Is A Routine De-Functioning Stoma Benefit for Rectal Cancer Surgery: Results Basing On Meta-Analysis of Postoperative Complications and Quality of Life with A Stoma

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1. Abstract
1.1. Aim: This study aims to investigate the effect of a de-functioning stoma for low anterior resection and quality of life through a systematic meta-analysis.
1.2. Method: Literatures comparing the effect and quality of life between stoma and non-stoma from January 2000 to May 2019 were searched through the Cochrane Library, EMBASE and PubMed databases. The data of postoperative complications and quality of life were analyzed by RevMan5.3 software.
1.3. Results: In total, 17 studies (8578 patients, 3856 stoma vs. 4722 non-stoma) were collected according to the criterion of postoperative complications on a de-functioning stoma. In addition, 7 studies (1268 patients, 616 stoma vs. 652 non-stoma) on quality of life with a stoma (temporary or permanent stoma) were chosen for further analysis. Compared with the non-stoma patients, the total complication rate in de-functioning stoma patients increased (OR=1.07, 95%CI [1.01,2.18], I²=36%, P=0.04). However, the anastomotic leakage (OR=0.82, 95%CI [0.37,0.68], I²=29%, P=0.0001), mortality (OR=0.88, 95%CI [0.28,1.62], I²=0%, P=0.38) and reoperation rate (OR=1.21,95%CI [0.36,0.70], I²=16%, P<0.0001) decreased, respectively. In addition, for patients with a stoma, the scores of emotion functioning (OR=0.95, 95%CI [-6.65,2.18], I²=90%, P<0.00001), global health (OR=0.94, 95%CI [-6.11,0.74], I²=98%, P<0.0001), male sexual functioning (OR=1.23, 95%CI [-10.04,21.48], I²=84%, P=0.0003), pain score (OR=0.94, 95%CI [-1.61,3.10], I²=96%, P<0.00001), physical functioning (OR=0.94, 95%CI [-5.18, -1.12], I²=71%, P=0.002) and social functioning (OR=0.95, 95%CI [-18.84, -2.39], I²=100%, P=0.01) decreased, respectively.
1.4. Conclusion: This meta-analysis suggests that a de-functioning stoma reduces the incidence of reoperation, mortality and anastomotic leakage, while increase the total complication rate. Overall, the quality of life of patients with stoma seems poorer. Thus, a routine de-functioning stoma for all cases of low anterior resection may not be recommended.

2. Introduction
The incidence of colorectal cancer is gradually increasing and occupies as the third malignant neoplasm in the world [1-3]. Total Mesorectal Excision (TME) has become the standard surgical method for rectal cancer, and postoperative anastomotic leakage remains the main complication of TME [4, 5]. Thus, prevention of postoperative anastomotic leakage has drawn broad attention.
The effect of de-functioning stoma in reducing incidence of anastomotic leakage is still controversial. Several previous studies identified the absence of de-functioning stoma as a risk factor for anastomotic leakage and mortality after low anterior resection [7-9]. Thus, in many institutions of China, a de-functioning stoma is routinely performed for rectal cancer patients. However, these studies do not include analysis of quality of life for patients, no matter the fact that a de-functioning stoma may be unnecessary for part of these patients and also impair the quality of life. Moreover, the presence of stoma may increase the risk of complications led by the subsequent stoma closure [10, 11]. Thus, it may be inferred that a de-functioning stoma has a negative effect on quality of life for patient underwent rectal cancer resection [12, 13].

Taking together, the benefit of a de-functioning stoma in low anterior resection for rectal cancer is still largely elusive. Consequently, this updated study aims to evaluate the validity of a de-functioning stoma for low anterior resection in two aspects: postoperative complications and quality of life.

3. Methods

Different related key words or MeSH terms containing “low anterior resection”, “rectal cancer”, “protective stoma”, “anastomotic leak”, “mortality”, “complication”, “quality of life”, and “reoperation rate” were searched with various combinations in three search engines: PubMed databases, Embase, Cochrane Library. The searching period was from January 2000 to May 2019.

3.1. Inclusion and Exclusion Criteria

3.1.1. Inclusion: i) Studies that compared LAR with or without a defunctioning stoma from 2000 to 2019. ii) Scores of quality of life were evaluated with (QLQ)C30 and (QLQ)C38. iii) Adult patients (>16y).

3.1.2. Exclusion: i) Lack of data in articles. ii) Not full text or non-comparative studies. iii) Emergency cases to surgery, such as: intestinal obstruction, intestinal perforation and so on. iv) Review or commentary.

3.2. Statistical analysis

Rate of reoperation, mortality, anastomotic leak and other complications were analyzed as binary variable data. (QLQ) C30 and QLQ-CR38 were used as standards of scores in quality life. The mean and SD were required to each study of pool continuous data. Since five clinical trials on quality of life just reported the size of the trial, the median and range, without the mean and SD [14-20], estimates of the mean and SD were obtained using formulas proposed by Hozo's Method, which referred to Cochrane hood book [21]. In addition, there was only one research directly reported the quality of life of a de-functioning stoma [17]. Thus, we decided to research the quality of life with a permanent or temporary stoma instead, to calculate the result of quality of life with a de-functioning stoma.

The forest figure was drawn to check the statistic homogeneity. 95%CIs and P-value were extract on every study. F statistic was used to estimate the percentage of total variation across studies, owing to heterogeneity rather than chance, with values greater than 50% considered as substantial heterogeneity. All statistical analysis was conducted with Review Manager Version 5.3.3 (Cochrane Collaboration, Software Update, Oxford, United Kingdom).

4. Results

4.1. Eligible Studies

In total, 17 studies (8578 patients, 3856 stoma vs. 4722 non-stoma) published from 2004 to 2016 were included, according to the criterion of postoperative complications [22-38]. 7 studies (1268 patients, 616 stoma vs. 652 non-stoma) on quality of life published from 2004 to 2016 were included [14-20]. The flow chart of the study selection was revealed on Figure 1. There were 3 randomized controlled trials and 14 comparative studies on postoperative complications. The main characteristics, containing anastomotic leak, mortality, complication and reoperation rate in this meta-analysis were analyzed as binary variable data. The main characteristics of the 7 included studies on quality of life were listed in Table 1. Correspondingly, the main characteristics of the 7 included studies on quality of life were listed in Table 2.

<table>
<thead>
<tr>
<th>study</th>
<th>year</th>
<th>all</th>
<th>Type of study</th>
<th>Type of resection</th>
<th>T sample (stoma)</th>
<th>C sample (non-stoma)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anderin [22]</td>
<td>2015</td>
<td>287</td>
<td>CS</td>
<td>TME</td>
<td>139</td>
<td>148</td>
</tr>
<tr>
<td>Beirens [23]</td>
<td>2012</td>
<td>1,912</td>
<td>CS</td>
<td>LAR</td>
<td>1,183</td>
<td>729</td>
</tr>
<tr>
<td>Eriksen [24]</td>
<td>2005</td>
<td>1,958</td>
<td>CS</td>
<td>LAR</td>
<td>622</td>
<td>1,336</td>
</tr>
<tr>
<td>Gong [25]</td>
<td>2013</td>
<td>62</td>
<td>CS</td>
<td>uLAR</td>
<td>26</td>
<td>36</td>
</tr>
<tr>
<td>Gumbau [26]</td>
<td>2015</td>
<td>104</td>
<td>CS</td>
<td>TME</td>
<td>58</td>
<td>46</td>
</tr>
<tr>
<td>Ihnat [27]</td>
<td>2016</td>
<td>151</td>
<td>CS</td>
<td>TME</td>
<td>78</td>
<td>73</td>
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<tr>
<td>Karahasanoglu [28]</td>
<td>2011</td>
<td>77</td>
<td>CS</td>
<td>LAR</td>
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<td>54</td>
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<tr>
<td>Kim [29]</td>
<td>2015</td>
<td>102</td>
<td>CS</td>
<td>LAR</td>
<td>67</td>
<td>35</td>
</tr>
<tr>
<td>Matthiessen [31]</td>
<td>2004</td>
<td>432</td>
<td>CS</td>
<td>LAR</td>
<td>72</td>
<td>360</td>
</tr>
</tbody>
</table>
Mrak [33] 2016 166 RCT TME 94 72
Nurkin [34] 2013 1791 CS LAR 958 833
Seo [35] 2013 836 CS uLAR 246 590
Shiomi [36] 2010 222 CS LAR 80 142
Thoker [37] 2014 78 RCT LAR 34 44
Ulrich [38] 2009 34 RCT LAR 18 16

(TME: total mesorectal excision; LAR: low anterior resection; uLAR: Ultralow anterior resection; RCT: randomized controlled trial; CS: comparative study.)

Table 2: Main characteristics of the 7 included studies about quality of life

<table>
<thead>
<tr>
<th>study</th>
<th>year</th>
<th>all</th>
<th>T sample</th>
<th>C sample</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johanne G. [15]</td>
<td>2009</td>
<td>121</td>
<td>51</td>
<td>70</td>
</tr>
<tr>
<td>Lucas Sideris [16]</td>
<td>2005</td>
<td>132</td>
<td>42</td>
<td>90</td>
</tr>
<tr>
<td>Philippe Rauchs [17]</td>
<td>2004</td>
<td>121</td>
<td>55</td>
<td>66</td>
</tr>
<tr>
<td>Pia Na’svalls [18]</td>
<td>2016</td>
<td>453</td>
<td>336</td>
<td>117</td>
</tr>
<tr>
<td>Thomas Yaus [19]</td>
<td>2009</td>
<td>186</td>
<td>93</td>
<td>93</td>
</tr>
<tr>
<td>Xinxin Li [20]</td>
<td>2010</td>
<td>269</td>
<td>45</td>
<td>224</td>
</tr>
</tbody>
</table>

Figure 1: The flow chart of the study
4.2. Meta-Analysis

Compared with the non-stoma patients, the total complication rate in de-functioning stoma patients increased (OR=1.07, 95% CI [1.01, 2.18], I²=36%, P=0.04, Figure 2). However, the anastomotic leakage (OR=0.82, 95% CI [0.37, 0.68], I²=29%, P<0.0001, Figure 3), mortality (OR=0.88, 95% CI [0.28, 1.62], I²=0%, P=0.38, Figure 4) and reoperation rate (OR=1.21, 95% CI [0.36, 0.70], I²=16%, P=0.0001, Figure 5) decreased, respectively.

Quality of life with or without stoma were compared. The results revealed that for patients with stoma, the incidence of constipation (OR=1.73, 95% CI [-15.61, -2.37], I²=84%, P=0.0004, Figure 6) and diarrhea (OR=1.73, 95% CI [-8.98, 6.45], I²=79%, P=0.003, Figure 7) decreased. However, the scores of emotion functioning (OR=0.95, 95% CI [-6.65, 2.18], I²=90%, P<0.0001, Figure 8), global health (OR=0.94, 95% CI [-6.11, 0.74], I²=98%, P<0.00001, Figure 9), male sexual functioning (OR=1.23, 95% CI [-10.04, 21.48], I²=84%, P=0.0003, Figure 10), pain score (OR=0.94, 95% CI [-1.61, 3.10], I²=96%, P=0.00001, Figure 11), physical functioning (OR=0.94, 95% CI [-5.18, 1.12], I²=71%, P=0.002, Figure 12) and social functioning (OR=0.95, 95% CI [-18.84, -2.39], I²=100%, P=0.01, Figure 13) decreased, respectively.

4.3. Publication Bias

The summary of selection bias, performance bias, detection bias, attrition bias, reporting bias and other biases in each study on complications had been identified and showed in Figure 14. Funnel plots (Figure 15 - 18) and Egger’s tests were performed to evaluate the publication bias on this meta-analysis. The shape of the funnel plot did not reveal any evidence of obvious asymmetry.

![Figure 2: The flow chart of complication rate in de-functioning stoma patients](image2)

![Figure 3: The flow chart of anastomotic leakage](image3)
Figure 4: The flow chart of Mortality

Figure 5: The flow chart of reoperation rate

Figure 6: The flow chart of incidence of constipation
Figure 7: The flow chart of diarrhea

Figure 8: The flow chart of emotion functioning

Figure 9: The flow chart of global health

Figure 10: The flow chart of male sexual functioning
Figure 11: The flow chart of pain score

Figure 12: The flow chart of physical functioning

Figure 13: The flow chart of social functioning
Figure 14: The flow chart of the study

Figure 15: The flow chart of complications
Total Mesolectal Excision (TME) plays an important role in treatment of patients with mid-low rectal cancer [39]. As the most common complication for TME, anastomotic leakage and its prevention has drawn broad attention [40]. Some studies revealed that a de-functioning stoma was effective for prevention of postoperative leakage [41]. However, other studies demonstrated that a de-functioning stoma could not reduce incidence of postoperative leakage [42]. Some surgeons preferred to perform a routine de-functioning stoma to avoid the confusing situation of leakage and mortality. However, a de-functioning stoma may increase the incidence of either total or stoma-related complications [43, 44]. In addition, the presence of a de-functioning stoma demanded additional subsequent surgery for stoma closure, and thus may lead to additional complications [45-47]. Potential disadvantages of a de-functioning stoma include the need for re-operation, longer hospital stay and stoma-related complications such as dehydration, which could be fatal [48]. This meta-analysis demonstrated that with a de-functioning stoma, the incidences of anastomotic leak, re-operation rate and mortality decreased. However, the incidence of total complications increased. The incidence of total complications, containing bleeding, incisional hernia, abscesses, etc., may increase due to the surgery of both resection and stoma [50-54]. It should be noted that among 17 studies on postoperative complications included in this study, there were only 3 randomized controlled trials. The other 14 studies were comparative studies, which may have a potential risk of selection bias. Thus, the data of this meta-analysis should be objectively treated. Given to the considerable selection bias existing in some included studies, we should keep the caution and critically attitude with these results. More RCT studies should be performed to confirm the influence of a de-functioning stoma on postoperative complications.

Compared with postoperative complications, surgeons have paid less attention on the virtual problem: quality of life with a de-functioning stoma. There was no meta-analysis on quality of life with de-functioning stoma. Thus, we doubted the contribution of a de-functioning stoma, especially the possibility of an impaired quality of life [49]. Unfortunately, there was only one study directly reported the quality of life with a de-functioning stoma [15]. Thus, we compared the quality of life with or without a stoma instead, no matter the stoma was permanent or temporary. The results revealed that for patients with a stoma, the scores of emotion functioning, global health, male sexual functioning, pain score, physical functioning and social functioning decreased, suggesting a negative effect of stoma on postoperative quality of life. Thus, a routine de-functioning stoma for all cases of low anterior resection may not be recommended.

The high I² values of Figure 7, 13 and 14 demonstrated that the heterogeneity from samples were extremely high. That may be ascribed to the truth that some endpoints could not be pooled for analysis due to lack of reporting in the included studies, such as perforation, obstruction, excoriation, prolapse rates, readmission...
rates, and stoma related complications such as peristomal ulcerations, abscess and high output leading to kidney injury [56-60]. In addition, among the 7 studies on quality of life included in this study, only two articles have directly provided the data of mean and SD [14, 17], while the related data of the other 5 articles were absent. Thus, the missing data were estimated using formulas proposed by Hozo's Method, a measure referred to the Cochrane handbook. We initially considered the lack of data (mean and SD) may be an important risk of bias. The accuracy of data on forest

There are some factors which may have influence on quality of life and thus cause heterogeneity of samples. The operation time, bleeding and chemo radiotherapy of rectal cancer patients have been proved to have significant influences on quality of life [61]. The inconvenience of an ostomy bag hanging on the abdominal wall actually has a negative effect on emotion, sexual desire and social status for patients. However, the data of these factors were not complete in the included articles, thus a subgroup analysis was unenforceable.

Another limitation of this study is that there were no enough articles studying the quality of life of a de-functioning stoma. Therefore, we compared the quality of life with or without a stoma instead, no matter the stoma was permanent or temporary. The quality of life was evaluated with questionnaires of (QLQ) C30 and QLQ-CR38, at least 1 year postoperatively. However, for most cases of a de-functioning stoma, the operation time for stoma closure was within 6 months after total mesolectal excision. Thus, whether short-term de-functioning stomas do have a negative influence on quality of life as permanent stomas do, is still largely elusive. In theory, the earlier we reverse the de-functioning stoma, the more benefits the patients may gain [62-64]. However, although the quality of life improves after reversal of stoma, some problems may remain or even get worse due to early reversal, such as temporary alteration in bowel function with economic burdens. Thus, more well designed RCT studies were in emergent need to confirm the influence of a de-functioning stoma on quality of life for rectal cancer patients, and as well provide guidance for operation time of stoma reversal.

6. Conclusions
Despite of the limitations of high heterogeneity of stoma literatures, this meta-analysis has proved that a de-functioning stoma could reduce the incidence of reoperation, mortality and anastomotic leakage, but increase the total complication rate. Overall, the quality of life of patients with stoma seems poorer. Thus, a routine de-functioning stoma for all cases of low anterior resection surgeries may not be recommended. However, more RCT studies are needed to confirm the conclusion.

7. Acknowledgment
This study was supported by grants from the National Natu-

References


