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REVIEW ARTICLE

Can rectal washout reduce anastomotic recurrence after anterior resection for rectal cancer? A review of the literature

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Abstract

Local recurrence rates of rectal cancer after anterior resection remain high, despite the continued efforts of surgeons to devise preventive measures. Anastomotic recurrence, a form of local recurrence, may be caused by the implantation of exfoliated cancer cells during resection, and rectal stump washout has been proposed as a way to reduce the risk of this occurring. In this review article, we explore the mechanism of anastomotic recurrence after low anterior resection for rectal cancer, and examine the history and effectiveness of rectal washout on reducing recurrence rates, with a focus on washout solutions, procedures, and devices. Despite the lack of evidence from randomized trials, rectal washout with normal saline or diluted iodine is performed almost routinely during low anterior resection. Clamping is usually done using cross-clamps, linear staplers, tourniquets, and other devices. Although viable cancer cells may be shed into the rectal lumen during surgical resection, their impact on anastomotic recurrence remains uncertain. However, washout poses little or no harm to patients, and appears acceptable as a routine procedure. Randomized controlled trials or large observational studies may help to clarify the best practices for rectal washout.

Keywords Rectal washout · Anterior resection · Rectal cancer · Exfoliated cancer cells · Implantation

Introduction

Colorectal cancer is the third most common cancer globally [1] and approximately one-third of all colorectal cancers are located in the rectum [2]. Local recurrence after resection for rectal cancer is a serious issue [3] and recurrence rates after anterior resection remain relatively high, despite improvements in patient management such as total mesorectal excision [4], preoperative or postoperative radiotherapy [5], and preoperative chemoradiotherapy [6]. As a result of these efforts, 5-year local recurrence rates have dropped to below 10% [4, 7], but surgeons continue to devise additional measures to reduce the risk of recurrence. Local recurrence is defined as a recurrent tumor in and around the tumor bed, including the pericolic fat, the adjacent mesentery, and lymph nodes (extramural recurrence); or at the suture or staple line of anastomosis (intramural recurrence) [8].

It has been suggested that anastomotic recurrence after anterior resection of the rectum is caused by the implantation of exfoliated cancer cells and rectal stump washout has been proposed to prevent implantation [9]. Despite the lack of evidence from randomized trials, rectal stump washout is performed routinely by 60–87% of surgeons in the UK and US [10–12]. In a consecutive case series of rectal cancer patients reported by Heald and Ryall [4], the distal rectum of each patient was routinely clamped and washed out with water following total mesorectal excision. However, a study on a Swedish database of colorectal cancer patients indicated that rectal washout after Hartmann's procedure did not reduce the rate of local recurrence (including at the anastomotic site, perirectal tissue, and lesser pelvis), distant metastasis, and overall recurrence; nor did it improve the overall and 5-year cancer-specific survival rates [13]. Conversely, another study on the same database showed that rectal washout after anterior resection may reduce local recurrence rates [14]. These two studies did not focus only on anastomotic

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recurrence, but examined cases of local recurrence, which has a broader definition. The latest version of clinical practice guidelines published by the American Society of Colon and Rectal Surgeons [15] includes a weak recommendation, based on low-quality evidence, for rectal washout in patients undergoing total mesorectal excision. On the other hand, few studies have examined the benefits of washout during resection of the colon or other parts of the gastrointestinal tract.

We conducted an in-depth review of the literature to explore the mechanism of anastomotic recurrence after anterior resection for rectal cancer, and to examine the history and effectiveness of rectal stump washout procedures in reducing anastomotic recurrence rates. We focused on the commonly used washout solutions and volumes, as well as the procedures and devices used for clamping and washing. Although the definitions of local recurrence and anastomotic recurrence were ambiguous in some previous studies, our review distinguishes between these terms based on the context used in each study.

Mechanism of anastomotic recurrence through the implantation of exfoliated cancer cells

Ryall [16] was the first to suggest that cancer recurrence may be caused by the implantation of exfoliated cancer cells. Subsequently, Golingher [9] reported that almost half of all local recurrences in rectal cancer patients may be attributed to the implantation of loose carcinoma cells on a raw surface at the bowel suture lines, and recommended rectal stump washouts following anterior resection to reduce the risk of anastomotic recurrence. Washouts with 1:500 mercury bichloride were subsequently found to reduce the rate of anastomotic recurrence substantially [9].

Exfoliated cancer cells with high viability have been detected at intestinal anastomotic sites [17]. These cells may cause recurrence by implanting in the suture line [18] and/or attaching to the raw lumen surface [18, 19]. Gertsch et al. [20] reported finding malignant cells in the saline used to wash the surgical staplers and doughnuts after anterior resection of colorectal cancer, and postulated that the malignant cells collected by these staplers can be implanted during anastomosis. Similarly, recurrence at the endoscopic mucosal resection site of rectal cancer may also be caused by tumor-cell implantation, where a post-dissection ulcer provides a raw surface onto which free viable cancer cells can implant [21].

Because more manipulation is required in the narrow lesser pelvic cavity during rectal surgery than colonic surgery, the former can result in a larger quantity of exfoliated cancer cells. Therefore, washing out these cancer cells may be a key to reducing the anastomotic recurrence rates of rectal cancer [22].

Viability of exfoliated cancer cells in washout solutions

Although Rosenberg et al. [23] showed through a trypan blue exclusion test that there were no viable cancer cells in tumor homogenate suspensions, other researchers have verified the viability of exfoliated cancer cells in washout solutions. Skipper et al. [24] and Umpleby et al. [17] reported, respectively, that 40% and 70% of exfoliated colorectal cancer cells are viable. Symes et al. [25] also demonstrated that exfoliated human colon cancer cells can develop into pulmonary metastases in immune-deprived mice. Similarly, Fermor et al. [26] observed that exfoliated colorectal cancer cells can proliferate and metastasize in immune-deprived mice.

Types and volumes of rectal washout solutions

A survey conducted in the UK between 2012 and 2013 found that surgeons used povidone-iodine (PVP-I) diluted with water or saline, chlorhexidine, cetrimide, or water only, for rectal washout during surgery for rectal cancer [10]. Following is an overview of the various types of solutions used for rectal washout.

Mercury bichloride

Mercury bichloride ($HgCl_2$), used originally as a bactericidal agent, was reported to eliminate the implantation of exfoliated cancer cells in the bowel lumen after surgical excision of colorectal cancers [27]. In 1948, Turner et al. [28] advocated clamping below the tumor before irrigating the distal rectum with 1:1000 mercury perchloride during radical excision of the rectum with conservation of the sphincters. Morgan [19] also reported that mercuric washout reduced the recurrence rate of colorectal cancers from 21.4 to 2.09%. Keynes [27] found that washout using mercury bichloride lowered the incidence of local recurrence from 10–16 to 2.6% in patients with cancer of the rectosigmoid and rectum, and also noted the absence of toxic effects from mercury poisoning after using 1:500 mercury bichloride to irrigate mastectomy wounds. However, Keynes [27] did not clarify the definition and details of local recurrence. Hale [29] reported that irrigation with mercury perchloride was more effective than that with normal saline in reducing anastomotic recurrence in Wistar rats injected with tumor cells into the large

bowel. However, mercury is now known to be a toxic agent [30], and is no longer used in washouts.

Cetrimide

Cetrimide was reported to be as effective as mercury bichloride in reducing tumor recurrence [29]. However, Agaba [31] did not find any evidence that rectal washout using 500 mL of 1% cetrimide reduces local recurrence, although this may have been influenced by a relatively small sample size ($n = 141$). Agaba [31] did not clarify the definition and details of local recurrence. Another study reported that rectal lavage using cetrimide was accompanied by blood pressure instability and cardiac ischemia [32].

Formalin

Long and Edwards [33] demonstrated that proximal and distal bowel irrigation with 1–3% formalin solution in colorectal cancer patients reduced the local recurrence rate from 14.3 to 2.6%, but they did not clarify the definition and details of local recurrence. The use of formalin is associated with adverse effects such as intestinal stenosis and diarrhea.

Chlorhexidine

Chlorhexidine is used widely as an antiseptic and has been utilized by many surgeons for rectal washout [10, 34, 35]. However, chlorhexidine is not used for rectal lavage in Japan because its direct application on mucous membranes is not approved [36]. Liu et al. [37] reported a case of severe anaphylactic reaction to chlorhexidine after it was used for rectal stump lavage. Surgeons must consider the potential dangers of allergic reactions to antiseptics.

Povidone-iodine solution

PVP-I solution has been used widely for the prevention or management of wound infections since the 1950s [38], and is still one of the most common antiseptics. Although PVP-I has been reported to have a tumoricidal effect [11], Terzi et al. [39] did not observe any beneficial effects of rectal washout using 500 mL of 5% PVP-I solution on the local recurrence of rectal cancer; however, this may have been affected by a relatively small sample size ($n = 96$). Terzi et al. [39] did not clarify the definition and details of local recurrence. Basha et al. [40] suggested that PVP-I at a concentration of 5% or more can kill viable exfoliated tumor cells.

Based on an in vivo study of Fischer rats, Cho [41] found that irrigation with PVP-I solution did not result in injury of the cecal epithelium. Basha et al. [42] similarly investigated the local and systemic effects of washout using 5% PVP-I solution on Fischer rats. After 30 min of washout, the epithelial cell layer of the colon became detached in each rat, resulting in severe injury to the colonic mucosa that healed after a week. Exposure to the PVP-I solution also caused transient decreases in the levels of thyroid hormones, but these normalized within a week [42]. Another study showed that colorectal cancer surgery patients had elevated serum iodine levels after intraoperative bowel irrigation with 5% PVP-I solution, but did not suffer thyroid dysfunction or toxic chemical syndrome (such as metabolic acidosis and hypernatremia) [43]. Mariani et al. [44] reported that colorectal cancer patients who received whole-colon irrigation with PVP-I solution had reduced levels of total serum triiodothyronine, but these normalized after 7 days. Similarly, Banich and Mendak [45] found that intraoperative colonic irrigation with 500–1000 mL of 10% PVP-I solution did not cause systemic toxicity or mucosal damage.

Normal saline

Previous studies have reported on the use of 200–2000 mL [46–49] of normal saline for rectal irrigation. Maeda et al. [22] proposed that more than 1000 mL and 2000 mL of saline, respectively, is needed to effectively irrigate exfoliated cancer cells for rectal cancer located below and above the peritoneal reflection. In Japan, many surgeons irrigate the rectal stump using 1000–2000 mL of saline [50–52]. However, Shinto et al. [52] reported that even after washout using 2000 mL of saline, scraping smear tests of the anastomotic site still detected exfoliated cancer cells in 70% of patients who had undergone low anterior resections for rectal cancer. In contrast, Zhou et al. [53] reported that rectal washout with 1500 mL of normal saline reduced local recurrence in patients who had undergone anterior resection for rectal cancer, but they did not clarify the definition and details of local recurrence.

Water

Heald et al. [3, 4] described the use of water to perform rectal washout in rectal cancer patients; however, these studies did not show the effectiveness of washout using water on recurrence rates.

Which solution is best?

Umpleby and Williamson [11] compared the cytotoxicity of several agents, including chlorhexidine–cetrimide, PVP-I solution, sterile water, mercury perchloride, and noxythiolin, on colorectal cancer cells, and reported that chlorhexidine–cetrimide and PVP-I solution were the most rapidly lethal to these cells. However, there is little definitive

evidence that any one solution is superior to the others in the clinical setting.

Procedures and devices for clamping

During surgery for rectal cancer, a clamp or stapler is applied below the tumor and above the dissection line. Whether in open or laparoscopic surgery, the clamps should be designed so that they are easy to operate and do not hinder anastomosis.

During open surgery

The rectum can be clamped with a curved Parker Kerr crushing clamp [9], a cross-clamp [31, 39, 46], or a right-angle clamp [4, 22, 37, 47, 48, 50, 51, 54, 55]. Encircling nylon tape can be used if a clamp cannot be placed distal to the tumor because of a narrow pelvis [39]. A piece of tubing from the intravenous line can also be used as an occlusive tourniquet [56]. Shinto et al. [52] reported using a linear stapler to staple the rectum directly, without any other clamping device.

During laparoscopic surgery

Laparoscopic rectal surgery has become popular in recent years, and there is a growing demand among surgeons for devices that are suitable for laparoscopic surgery. However, laparoscopic manipulation can increase tumor exfoliation, thereby elevating the importance of lavage [55]. Simillis et al. [10] reported that in the UK, the rectum is clamped laparoscopically using a Johann grasper, Hayes clamp, tightened nylon tape, endostapler, open linear stapler, or ligatures. When using staplers for clamping during rectal surgery, the same stapler can be moved or a second stapler can be placed distally [55]. Sakai et al. [57] reported that a specialized Gut Clamper® (Kobe Biomedix Co. Ltd., Kobe, Japan) provides stable and tight clamping of the rectum. Following irrigation, this device conveniently allows adjustments to a linear stapler. Detachable bowel clamps [55] and occlusive tourniquets can also be used [56] during laparoscopic surgery for rectal cancer.

Procedures and devices for washouts

Rectal washouts have been performed using Foley catheters [46, 58, 59], 30-mL syringes [51], double concentric sump tubes [48], a proctoscope with an irrigator designed for rectal washout (I-type proctoscope for rectal washout; Yufu Itonaga Inc., Tokyo, Japan) [22, 49, 54], and the Colo-Shower® (Sapi-Med, Alessandria, Italy) [60]. Simillis et al. [10] reported on the use of rectal tubes, Ross irrigating proctoscopes, Proctowash, and 50-mL bladder-ended syringes. Whole-colon irrigation can also be performed using commercial colostomy irrigation sets (Coloplast, Ruisbroek, Belgium) [44].

Washout during resection of other gastrointestinal cancers

Although many surgeons perform washout during rectal resection, this procedure is less common during colonic resection. There are several possible reasons for this disparity: First, suture-line recurrence is less common after colonic resection than after anterior resection of the rectum [27]. Second, anterior resections require more manipulation in the narrow pelvis [22]. Moreover, the intestine is generally excised nearer the tumor in anterior resection than in colectomy, and more exfoliated cancer cells can spread within the lumen [61]. Third, the procedure for total colonic washout is more complicated than that for rectal washout. However, cases of anastomotic recurrence have been reported after functional end-to-end anastomosis for colon cancer [18, 62]. Saito et al. [18] described wiping the staple line with PVP-I to prevent anastomotic recurrence, and noted that a clearly defined standard procedure is needed to reduce recurrence after functional end-to-end anastomosis.

Double-stapling technique and anastomotic recurrence

Hirai et al. [50] suggested that recurrence at the anastomotic site was influenced not by the tumor location, but by the anastomotic technique. Specifically, they noted that the double-stapling technique resulted in anastomotic recurrence more often than other anastomotic procedures such as single stapling and hand suturing [50]. Gertsch et al. [20] suggested that exfoliated cancer cells may be implanted at the anastomotic line by staplers, increasing the risk of anastomotic recurrence.

Washout of the proximal colon and anastomotic recurrence

In a consecutive case series, McGrew et al. [61] reported positive smears in 42% of the proximal ends and 76% of the distal ends of resected rectums, even though the average distances from the tumors were 23 cm and 6 cm, respectively. Because exfoliated cancer cells are often detected in the proximal colon, its irrigation may help to reduce the recurrence rate at the anastomotic site; however, there is

currently insufficient clinical evidence on the effectiveness of this method.

Conclusion

Local recurrence includes extramural and intramural/anastomotic recurrence, which can be attributed to various factors. Thus, it is difficult to accurately quantify the proportion of local recurrence (or anastomotic recurrence) due solely to the implantation of exfoliated cancer cells. The existing literature suggests that viable cancer cells may be shed into the rectal lumen from tumors during surgical resection, but there is little evidence to prove that this increases anastomotic recurrence. Few studies have reported a significant reduction in anastomotic recurrence after rectal washout because of the generally small number of cases of anastomotic recurrence. Despite the lack of high-quality evidence, washout appears not to damage the rectum and, therefore, may be used as a routine procedure during anterior resection of rectal cancer. Randomized controlled trials or large observational studies could identify the best practices for rectal washout. Based on current knowledge, it appears reasonable to perform rectal washout using normal saline or 5% PVP-I solution, which has shown cytotoxic effects against cancer cells.

Compliance with ethical standards

Conflict of interest Kae Okoshi and co-authors have no conflicts of interest to declare.

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