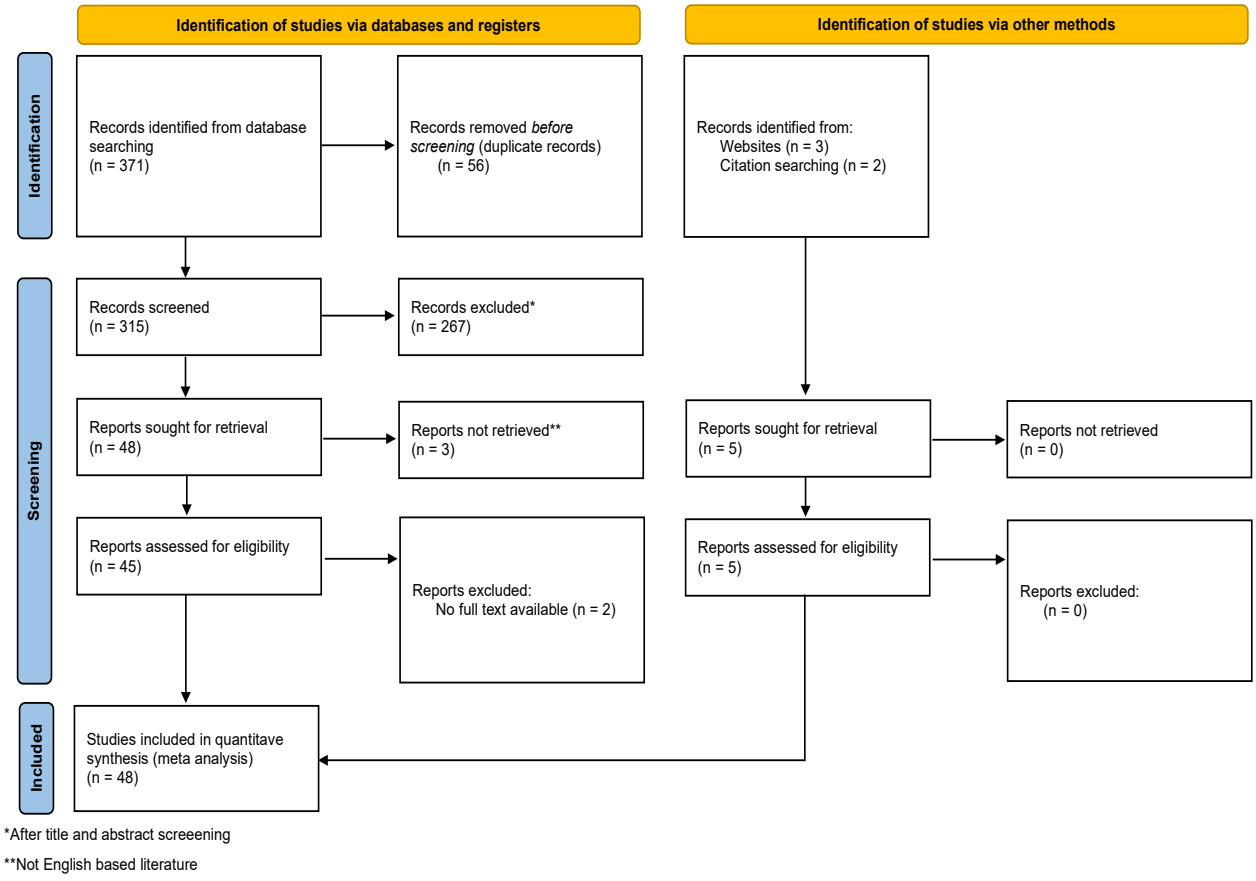


Figure 1: PRISMA flowchart of this study

recurrence rate, disease-free survival, five-year survival, and overall survival.

Data extraction

Relevant studies were limited to the studies published in the last 20 years. Two authors extracted the following information independently by using a predesigned table. Duplicate journal was managed by EndNote. There was a total of 320 records from literature searches based on the keywords applied. After screening the title and abstract, the authors included 53 studies that were relevant to the aim of this study. Three studies were excluded to not English-

based literatures. Then, only 48 studies were included in the quantitative synthesis due to no full -text available in the other two studies.

Any divergence or disagreements between authors was resolved by consulting a third author. The data collected in this meta-analysis were author, year, country, duration of follow up, included rectal tumor based on the distance from the anal verge, measured pathology specimen, the stage, number of cases, and total cases analyzed. For the lower rectal cancer, abdominoperineal resection or Miles procedure was carried out. For the middle rectal cancer, ultra-low anterior resection was done. For the upper rectal cancer, anterior resection was done.

Data analysis

All extracted data were entered into RevMan 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012) for statistical analysis. Studies with proportion will be analyzed by dichotomous analysis using random-effects model based on Mantel-Haenszel statistical approach was selected to combine the data. A significant p of 0.05 was taken as the standard.

Results

The local recurrence rate of the group with DRM more and less than 1 cm

There was a total of 23 studies that included in the meta-analysis of local recurrence rate between the group with DRM less than 1 cm and that with DRM more than 1 cm. The years of study ranged from 1992 to 2021. Duration of follow up ranged from 33-192 months. The total subjects from overall studies were 12,155 subjects. Most studies (60.9%) measured the DRM in fresh specimens. The most discrepancies in the included studies were that some only included the lower rectal cancer, while others included all regardless of the distance from the anal verge. Moreover, in some studies, authors used 6 cm as the cut-off point for lower to middle rectal cancer and middle to upper rectal cancer. One study used 7 cm, bust mostly used 5 cm. Only 1 study that subclassified again the recurrence rate based on the distance from anal verge. Besides that, not all subjects received neoadjuvant chemoradiation (NACRT). NACRT was given mainly to the subject's stage III-IV (Table 1) (8, 14-43).

This meta-analysis showed that the local recurrence rate was higher in the group who had DRM less than 1 cm compared to the group with DRM more than 1 cm (OR 1.34; 95%CI 0.95-1.89), but it was not statistically significant (p=0.10; I^2 51%; Figure 2). Then, authors were limited to three studies with only lower rectal cancer, wherein the local recurrence rate was also not significantly different (OR 1.69; 95%CI 0.62-4.59; p=0.31; I^2 0%). However, when the studies analyzed were only those which measured DRM in the fresh specimen (excluding fixed specimen), the local recurrence rate was significantly higher in the group with DRM less than 1 cm to the group with DRM more than 1 cm (OR 1.92; 95%CI 1.21-3.06; p=0.006; I^2 35%).

The local recurrence rate of the group with DRM more and less than 5 mm

There was a total of 11 studies that included in the meta-analysis of local recurrence rate between the group with DRM less than 5 mm and that with DRM more than 5 mm (Table 2). This meta-analysis showed that the local recurrence rate was significantly higher in the group who had DRM less than 5 mm compared to the group with DRM more than 5 mm (OR 1.52; 95%CI 1.05-2.29; p=0.03; I^2 34%; Figure 3). The same significant result is also shown in the study that take fresh specimen only (OR 2.63; 95%CI 1.54-4.50; p=0.0004; I^2 0%). However, the meta-analysis of only three studies taking tumors limited to lower rectal cancer showed no significant difference (OR 1.54; 95%CI 0.76-3.12; p=0.23; I^2 0%) (14, 16, 21, 24, 32-36).

The local recurrence rate of the group with DRM more and less than 2 cm

There was a total of 6 studies included in the meta-analysis of local recurrence rate between the group with DRM less than 2 cm and that with DRM more than 2 cm (Table 3). This meta-analysis showed that the local recurrence rate was significantly higher in the group who had DRM less than 2 cm compared to the group with DRM more than 2 cm (OR 2.24; 95%CI 1.01-4.93; p=0.05; I^2 80%; Figure 4). Furthermore, the significant results were also shown if the meta-analysis was done only in studies with fresh specimen (OR 2.66; 95%CI 0.99-7.11; p=0.05; I^2 84%) (8, 15, 17, 29, 38, 39).

The local recurrence rate of the group with various cut off point of CRM

A total of 5 studies was included in the meta-analysis of the local recurrence rate of the group with various circumferential resection margin (CRM) cut-off points (Table 4). This meta-analysis showed that the local recurrence rate was significantly higher in the less CRM, either by using the cut-off point of 1 cm (OR 3.01; 95%CI 1.77-5.11; p=0.0001; I^2 20%); 5 mm (OR 4.15; 95%CI 2.69-6.41; p<0.00001; I^2 0%); 2 mm (OR 2.17; 95%CI 1.67-4.40; p<0.0001; I^2 0); or 1 mm (OR 3.51; 95%CI 2.30-5.35; p<0.00001; I^2 55%; Figure 5) (29, 39-42).

The distant recurrence rate of the group with various cut off point of DRM

A total of 6 studies was included in the meta-analysis regarding distant recurrence rates with various DRM cut-off points (Table 5). This meta-analysis showed that no significant difference in distant recurrence rate with the cut-off point of 1 cm (Figure 6). However, meta-analysis was not carried out by the cut-off point of 2 cm and 5 mm because only 1 study fulfilled the criteria (15, 16, 18, 21, 28, 29).

Table 1: The data of the studies regarding the local recurrence rate of the group with DRM more and less than 1 cm

Author	Country	Duration of follow up (months)	Distance from the anal verge	Measured pathology specimen	Stage	DRM <1 cm		DRM >1 cm	
						n	Total	n	Total
Andreola et al. 2001 (14)	Italy	51	5 cm	Fixed	All	4	35	3	41
Bernstein et al. 2012(15)	Norway	60	15 cm (94.6% mid-upper; 5.4% lower)	Fixed	I-III	76	519	243	2823
Bhamre et al. 2019 (16)	India	62	10 cm (55.4% mid; 44.6% 108 lower)	Fixed	All	1	41	3	201
Bokey et al. 1999 (17)	Australia	60	15 cm (Lower 31.5%; Mid 29.9%; Upper 38.6%)	Fresh	All	9	39	50	557
Han et al. 2013 (18)	Korea	60	15 cm (Mean 7.8 cm)	Fixed	T3	8	129	17	198
Hong et al. 2014 (19)	Korea	37	12 cm (Mean 7.2 cm)	Fresh	All	1	81	4	137
Huh et al. 2008 (20)	Korea	56	6 cm (Median cm)	Fixed	All	3	18	0	25
Kang et al. 2016 (21)	Korea	60	NA	Fixed	All	9	132	18	283
Karanjia et al. 1990 (22)	UK	60	10 cm (Mean 7.1 cm)	Fixed	All	0	42	4	110
Kim et al. 2009 (23)	Korea	65	15 cm (Mean 7.2 cm)	Fixed	All	7	163	28	744
Kim et al. 2014 (24)	Korea	192	10 cm (Mean 5 cm)	Fixed	All	203	2208	34	368
Kiran et al. 2011 (25)	USA	49	10 cm (Mean 7 cm)	Fixed	All	7	784	19	586
Kuvshinoff et al. 2001 (26)	USA	33	8 cm (Median 4.4 cm)	Fixed	All	6	16	1	12
Law et al. 2002 (27)	Hong Kong	35	8 cm (Median 6 cm)	Fresh	All	6	60	6	207
Leo et al. 2009 (28)	Italy	92	5 cm	Fresh	All	7	94	6	84
Lim et al. 2012 (29)	Singapore	45	12 cm	Fixed	I-III	12	148	9	172
Manegold et al. 2019 (30)	Germany	96	12 cm (Mid 64.8%; Lower 35.2%)	Fixed	II-III	2	33	3	55
Moore et al. 2003 (8)	USA	118	15 cm (Mean 6 cm)	Fresh	All	2	17	7	77
Piccolo et al. 2010 (31)	USA	109	10 cm (Mean 6 cm)	Fixed	All	0	10	0	40
Rutkowski et al. 2008 (32)	Poland	69	10 cm (Mean 6 cm)	Fresh	All	5	42	19	124
Silberfein et al. 2010 (33)	USA	94	5 cm (Median 2 cm)	Fresh	All	3	37	6	82
Stocchi et al. 2001 (34)	USA	60	12 cm	Fresh	All	13	54	29	298
Vernava et al. 1992 (35)	USA	42	10 cm (Median 8 cm)	Fresh	All	6	20	22	219

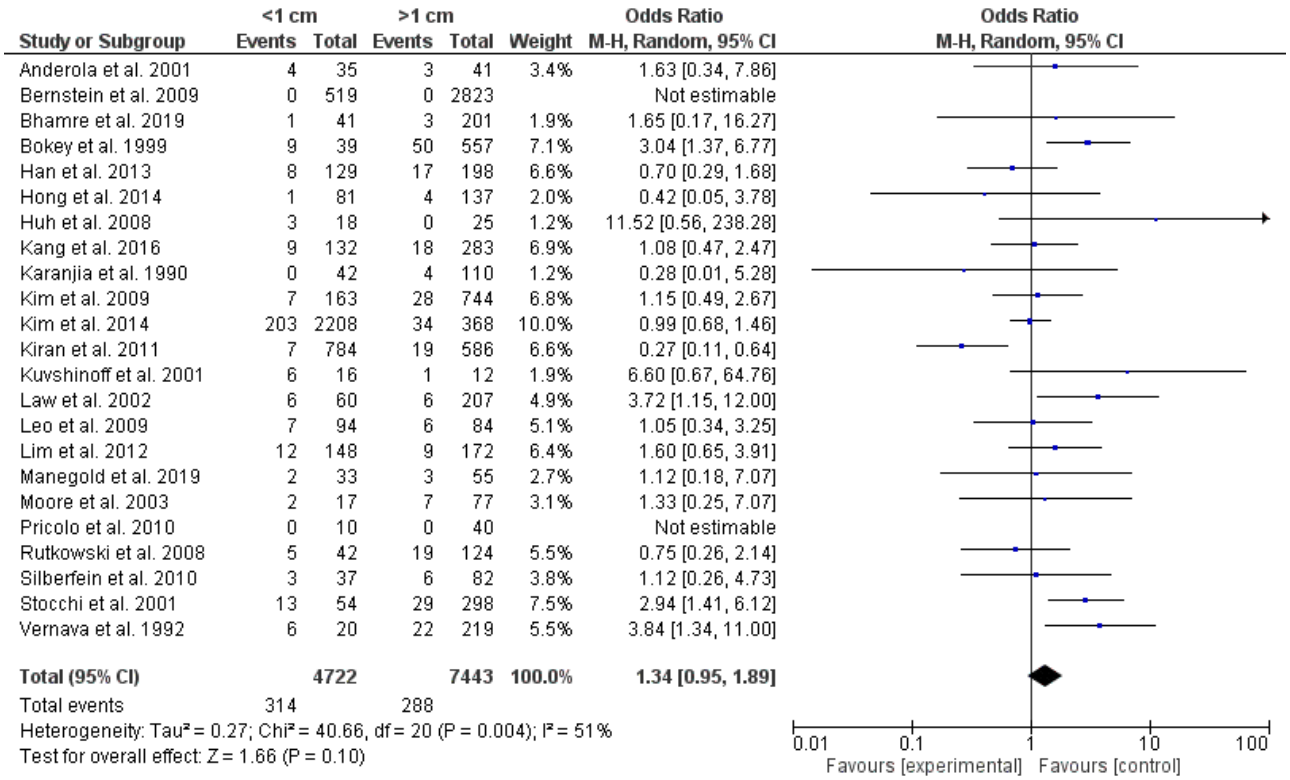


Figure 2: Forest plot of the local recurrence rate of the group with DRM more and less than 1 cm (8, 14-43)

Table 2: The studies regarding the local recurrence rate of the group with DRM more and less than 5 mm

Author	Country	Duration of follow up (months)	Distance from the anal verge	Measured pathology specimen	Stage	DRM <5 mm		DRM >5 mm	
						n	Total	n	Total
Andreola et al. 2001 (14)	Italy	51	5 cm	Fixed	All	4	24	3	49
Bhamre et al. 2019 (16)	India	62	10 cm (55.4% mid; 44.6% 108 lower)	Fixed	All	0	16	4	226
Kang et al. 2016 (21)	Korea	60	NA	Fixed	All	3	45	24	370
Kim et al. 2014 (24)	Korea	192	10 cm (Mean 5 cm)	Fixed	All	169	1840	68	736
Kiran et al. 2011 (25)	USA	49	10 cm (Mean 7 cm)	Fixed	All	4	77	22	706
Kuvshinoff et al. 2001 (26)	USA	33	8 cm (Median 4.4 cm)	Fixed	All	1	9	0	19
Kwak et al. 2012 (36)	Korea	138	5 cm (Mean 2.6 cm)	Fixed	I-III	6	61	23	315
Rutkowski et al. 2008 (32)	Poland	69	10 cm (Mean 6 cm)	Fresh	All	5	42	19	124
Silberfein et al. 2010 (33)	USA	94	5 cm (Median 2 cm)	Fresh	All	3	37	6	82
Stocchi et al. 2001 (34)	USA	60	12 cm	Fresh	All	29	167	13	185
Vernava et al. 1992 (35)	USA	42	10 cm (Median 8 cm)	Fresh	All	6	20	23	219

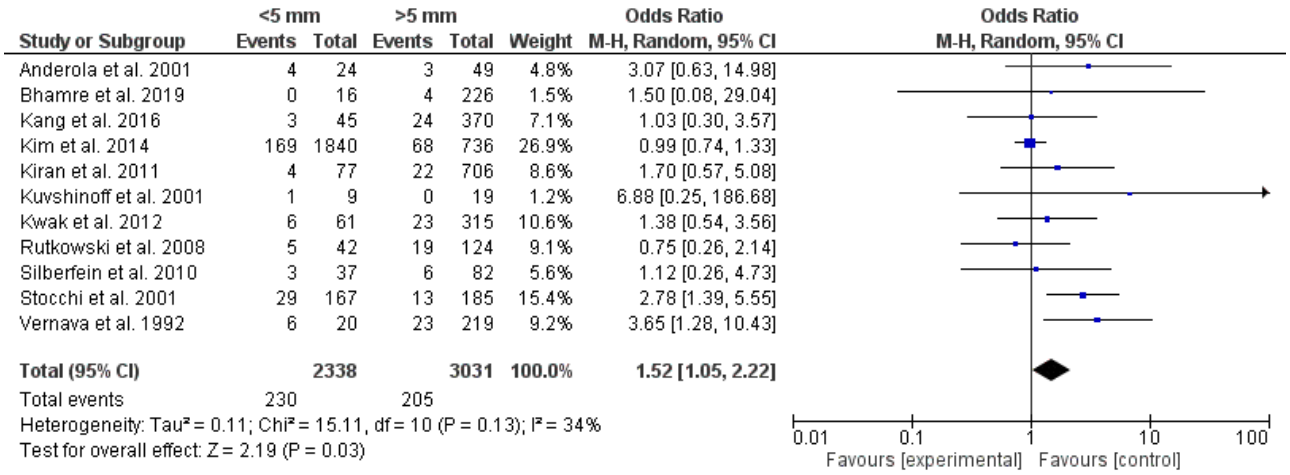


Figure 3: Forest plot of the local recurrence rate of the group with DRM more and less than 5 mm (14, 16, 21, 24, 32-36)

Table 3: The studies regarding the local recurrence rate of the group with DRM more and less than 2 cm

Author	Country	Duration of follow up (months)	Distance from the anal verge	Measured pathology specimen	Stage	DRM <2 cm		DRM >2 cm	
						n	Total	n	Total
Bernstein et al. 2009 (15)	Norway	60	15 cm (94.6% mid-upper; 5.4% lower)	Fixed	I-III	153	1315	166	2027
Bokey et al. 1999 (17)	Australia	60	15 cm (Lower 31.5%; Mid 29/9%; Upper 38.6%)	Fresh	All	12	124	47	472
Ghahramani et al. 2015 (37)	Iran	24	15 cm (Mean 6.4 cm)	Fixed	I-III	36	37	16	45
Lim et al. 2012 (29)	Singapore	45	12 cm	Fixed	I-III	14	191	7	129
Moore et al. 2003 (8)	USA	118	15 cm (Mean 6 cm)	Fresh	All	4	53	5	41
Safioleas et al. 2005 (38)	Greece	60	15 cm	Fresh	All	8	15	4	51

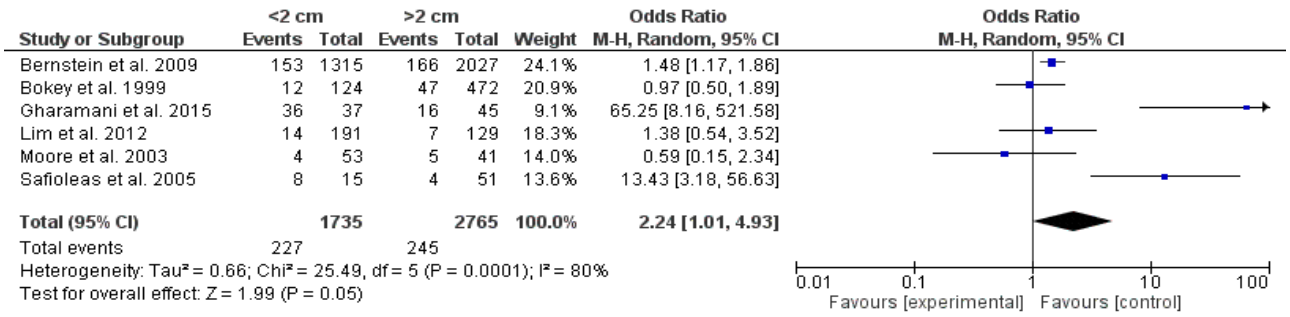
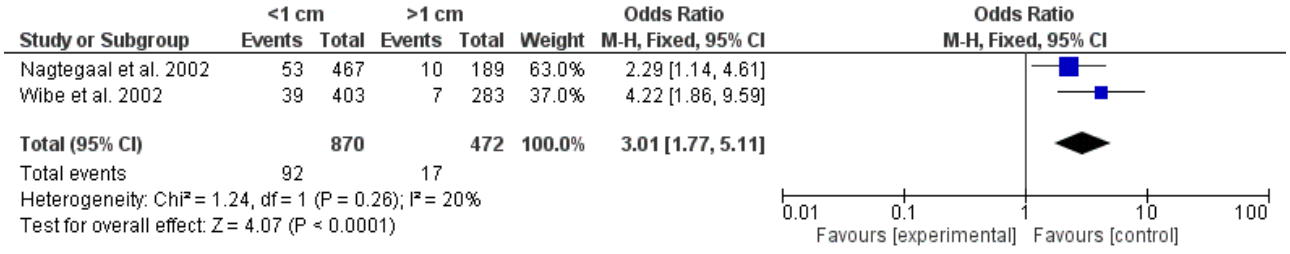
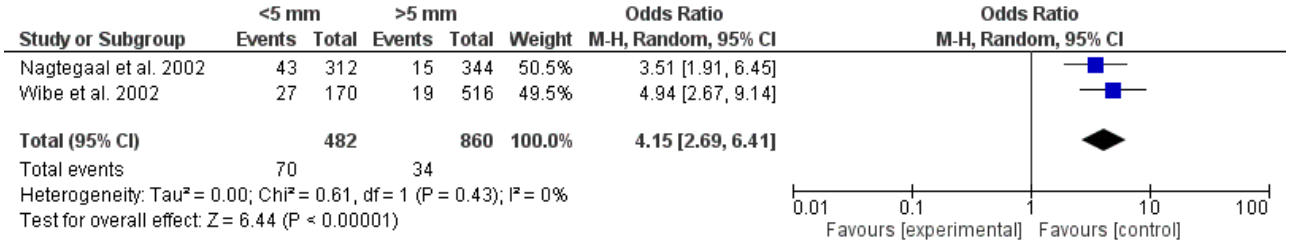


Figure 4: Forest plot of the local recurrence rate of the group with DRM more and less than 2 cm (8, 15, 17, 29, 38, 39)

Table 4: The data of the studies regarding the local recurrence rate of the group with various cut off point of CRM

Author	Country	Duration of follow up (months)	Distance from the anal verge	Measured pathology specimen	Stage	CRM <1 cm		CRM >1 cm	
						n	Total	n	Total
Nagtegaal et al. 2002 (39)	Netherlands	36	15 cm	Fixed	All	53	467	10	189
Wibe et al. 2002 (40)	Norway	39	16 cm	Fixed	All	39	403	7	283
Author	Country	Duration of follow up (months)	Distance from the anal verge	Measured pathology specimen	Stage	CRM <5 mm		CRM >5 mm	
						n	Total	n	Total
Lim et al. 2012 (29)	Singapore	45	12 cm	Fixed	I-III	16	185	5	116
Nagtegaal et al. 2002 (39)	Netherlands	36	15 cm	Fixed	All	28	173	30	483
Author	Country	Duration of follow up (months)	Distance from the anal verge	Measured pathology specimen	Stage	CRM <2 mm		CRM >2 mm	
						n	Total	n	Total
Nagtegaal et al. 2002 (39)	Netherlands	36	15 cm	Fixed	All	43	312	15	344
Wibe et al. 2002 (40)	Norway	39	16 cm	Fixed	All	27	170	19	516
Author	Country	Duration of follow up (months)	Distance from the anal verge	Measured pathology specimen	Stage	CRM <1 mm		CRM >1 mm	
						n	Total	n	Total
Birbeck et al. 2002 (41)	UK	60	12 cm	Fixed	All	63	163	42	421
Lim et al. 2012	Singapore	45	12 cm	Fixed	I-III	12	103	9	198
Nagtegaal et al. 2002 (39)	Netherlands	36	15 cm	Fixed	All	20	120	38	536
Wibe et al. 2002 (40)	Norway	39	16 cm	Fixed	All	14	65	32	621
Zeng et al. 2017 (42)	China	60	12 cm	Fixed	All	22	97	18	145





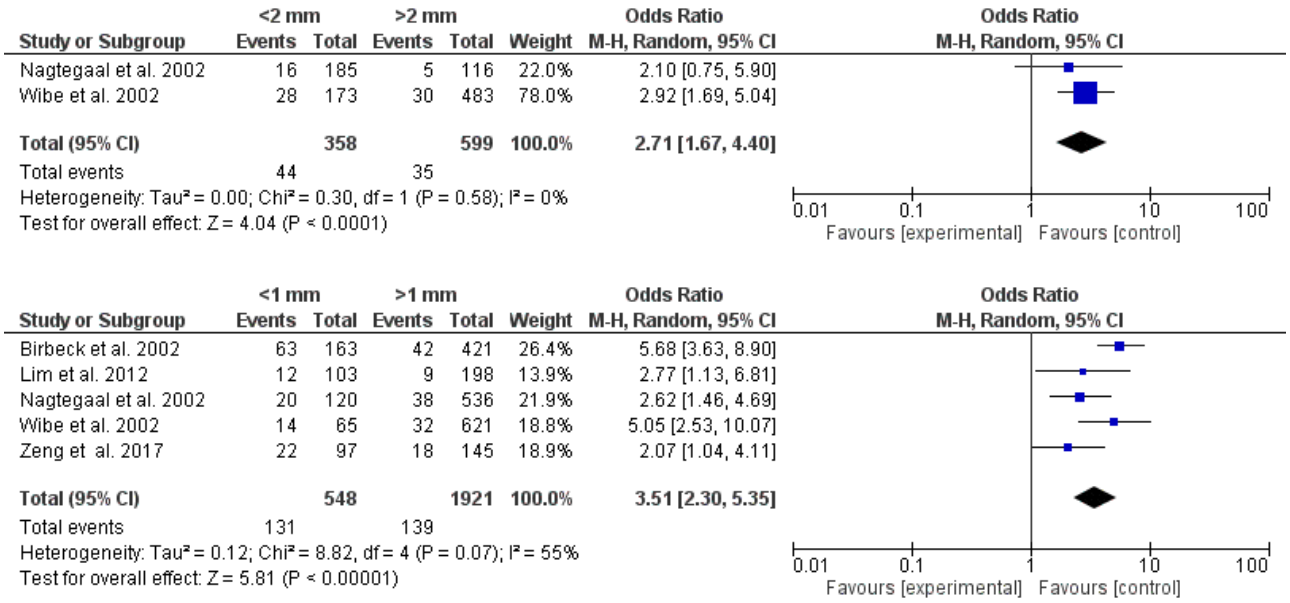


Figure 5: Forest plot of the local recurrence rate of the group with various cut off points of CRM (a) 1 cm, (b) 5 mm (c) 2 mm, (d) 1 mm (29, 39-42)

Table 5: The data of the studies regarding the distant recurrence rate of the group with various cut off point of DRM

Author	Country	Duration of follow up (months)	Distance from the anal verge	Measured pathology specimen	Stage	DRM <2 cm		DRM >2 cm	
						n	Total	n	Total
Lim et al. 2012 (29)	Singapore	45	12 cm	Fixed	I-III	38	191	35	129
Author	Country	Duration of follow up (months)	Distance from the anal verge	Measured pathology specimen	Stage	DRM <1 cm		DRM >1 cm	
						n	Total	n	Total
Bernstein et al. 2009 (15)	Norway	60	15 cm (94.6% mid-upper; 5.4% lower)	Fixed	All	92	519	570	2823
Bhamre et al. 2019 (16)	India	62	10 cm (55.4% mid; 44.6% 108 lower)	Fixed	All	11	41	43	201
Han et al. 2013 (18)	Korea	60	10 cm	Fixed	All	24	129	42	198
Kang et al. 2016 (21)	Korea	60	NA	Fixed	All	16	132	140	283
Leo et al. 2009 (28)	Italy	92	5 cm	Fresh	All	21	94	15	84
Lim et al. 2012 (29)	Singapore	45	12 cm	Fixed	I-III	23	148	40	172
Author	Country	Duration of follow up (months)	Distance from the anal verge	Measured pathology specimen	Stage	DRM <5 mm		DRM >5 mm	
						n	Total	n	Total
Bhamre et al. 2019 (16)	India	62	10 cm (55.4% mid; 44.6% 108 lower)	Fixed	All	5	16	49	226

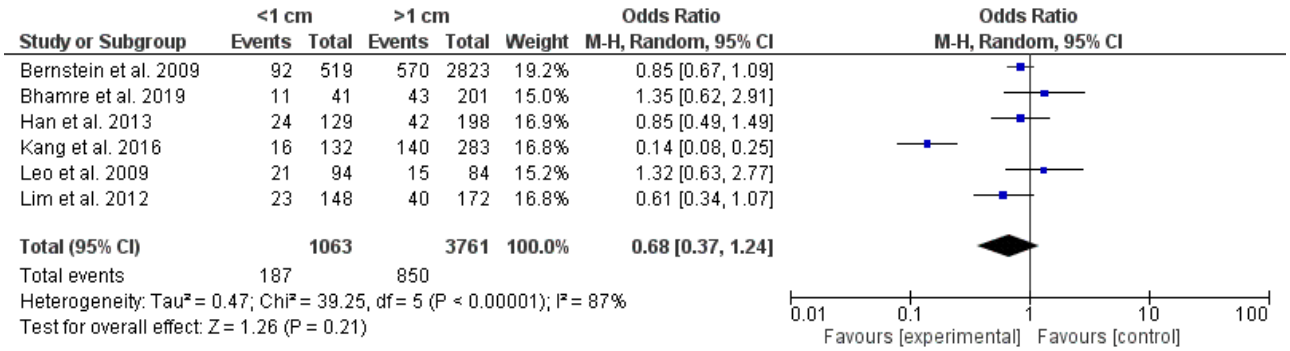


Figure 6: Forest plot of the distant recurrence rate of the group with 1 cm cut off point of DRM (15, 16, 18, 21, 28, 29)

The distant recurrence rate of the group with various cut-off points of CRM

There was a total of 4 studies that included in the meta-analysis of distant recurrence rate of the group with various CRM cut off points. This meta-analysis showed significant lower distant recurrence rate with the cut-off point of CRM by 1 mm (OR 2.67; 95%CI 1.34-5.31; p=0.005; I^2 79%), but not with cut-off point of CRM by 2 mm (Figure 7) (29, 39, 40, 42.

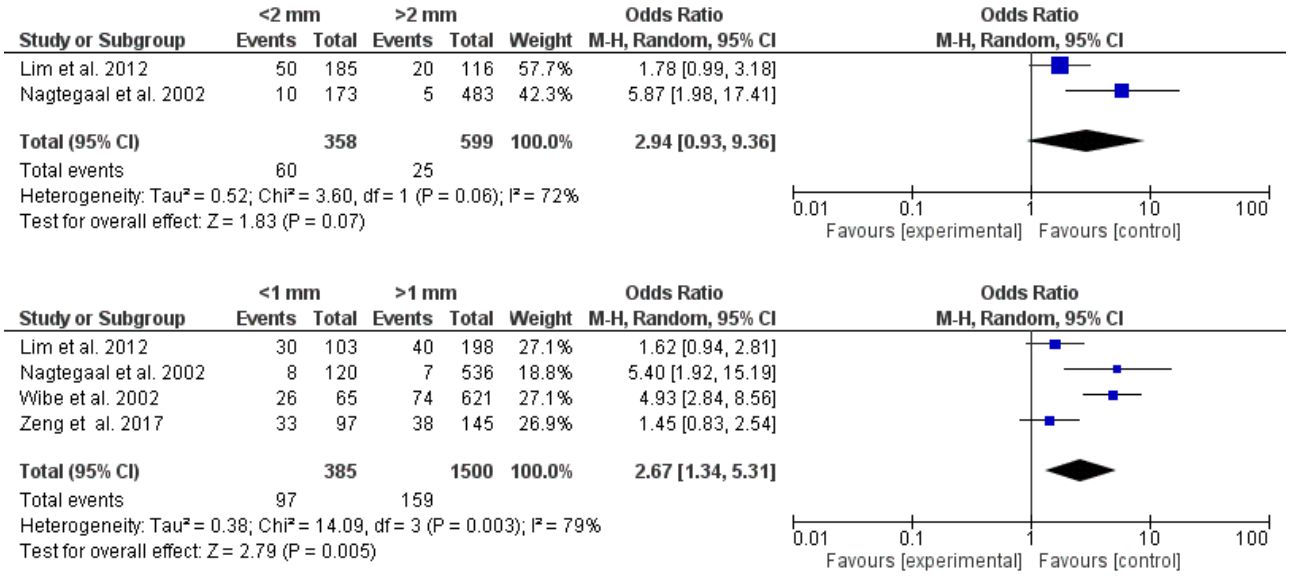


Figure 7: Forest plot of the distant recurrence rate of the group with 2 mm and 1 mm cut off point of CRM (29, 39, 40, 42)

The survival rate of the group with various cut off points of DRM and CRM

The survival rate of the group with various cut off points of DRM mostly were not statistically significant except for disease-free survival parameter in with the cut-off point of DRM by 1 cm (Figures 8-10) (8, 15, 18, 19, 21, 25, 26, 28, 29, 32, 34, 35-37, 43). Further, there was insufficient data for carrying out meta-analysis for survival rate with the parameter of CRM (Table 6) (39,40).

Bias assessment

The bias assessment of this meta-analysis was shown in Figure 11.

Discussion

The rectal cancer surgery was challenging due to rectum anatomical location at the distal area and confined to the pelvic cavity (45). The surgical procedures for rectal cancer highly developed since the introduction of Miles operation in 1908, focused not only on preserving function but also on oncological aspects (46). In 1948, Dixon reported the technique of anterior resection from abdominal approach (47). In 1982, Heald et al. introduced an important oncological adequacy, total mesorectal excision (TME), which has now become the standard method for rectal cancer surgery (3). Despite that, the high recurrence rate after the surgery has forced the operator to carry out the optimal resection margin. An increasing acceptance for a

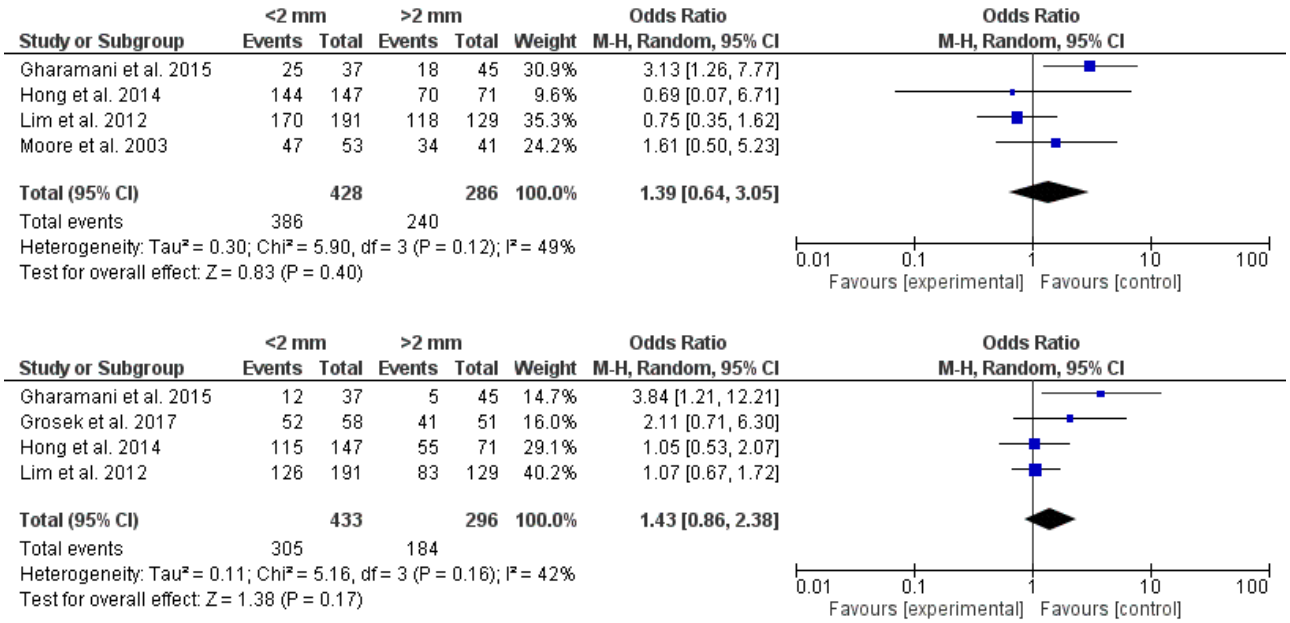


Figure 8: Forest plot of (a) Disease-free survival, (b) Overall survival of the group with cut off point of DRM by 2 mm (19, 29, 37, 43)

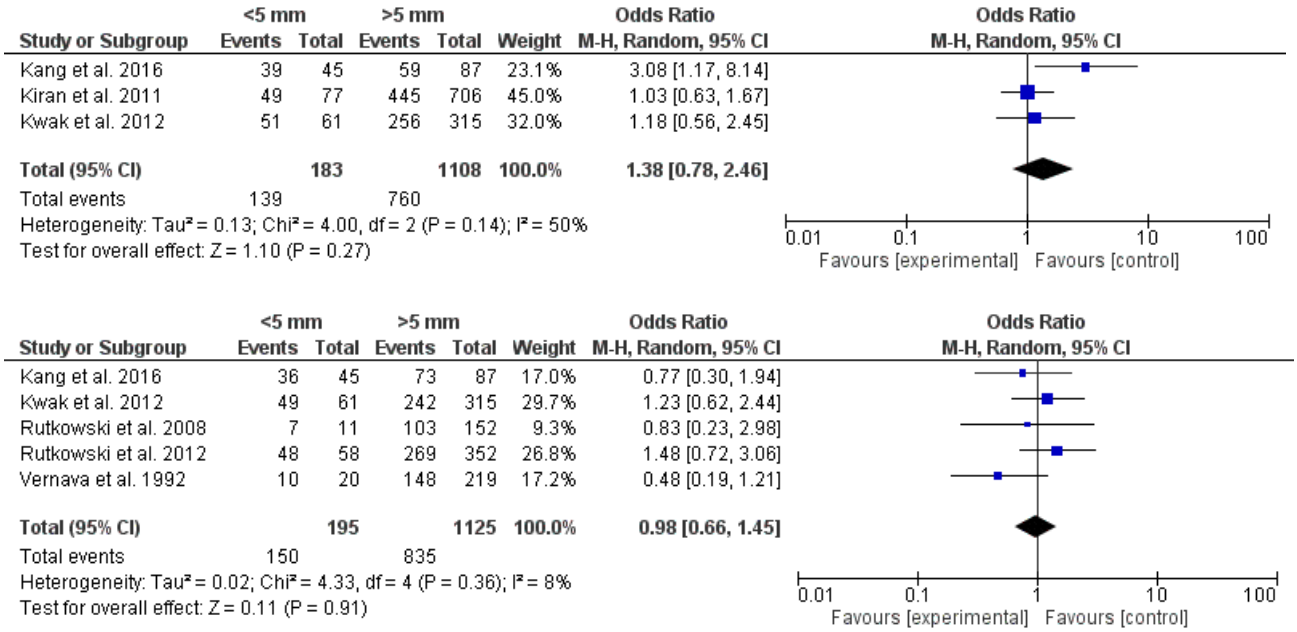


Figure 9: Forest plot of (a) Disease-free survival, (b) Overall survival of the group with cut off point of DRM by 5 mm (21, 25, 32, 35, 36, 44)

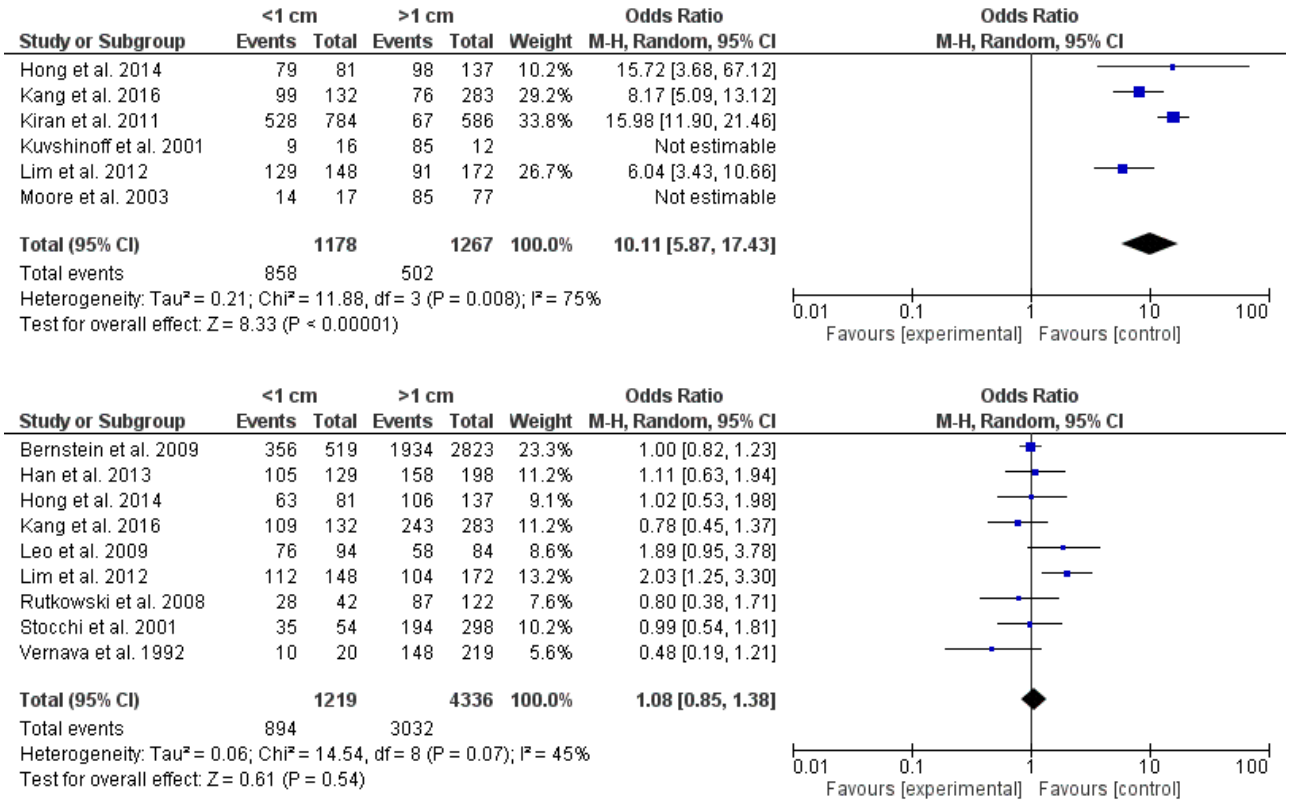


Figure 10: Forest plot of (a) Disease-free survival, (b) Overall survival of the group with cut off point of DRM by 1 cm (8, 15, 18, 19, 21, 25, 26, 28, 29, 32, 34, 35)

Table 6: The studies regarding the overall survival rate of the group with various cut off point of CRM

Author	Country	Duration of follow up (months)	Distance from the anal verge	Measured pathology specimen	Stage	CRM <5 mm		CRM >5 mm	
						n	Total	n	Total
Nagtegaal et al. 2002 (39)	Netherland	36	15 cm	Fixed	All	76.2	235	89.2	451
Author	Country	Duration of follow up (months)	Distance from the anal verge	Measured pathology specimen	Stage	CRM <2 mm		CRM >2 mm	
						n	Total	n	Total
Nagtegaal et al. 2002 (39)	Netherland	36	15 cm	Fixed	All	77.3	173	90.3	483
Author	Country	Duration of follow up (months)	Distance from the anal verge	Measured pathology specimen	Stage	CRM <1 mm		CRM >1 mm	
						n	Total	n	Total
Wibe et al. 2002 (40)	Norway	39	16 cm	Fixed	All	53	65	88.4	621

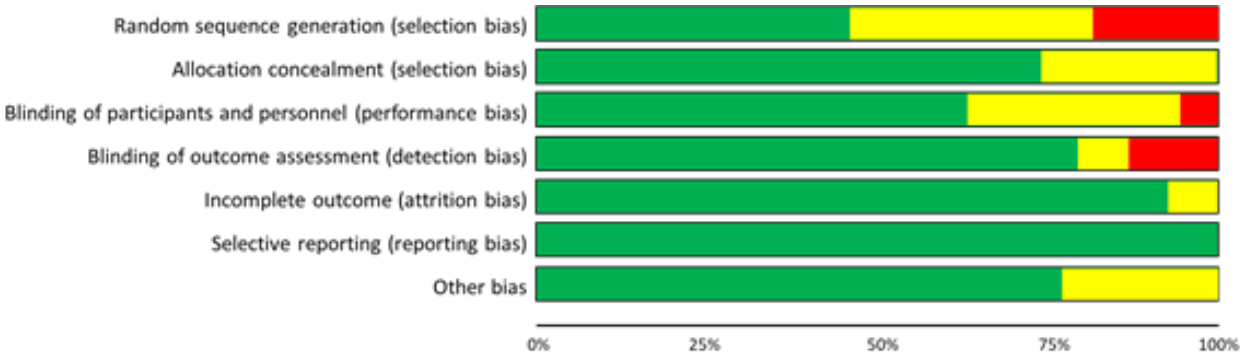


Figure 11: Bias assessment of this study. Green: low risk, yellow: unspecified, red: high risk

narrower margin of resection has been seen along with the encouraging results from most of the studies (35-38).

The distal resection margin (DRM) was defined as the most distal edge of surgical specimen of the tumor (25-28). The recommendation for DRM was evolving throughout the decades. In 1951, Goligher et al. recommended 5 cm, but this margin was debated following the recognition of total mesorectal excision and presurgical chemoradiation. By the findings of William et al (1983), DRM of 2 cm was taken as a cut off standard (9). Studies regarding the best minimal margin still advancing and many showed no inferior outcome even less than 1 cm DRM was performed (8, 26). However, a DRM of 2 cm is still recommended for subjects who have not received presurgical chemotherapy. Currently, Both the US National Cancer Institute and the 9th World Congress of Gastrointestinal Cancer recommended DRMs of 2-5 cm for mid and high rectal cancers, and a 1-cm margin for the distal tumours (45). Meta-analysis of Bujko et al even showed that DRM less than 1 cm even 5 mm was associated with neither local recurrence nor survival. However, the importance of patient selection for this approach should be emphasized (48).

In this study, the local (only fresh specimen measurement) of the group with DRM less than 1 cm was significantly higher than the group with DRM more than 1 cm (OR 1.92; 95%CI 1.21-3.06; p=0.006; I^2 35%). If data analysis was done thoroughly with the measurement of fixed specimen, an insignificant result was shown. This data emphasized the important standard of measurement for specimens. The frozen section result for the DRM may be falsely negative in 12% of all cases. If the specimen is not pinned, the length of the DRM can shrink by 10-50% in a non-radiated rectum after formalin fixation. On another side, pinning the specimen stretched the rectal mucosa more than unpinned status (49). Thus, the method of measurement of the distal margin requires specific definition, as different techniques provide different results. Unfortunately, most studies do not identify how the length of the distal margin was determined. Comparison of various measurement methods are urgently needed to determine oncologically safe DRM (50).

Further, the author analyzed taking the lower cut-off point, 5 mm. From 11 studies, this meta-analysis proved that the local recurrence rate was significantly higher in the group who had DRM less than 5 mm compared to the group with DRM more than 5 mm (OR 1.52; 95%CI 1.05-2.29; p=0.03; I^2 34%). This should be a good result to be considered in clinical practice. Not surprising, taking a larger 2 cm as a cut-off point showed that less than 2 cm gave a significantly worse result than more than 2 cm.

Currently, many studies proposed the use of CRM instead of DRM. In a study of 1,861 patients, 17% of patients with positive CRM had a 2-year local recurrence rate of 13% compared to 4% with a negative margin (51). This meta-analysis showed that taking the point of local recurrence rate, even CRM as minimal as 1 mm could be promising. The author believed that in future clinical practice, both DRM and CRM should be taken consideration in doing surgery.

For the parameter of distant recurrence rate and survival rate, the author could not make a conclusion due to the lack of data from previous studies. Nevertheless still, there was a trend that the larger the margin length, the better outcome. Further, the determination of previous treatment such as chemoradiation might be a favorable aspect in reducing DRM. Author also understood that distal tumoral spread was not only related to distal resection margin but also, the tumor size, infiltration to perirectal tissue, lymph node involvement, invasion of tumor to nerve branch, and histopathological results.

Larger and controlled studies were recommended for further research. Future research should elaborate subjects from worldwide and standardize measuring margins from fixed or fresh specimen.

Conclusion

This meta-analysis showed that taking 5 mm as a cut-off point was optimal to control the local recurrence rate in rectal cancer. The difference between distant recurrence and survival rate could not be determined due to lack of data from previous studies.

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Data availability

The data used in this paper is available from the corresponding author upon reasonable request.

Competing interests

The authors have declared that there is no conflict of interest regarding the publication of this paper.

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