Rectal washout during abdominoperineal resection for rectal cancer has no impact on the oncological outcome

Rebecca Svensson Neufert1,2 | Fredrik Jörgren2,3 | Pamela Buchwald2,4

INTRODUCTION

Viable intraluminal cancer cells with the ability to implant are suggested as a possible cause of local recurrence (LR) in rectal cancer [1–3]. Intraoperative rectal washout (RW) is performed to decrease the number and the viability of these cells, and thus to attempt to reduce the risk of LR, by irrigating with a cytotoxic fluid or thorough mechanical cleansing. RW is part of the total mesorectal excision (TME) technique, and its effect on the risk of LR after anterior resection has been studied, with conflicting results [4–8]. No randomized controlled trials have been done. The largest published study using the Swedish Colorectal Cancer Registry (SCCR) data showed reduced rates of LR with RW [4]. Only one study has addressed RW in Hartmann’s procedure [9]. No risk reductions in oncological outcomes, including LR, were shown but the authors suggested that the practice of RW was continued until more data were available. However, the possible benefit of RW in abdominoperineal resection (APR) has not been studied.

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Abdominoperineal resection is most often reserved for cancers located in the lower third of the rectum ≤5 cm from the anal verge [10]. In this area the mesorectum tapers, making it technically difficult to achieve a clear circumferential resection margin. The risk of intraoperative perforation is also increased, translating to poorer oncological outcomes, including higher rates of LR and impaired overall and disease-free survival [10–14]. Therefore, it is important to explore any possible impact of RW on oncological outcomes in APR. The Swedish national guidelines for rectal cancer care recommend RW in anterior resection but also advocate it at the discretion of the surgeon in APR [10]. RW is usually performed with the lumen occluded distal to the tumour. For low rectal cancers this is technically not always possible, and the alternative is to wash out the rectal lumen without an occlusive clamp before placement of a purse-string suture. The hypothesis behind RW in APR is elimination of intraluminal cancer cells that otherwise would have been left behind in the distal rectal stump and thereby increase the risk of LR if intraoperative perforation or leakage from the purse-string suture occur.

This registry study aims to assess the oncological outcome in terms of LR, distant metastasis (DM), overall recurrence (OAR) and overall and relative survival after RW in APR for rectal cancer and to find evidence for whether RW should be performed in APR or not.

METHOD

Swedish Colorectal Cancer Registry and study population

The study population comprised all patients registered in the Swedish Colorectal Cancer Registry (SCRCR) who underwent elective surgery with APR for rectal cancer (TNM Stages I–III) between 2007 and 2013. Data on tumour characteristics and demographics and preoperative, perioperative, postoperative and follow-up data were collected. The SCRCR is a national population-based registry and has a coverage ratio of 99.7% [15]. Primary data are reported 30 days after surgery or at diagnosis if no surgery is performed and follow-up data are registered 3 and 5 years postoperatively. The SCRCR has been described in detail in other publications [15,16].

Definitions

Rectal cancer is defined as an adenocarcinoma with its lower edge located within 15 cm of the anal verge as measured with a rigid sigmoidoscope during withdrawal.

Hospital volume is defined according to the number of APRs for rectal cancer performed annually. A volume of 1–10 procedures is referred to as low, 11–25 as medium and ≥26 as high.

A colorectal surgeon is defined as an accredited colorectal surgeon or a surgeon with a colorectal interest.

The definition of an intraoperative perforation is an unintentional perforation of the rectum that occurs during surgery.

R0 is defined as a locally radical procedure with neither macroscopic tumour tissue left behind according to the surgeon nor microscopic tumour tissue at the resection margins according to the pathologist.

Local recurrence is defined as tumour growth located below the level of the promontory related to the primary rectal tumour. Tumour tissue in the ovary, liver, peritoneum, bone, lung, brain or any other organ as well as in any lymph node that is not located in the pelvis is defined as DM. LR and DM are registered regardless of how the diagnosis was made (e.g. clinical, radiological, pathological or endoscopic examination). OAR includes either isolated LR or DM, or both LR and DM.

Statistical analysis

Categorical data are presented as numbers with percentages and continuous data are presented as median with interquartile range. The chi-square test, Fisher’s exact test and the independent sample t-test were used to compare groups when appropriate. Patients were followed for 5 years postoperatively. Survival analyses were performed. Kaplan–Meier with log-rank test and univariable and multivariable Cox regression analysis were used. In multivariable analysis, clinically relevant variables considered as potential confounders for LR, DM, OAR and overall and relative survival (i.e. age, gender, TNM stage, tumour height, neoadjuvant radiotherapy, neo-adjuvant chemotherapy, intraoperative perforation, adjuvant chemotherapy) were included in the model. Surgical competence was not included in multivariable analysis because only a few cases were treated by a general surgeon and all occurred in one group. Relative survival was calculated with the R package surv and the Andersen multiplicative model [17]. Population life tables from the Human Life-Table Database available at http://www.lifetable.de were used [18]. Calculations were performed using IBM SPSS Statistics for Windows, version 25.0. (IBM Corp., released 2017) and R version 4.0.1 (R Core Team 2020 [19]). A p-value of <0.05 was considered as significant and all tests were two-sided.

RESULTS

Study population

A total of 2425 patients with R0 resection, no LR, DM or death within 90 days postoperatively, valid 5-year follow-up and available RW data were grouped depending on whether RW was performed.
or not (Figure 1). The groups differed significantly with regard to tumour height, TNM stage, hospital volume, laparoscopic surgery and intraoperative perforation (Table 1).

Recurrence

As shown in Table 2, LR occurred in 97/2425 (4.0%) of the patients within 5 years postoperatively, with no significant difference between the RW and the no RW groups [10/265 (3.8%) vs. 87/2160 (4.0%), \( p = 0.84 \)]. Moreover, there were no significant differences between the groups, neither for DM [51/265 (19.2%) vs. 476/2160 (22.0%), \( p = 0.29 \)] nor for OAR [53/265 (20.0%) vs. 505/2160 (23.4%), \( p = 0.21 \)]. In subgroup analysis of low rectal cancers (0–5 cm), no differences in rates of LR, DM and OAR were observed between the RW and no RW groups (Table 3). Furthermore, subgroup analysis of the patients where intraoperative perforation occurred \( n = 133 \), showed no differences in rates of LR, DM and OAR between the RW and no RW groups (Appendix S1 in the Supporting Information).

Survival

Overall and relative survival are presented in Figure 2. The 5-year overall survival in the RW group was 0.72 compared with 0.72 in the no RW group \( (p = 1.00) \). The 5-year relative survival in the RW and the no RW group was 0.87 and 0.85, respectively \( (p = 0.67) \).

Univariable and multivariable analysis

In univariable and multivariable analysis, RW did not have a significant impact on the oncological outcome in terms of LR, DM, OAR and 5-year overall and relative survival (Table 4). The number of confounders that could be included in the multivariable analysis was limited owning to the small number of LR events. Multivariable analysis adjusted for laparoscopic surgery and hospital volume was performed but did not affect the results. Thus, these are not presented.

![FIGURE 1](image.png)  Flow chart (DM, distant metastasis; LR, local recurrence; RW, rectal washout; SCRCR, Swedish Colorectal Cancer Registry)
TABLE 1 Patient characteristics, treatment and tumour data on patients treated with elective R0 APR for rectal cancer (TNM Stages I–III) in Sweden, 2007–2013

|                              | All patients \( (n = 2425) \) | RW \( (n = 265) \) | No RW \( (n = 2160) \) | p-value |
|------------------------------|-------------------------------|-------------------|---------------------|---------|
| Median age at diagnosis      | 70 (15)                       | 71 (14)           | 70 (15)             | 0.68    |
| (years) (IQR)                |                               |                   |                     |         |
| Gender                       |                               |                   |                     |         |
| M                            | 1473 (60.7)                   | 175 (66.0)        | 1298 (60.1)         | 0.06    |
| F                            | 952 (39.3)                    | 90 (34.0)         | 862 (39.9)          |         |
| Tumour height                |                               |                   |                     |         |
| Low 0–5 cm                   | 1828 (75.4)                   | 157 (59.2)        | 1671 (77.4)         | <0.001  |
| Medium 6–10 cm               | 488 (20.1)                    | 88 (33.2)         | 400 (18.5)          |         |
| High 11–15 cm                | 71 (2.9)                      | 17 (6.4)          | 54 (2.5)            |         |
| Missing data                 | 38 (1.6)                      | 3 (1.1)           | 35 (1.6)            |         |
| TNM stage                    |                               |                   |                     |         |
| I                            | 851 (35.1)                    | 75 (28.3)         | 776 (35.9)          | 0.033   |
| II                           | 717 (29.6)                    | 81 (30.6)         | 636 (29.4)          |         |
| III                          | 857 (35.3)                    | 109 (41.1)        | 748 (34.6)          |         |
| Neoadjuvant radiotherapy     | 1987 (81.9)                   | 224 (84.5)        | 1763 (81.6)         | 0.25    |
| Missing data                 | 1 (0.0)                       | 0                 | 1 (0.0)             |         |
| Neoadjuvant chemotherapy     | 457 (18.8)                    | 50 (18.9)         | 407 (18.8)          | 1.00    |
| Missing data                 | 2 (0.1)                       | 0                 | 2 (0.1)             |         |
| Hospital volume              |                               |                   |                     |         |
| Low                          | 88 (3.6)                      | 16 (6.0)          | 72 (3.3)            | <0.001  |
| Medium                       | 389 (16.0)                    | 88 (33.2)         | 301 (13.9)          |         |
| High                         | 1948 (80.3)                   | 161 (60.8)        | 1787 (82.7)         |         |
| Surgical competence          |                               |                   |                     |         |
| Colorectal                   | 2404 (99.1)                   | 261 (98.5)        | 2143 (99.2)         | 1.00    |
| General                      | 5 (0.2)                       | 0                 | 5 (0.2)             |         |
| Missing data                 | 16 (0.7)                      | 4 (1.5)           | 12 (0.6)            |         |
| Laparoscopic surgery         | 279 (11.5)                    | 18 (6.8)          | 261 (12.1)          | 0.011   |
| Missing data                 | 18 (0.7)                      | 2 (0.8)           | 16 (0.7)            |         |
| Intraoperative perforation   | 133 (5.5)                     | 27 (10.2)         | 106 (4.9)           | <0.001  |
| Missing data                 | 17 (0.7)                      | 2 (0.8)           | 15 (0.7)            |         |
| Adjuvant chemotherapy        | 656 (27.1)                    | 76 (28.7)         | 580 (26.9)          | 0.53    |
| Missing data                 | 19 (0.8)                      | 2 (0.8)           | 17 (0.8)            |         |

Note: Values in parentheses are percentages unless indicated otherwise.

Abbreviations APR, abdominoperineal resection; IQR, interquartile range; RW, rectal washout.

Univariable and multivariable analysis of the subgroup of patients with low rectal cancers (0–5 cm) showed no impact of RW on the risk of LR, DM, OAR or overall survival (Appendix S2).

**DISCUSSION**

Whether or not RW was performed during APR for rectal cancer had no effect on oncological outcomes. To our knowledge, this is the first study to investigate the impact of RW in APR for rectal cancer.

The presence of exfoliated viable cancer cells in the rectal lumen adjacent to the tumour has been proven [1–3,20]. In rectal cancer surgery the lower tumours relevant for APR require more manipulation in the narrow pelvic cavity, which hypothetically may result in more intraluminal cancer cells being shed. The SCRCR includes data on whether or not RW was performed, but details on how the procedure was performed, washout fluid and volume are not available. Usually the rectum is cross-clamped distal to the tumour when RW is performed in anterior resection, but this may not be possible for lower tumours requiring APR. There are studies describing a decrease in the presence of exfoliated cancer cells after RW with the bowel clamped proximal to the tumour [21,22]. The performance of RW before an incidental perforation might decrease the number of exfoliated cancer cells and thus prevent implantation in the pelvis. However, a significant reduction in the rate of LR after RW and perforation has not been shown [23].
TABLE 2  Recurrence data on patients treated with elective R0 APR for rectal cancer (TNM Stages I–III) in Sweden, 2007–2013

|                  | All patients (n = 2425) | RW (n = 265) | No RW (n = 2160) | p-value |
|------------------|-------------------------|--------------|------------------|---------|
| Local recurrence |                         |              |                  |         |
| No               | 2325 (95.9)             | 255 (96.2)   | 2070 (95.8)      | 0.84    |
| Yes              | 97 (4.0)                | 10 (3.8)     | 87 (4.0)         |         |
| Missing data     | 3 (0.1)                 | 0            | 3 (0.1)          |         |
| Distant metastasis |                       |              |                  |         |
| No               | 1895 (78.1)             | 214 (80.8)   | 1681 (77.8)      | 0.29    |
| Yes              | 527 (21.7)              | 51 (19.2)    | 476 (22.0)       |         |
| Missing data     | 3 (0.1)                 | 0            | 3 (0.1)          |         |
| Overall recurrence |                      |              |                  |         |
| No               | 1864 (76.9)             | 212 (80.0)   | 1652 (76.5)      | 0.21    |
| Yes              | 558 (23.0)              | 53 (20.0)    | 505 (23.4)       |         |
| Missing data     | 3 (0.1)                 | 0            | 3 (0.1)          |         |

Note: Values in parentheses are percentages.
Abbreviations: APR, abdominoperineal resection; RW, rectal washout.

TABLE 3  Recurrence data on the subgroup of patients with low rectal cancers (0–5 cm), treated with elective R0 APR for rectal cancer (TNM Stages I–III) in Sweden, 2007–2013

|                  | All patients (n = 1828) | RW (n = 157) | No RW (n = 1671) | p-value |
|------------------|-------------------------|--------------|------------------|---------|
| Local recurrence |                         |              |                  |         |
| No               | 1754 (96.0)             | 150 (95.5)   | 1604 (96.0)      | 0.73    |
| Yes              | 72 (3.9)                | 7 (4.5)      | 65 (3.9)         |         |
| Missing data     | 2 (0.1)                 | 0            | 2 (0.1)          |         |
| Distant metastasis |                       |              |                  |         |
| No               | 1423 (77.8)             | 128 (81.5)   | 1295 (77.5)      | 0.26    |
| Yes              | 403 (22.0)              | 29 (18.5)    | 374 (22.4)       |         |
| Missing data     | 2 (0.1)                 | 0            | 2 (0.1)          |         |
| Overall recurrence |                      |              |                  |         |
| No               | 1399 (76.5)             | 127 (80.9)   | 1272 (76.1)      | 0.19    |
| Yes              | 427 (23.4)              | 30 (19.1)    | 397 (23.8)       |         |
| Missing data     | 2 (0.1)                 | 0            | 2 (0.1)          |         |

Note: Values in parentheses are percentages.
Abbreviations: APR, abdominoperineal resection; RW, rectal washout.

FIGURE 2  Five-year survival after elective R0 APR for rectal cancer (TNM Stages I–III) in Sweden, 2007–2013: (A) overall survival, p = 1.00; (B) relative survival, p = 0.67 (APR, abdominoperineal resection)
Intraoperative perforation was an infrequent event in the present study, occurring in only 133 patients. The recurrence rate was also low, with only 12 LR and 21 DM in the perforation group. Thus, multivariable analysis was not possible, but subgroup analysis demonstrated insignificant differences in rates of LR, DM and OAR between the RW and no RW groups.

A variety of different washout fluids are used in RW, for example cetrimide, chlorhexidine, povidone–iodine solution, saline, sterile water and ethanol [20,24,25]. Recent studies recommend a washout volume of >1500–2000 ml [24]. RW with dilute Betadine in APR for the purpose of removing residual stool has been described by Perry et al. [26], and a study of RW before colorectal anastomosis showed a reduction in bacterial counts in the rectal stump when sodium hypochlorite and povidone–iodine were used [27]. Further studies are necessary to investigate other possible benefits of RW before the procedure is completely dismissed in APR. From our data we cannot exclude the possibility that RW may be important in other aspects, such as reducing perineal infections.

To obtain the 5-year oncological outcome this study included patients undergoing APR between 2007 and 2013. Since then, neoadjuvant therapy has improved and is in transition due to the results of the RAPIDO trial where neoadjuvant short-course radiotherapy followed by chemotherapy was given [28]. Also, minimally invasive surgery has continued to increase and is currently the surgical technique of choice in over 50% of rectal cancer resections in Sweden [15]. In Sweden, Denmark, Australia, New Zealand and the United States, APR has been reported to account for 19%–38% of rectal cancer resections [14,15,29,30]. In our previous survey of the current practice of RW in Sweden, 6% of the responding units routinely performed RW in open APR, and 16% in minimally invasive APR [25]. In this study, RW was performed in 10.9% of the procedures. RW was performed in 6.5% of the laparoscopic procedures, compared with 11.5% of the open procedures. Data on whether conventional, extralevator or intersphincteric APR was performed were unavailable for this study. Since 2017, the SCRCR has recorded if intersphincteric APR is performed.

This study analysed data from the national, population-based SCRCR. The registry has a high coverage ratio with a large cohort of unselected patients. The validity and comparability have been evaluated in other publications [16]. The studied cohort contains patients with different tumour heights. In the RW group, tumours located higher in the rectum and with more advanced TNM stages were observed. It is possible that some of the patients in this study were intended for an anterior resection and consequently RW was performed, but because of intraoperative events they were converted to an APR. To distinguish patients who were originally planned for an APR, subgroup analysis was performed on patients with tumours situated 0–5 cm from the anal verge. However, this subgroup showed no differences in rates of LR, DM or OAR between the RW and no RW groups. Other factors and intraoperative adverse events, not accounted for in this study, may have biased the decision to perform RW or not.

The RW and no RW groups differed, and there were few LR events among the patients in this study. Fewer laparoscopic procedures, more intraoperative perforations and more low- or medium-volume hospitals were seen in the RW group. Multivariable analysis was used to adjust for possible confounders.

The best way to perform RW is still unknown. As mentioned by Kodeda et al. [31], to resolve this question negative and conflicting results also need to be published, and clinical studies investigating details on how to perform RW should continue to be conducted. Large international multicentre studies will be required to achieve evidence-based guidelines on the role of RW in rectal cancer surgery, including indications, the most effective washout fluid and volume in terms of reducing the risk of LR.

In conclusion, our data do not support routine RW in APR in order to improve oncological outcomes.

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**CONFLICT OF INTERESTS**

The authors declare that they have no conflicts of interest.

**AUTHOR CONTRIBUTION**

FJ and PB were responsible for the concept and the design of the study. RSN collected and analysed the data. RSN wrote the first draft of the manuscript. All authors contributed to the interpretation of the data.
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SUPPORTING INFORMATION
Additional supporting information may be found in the online version of the article at the publisher’s website.

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