

# Abdominoperineal Resection in Rectal Cancer: Systematic Review

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**Abstract:** Impaired perineal wound healing has become a significant clinical problem after abdominoperineal resection for rectal cancer. The increased use of neoadjuvant radiotherapy and wider excisions might have contributed to this problem. The primary aim of this systematic review with meta-analysis was to determine the impact of radiotherapy and an extralevator approach on perineal wound healing after abdominoperineal resection for rectal cancer. The primary end point was overall perineal wound problems within 30 days after conventional or extralevator abdominoperineal resection with or without neoadjuvant radiotherapy. Secondary end points were primary wound healing, perineal hernia rate, and the effect of biological mesh closure on perineal wound problems. In conclusion, neoadjuvant radiotherapy significantly increases perineal wound problems after abdominoperineal resection for rectal cancer, whereas the extralevator approach seems not to be of significant importance.

**Keywords:** Abdominoperineal Resection, Rectal Cancer, increases perineal.

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## 1. INTRODUCTION

Perineal injury issues after abdominoperineal resection (APR) for rectal cancer is reported in up to 57% of patients<sup>(1)</sup>. If the perineum does not heal primarily, secondary wound healing might lengthen medical facility stay, may require surgical reintervention, and frequently requires intensive wound care for several months, with the risk of developing a persistent sinus after 1 year<sup>(2-4)</sup>. In the past years, perineal wound recovery after APR has actually gained more attention since of the intensified treatment of distal rectal cancer. After the widespread adoption of the method of total mesorectal excision and the increasing use of neoadjuvant radiotherapy, locoregional disease control and survival of rectal cancer have improved<sup>(5,6)</sup>. The oncological outcome stayed bad due to positive circumferential resection margins and tumor perforations in patients with low rectal cancer undergoing APR<sup>(7)</sup>. When the total mesorectal excision airplane is followed all the method down to the pelvic flooring, as performed in conventional APR (cAPR), a normal coning of the specimen occurs by which the resection margins are compromised. To overcome this issue, larger excisions with en bloc resection of the distal anus, sphincter complex, and levator muscles have actually been presented, leading to a round specimen, this extralevator APR (eAPR) minimizes the rate of positive resection margins and growth perforation in distal rectal cancer, and improves oncological outcome<sup>(8,9)</sup> as a disadvantage of enhanced oncological result, both radiotherapy and extended resections have actually been suggested to increase perineal wound recovery issues after APR<sup>(10)</sup>. The goal of this organized review with meta-analysis was to determine the effect of these changes in rectal cancer management on perineal injury healing after APR. secondarily, the recent intro of biological mesh reconstruction of the pelvic flooring, aiming at enhanced perineal injury recovery and the prevention of perineal hernia, was assessed.

## 2. METHODOLOGY

All studies reporting on perineal wound healing after either cAPR or eAPR for rectal cancer were considered eligible for review. The electronic databases of the national institutes of health Pubmed (1952–2014), emBase (1984–2014), Cochrane library (2008–2013), and Sciencedirect (2013–2016) were systematically searched up to March 2016. The following medical subject heading (mesh) terms were used; rectal neoplasms, rectal, neoplasms, abdomen, perineum, colorectal surgery, surgical procedures operative, general surgery, wound healing, reconstructive surgical procedures,

wounds, and injuries. Other search terms were abdominal perineal resection, abdominoperineal resection, abdominoperineal excision, abdominal perineal excision, perineum surgery, perineal surgery, primary healing, repair, wound, and healing. No restrictions considering patient age or technique of APR were applied.

### 3. RESULTS AND DISCUSSION

#### I. Study Characteristics APR With Primary Perineal Closure:

Of the 32 consisted of studies, primary perineal wound closure after cAPR was described in 21 research studies, with an overall variety of 2989 patients (table 1).<sup>(1,2,9,10,13-- 20,22,25,29,30,32-36)</sup> five research studies explained using an extralevator approach (eAPR) in 728 patients<sup>(4,21,32,37,38)</sup>. All patients underwent APR for primary rectal cancer, with the exception of 2 studies in which a minority of patients had frequent rectal cancer (n = 41; 1%)<sup>(25,39)</sup>. Just 3% (n = 115) of the patients went through minimally invasive surgery as described in 3 studies<sup>(9,25,32)</sup>. Using an omental plasty was described in 3 studies and varied between 20% and 88%<sup>(14,35,37)</sup>. Using a presacral drain was described in 14 research studies (56%-100%)<sup>(1,13-15,18,21,29,32-38)</sup> and a perineal wound drain in 3 research studies.<sup>(20,36,38)</sup> Radiotherapy was used in 16 research studies, and the percentage of patients getting radiotherapy varied from 28% to 100%<sup>(1,2,4,9,10,16--21,32,33,36-38)</sup>.

**Table 1 Perineal wound problems after APR with primary perineal closure for rectal cancer**

Included studies	Year	n	Study design	Consecutive series	Operation (CAPR/eAPR)	Preoperative Antibiotics (yes/no)	Radiotherapy	Concomitant Chemotherapy	Follow-up, mo (range)
Hawkins et al <sup>25</sup>	2013	239 of 249	Cohort	yes	cAPR	-	-	-	45 (1-130) <sup>b</sup>
Han et al <sup>16</sup>	2012	32 of 67	RCT	-	cAPR	-	9 (28)	9 (28)	29 (12-48) <sup>b</sup>
Asplund et al <sup>32</sup>	2011	79 of 158	Cohort	no	cAPR	-	66 (84)	5 (6)	45 (1-89) <sup>b</sup>
Pramateftakiet al <sup>18</sup>	2011	75	RCT	-	cAPR	yes	25 (33)	25 (33)	60 <sup>c</sup>
Zorcolo et al <sup>36</sup>	2010	155	Cohort	no	cAPR	yes	68(44)	40 (26)	34 (25-57) <sup>d</sup>
El-Gazzaz et al <sup>2</sup>	2009	696	Cohort	yes	cAPR	-	273 (39)	273 (39)	-
Sebag-Montore et al <sup>19</sup>	2009	202 of 1350	RCT	-	cAPR	-	202 (100)	-	60 <sup>c</sup>

#### II. Perineal Wound Problems After APR With Primary Perineal Wound Closure:

The portions of perineal injury problems after primary perineal wound closure for each individual research study are displayed in table 1. After cAPR without neoadjuvant radiotherapy (6 research studies, 1000 patients; table 2), overall perineal wound issues happened in a pooled portion of 15.3% (95% Ci, 12.1- 19.2; i2 = 50%,  $\chi^2 = 0.07$ )<sup>(2,10,14,15,17,36)</sup>. Presuming that radiotherapy was not used in an additional 4 studies published between 1991 and 1995, although this was not clearly described, the pooled portion of all perineal wound issues was 18.7% (95% Ci, 13.9-24.9; i2 = 78%,  $\chi^2 < 0.01$ ; 10 research studies, n = 1218)<sup>(2,10,13-15,17,29,34-36)</sup>. shallow perineal injury issues accompanied a pooled portion of 15.0% (95% Ci, 10.3-21.6; i2 = 78%,  $\chi^2 < 0.01$ ; 8 research studies, n = 1032)<sup>(2,10,15,17,29,34-36)</sup> and deep perineal wound problems with a pooled portion of 8.8% (95% Ci, 2.7-25.0, i2 = 92%,  $\chi^2 < 0.01$ ; 5 research studies, n = 744)<sup>(2,13-15,36)</sup>. After cAPR with neoadjuvant radiotherapy in all patients, the pooled percentage of perineal injury issues was 30.2% (95% Ci, 19.2-44.0; i2 = 90%,  $\chi^2 < 0.01$ ; 5 research studies, n = 730)<sup>(1,2,10,17,36)</sup>. shallow perineal wound issues had a pooled percentage of 19.4% (95% Ci, 14.5-- 25.4; i2 = 64%,  $\chi^2 = 0.026$ ; 5 studies, n = 730)<sup>(1,2,10,17,36)</sup> and deep perineal wound problems had a pooled percentage of 7.1% (95% Ci, 1.3-- 31.1; i2 = 87%,  $\chi^2 < 0.01$ ; 3 research studies, n = 362)<sup>(1,2,36)</sup> Radiotherapy revealed a substantial increase in overall perineal injury issues after caPR (oR, 1.74; 95% Ci, 1.29-2.34; p = 0.0003; i2 = 13%,  $\chi^2 = 0.33$ ; 4 research studies, n = 1496)<sup>(2,10,17,36)</sup>. The pooled percentage of general perineal injury issues after eAPR without neoadjuvant radiotherapy was 14.8% (95% Ci, 9.5-22.4; i2 = 30%,  $\chi^2 = 0.233$ ; 2 studies, n = 217)<sup>(4,37)</sup> in patients who went through neoadjuvant radiotherapy, the pooled percentage of perineal injury issues after eAPR was 37.6% (95%

Ci, 18.6-61.4;  $i^2 = 85\%$ ,  $\chi^2 = 0.01$ ; 2 research studies,  $n = 169$ )<sup>(4,37)</sup> neoadjuvant radiotherapy considerably increased the threat of perineal injury problems after both cAPR and eAPR (oR, 2.22; 95% Ci, 1.45-3.40;  $p = 0.0003$ ); the pooled portions with 95% CIs of the different subgroups.

**Table 2 Perineal wound problems after APR with primary perineal closure in patients being treated with or without neoadjuvant radiotherapy**

Included studies	cAPR/eAPR	n	Radiotherapy (yes/no)	sPWP	dPWP	cPWPa	PWH	Incisional hernia
Bullard et al <sup>10</sup>	cAPR	117	yes	16 (14)	-	55(47)	86(74)	1(1)
Chadwick et al <sup>33</sup>	cAPR	43	no	0	-	10(23)	36(84)	-
El-Gazzaz et al <sup>2</sup>	cAPR	37	yes	-	-	-	13(35)	-
Kapiteijn et al <sup>17b</sup>	cAPR	57	no	-	-	-	44(77)	-
Zorcolo et al <sup>36</sup>	cAPR	273	yes	49 (18)	14(5)	55(20)	234(86)	1(0.4)
De Broux et al <sup>37</sup>	eAPR	423	no	46 (11)	12(3)	51(12)	399(94)	6(1)
Nissan et al <sup>4</sup>	eAPR	251	yes	65 (26)	-	65(26)	-	-

### III. Perineal Wound Healing and Perineal Hernia After APR With Primary Perineal Wound Closure:

After cAPR without radiotherapy, main perineal wound healing had a pooled weighted estimate of 81.8% (95% Ci, 64.7-91.7;  $i^2 = 93\%$ ,  $\chi^2 < 0.01$ ; 5 studies,  $n = 736$ )<sup>(2,10,14,15,33)</sup> after neoadjuvant radiotherapy, main perineal wound recovery had a pooled estimate of 63.9% (95% Ci, 45.7-78.8;  $i^2 = 93\%$ ,  $\chi^2 < 0.01$ ; 5 studies,  $n = 650$ )<sup>(1,2,10,19,33)</sup> there was just 1 study reporting the primary perineal injury recovery rate after eAPR with all patients undergoing radiotherapy, which was 43% ( $n = 53/123$ ).<sup>4</sup> Radiotherapy showed a substantial reduction in main perineal injury healing after both cAPR and eAPR (oR, 0.27; 95% Ci, 0.16-0.45;  $p < 0.001$ ; fig. 4)<sup>(2,4,10,33)</sup> Perineal hernias after cAPR happened in a pooled percentage of 1.8% (95% Ci, 0.4-8.3;  $i^2 = 84\%$ ,  $\chi^2 < 0.01$ ; 4 studies,  $n = 1012$ )

<sup>(2,9,10,16)</sup> and in 2.0% after eAPR (95% Ci, 0.5-- 7.0;  $i^2 = 59\%$ ,  $\chi^2 = 0.09$ ; 3 studies,  $n = 367$ )<sup>(21,37,38)</sup>.

### IV. Perineal Wound Problems and Perineal Hernia After Biological Mesh-Assisted Closure:

Biological mesh-assisted perineal injury closure was performed in 224 patients from 8 studies<sup>(16,23,24,26-28,31,39)</sup> all 224 patients underwent eAPR. The use of a pre-sacral drain was reported in 2 studies<sup>(26,39)</sup> and a perineal injury drain was reported in 4 research studies<sup>(16,24,27,39)</sup>. The percentage of patients receiving radiotherapy ranged from 43% to 100%, and an omental plasty was utilized in 28% ( $n = 36$ ) and described in 2 studies<sup>(23,31)</sup>. The biological meshes consisted in 4 research studies of cross-linked porcine meshes<sup>(23,26,27,39)</sup> and 1 study of non-cross-linked porcine meshes<sup>(28)</sup>. In 1 research study, both cross-linked and non-cross-linked meshes were used<sup>(31)</sup>, and, in 2 studies, human dermal meshes were used<sup>(16,24)</sup>. Perineal wound problems after eAPR and in a minimum of 75% of the patients treated with radiotherapy happened in a pooled percentage of 24.3% (95% Ci, 14.1-38.6;  $i^2 = 21\%$ ,  $\chi^2 = 0.28$ ; 4 studies,  $n = 78$ )<sup>(24,28,31,39)</sup> if only 2 studies were consisted of in which all patients underwent neoadjuvant radiotherapy, perineal injury issues after eAPR occurred in a pooled percentage of 7.3% (95% Ci, 1.5-29.3;  $i^2 = 0\%$ ,  $\chi^2 = 0.81$ ;  $n = 20$ )<sup>(24,31)</sup> Perineal hernias after biological mesh closure following eAPR were reported in a pooled percentage of 8.2% (95% Ci, 4.8- 13.6;  $i^2 = 0\%$ ,  $\chi^2 = 0.45$ ; 6 studies,  $n = 188$ )<sup>(16,23,24,26,28,39)</sup>.

### Discussion:

Neoadjuvant radiotherapy significantly increased perineal wound problems after APR for rectal cancer with an oR of 2.22. An extralevator technique has also been associated with higher wound complication rates, likewise weighted pooled portions of perineal wound issues after cAPR and eAPR were found in uniform subgroups depending on whether or not radiotherapy was used. Without neoadjuvant radiotherapy, perineal wound problems happened in 15.3% after cAPR and 14.8% after eAPR; corresponding injury problem rates following radiotherapy were 30.2% and 37.6%. this suggests that, not the level of the resection, however generally neoadjuvant radiotherapy is the most important therapy-related threat element for perineal wound complications.

Most of the available studies have considerable methodological drawbacks, and these information must be analyzed with care, particularly the research studies with high analytical heterogeneity. The fairly high statistical heterogeneity could be the outcome of the non-standardized prospective assessment and registration of the perineal wounds and the nonuniform definitions used for categorizing perineal injury complications. Both the use of neoadjuvant radiotherapy and an extralevator method for the APR procedure have increased in time, with more focus on perineal wound issues in more recently published posts. A restriction of the research studies before 1990 was used, and subgroup analyses for the quantity of radiotherapy and the level of resection have actually been performed in this methodical review. A detailed description of the various types of perineal injury problems is lacking in a considerable number of research studies, such as superficial injury infection, dehiscence without infection, and deep pelvic abscess. This was the factor for choosing a combined endpoint of all perineal injury problems as primary outcome procedure for the present analysis. Although all these constraints may have influenced the pooled analyses, the presently reported data are the best offered evidence at this time.

Neoadjuvant radiotherapy may increase perineal injury problems and reduce perineal wound recovery due to the fact that it damages DNA and proteins, which could lead to apoptotic cell death<sup>(40)</sup>. Apoptosis in endothelial cells results in increased vascular permeability. this permeability results in apoplexy and intima expansion<sup>(40)</sup>. Furthermore, radiotherapy affects proinflammatory cytokines in the early phase<sup>(40)</sup>. Inflammation may not resolve adequately, leading to uncontrolled matrix build-up and brosis. in addition, decreased levels of nitric oxide and matrix metalloproteinase might contribute to the insufficient soft tissue reconstruction<sup>(41)</sup>.

Main perineal wound closure after APR has actually been the standard method for a long period of time. this requires a layered closure of the staying structures, specifically, the remnants of the pelvic floor, ischio-anal and subcutaneous fat, and perineal skin. after an extralevator approach, only the perineal and fat skin can be closed because the pelvic floor has actually been resected. Despite the much larger pelvic flaw, satisfying outcome on perineal injury healing has been released for primary perineal closure after eAPR<sup>(4,21,37)</sup>. This is not consistently reported, and others have actually used extra surgical procedures to improve perineal wound recovery after eAPR. autologous tissue flaps, such as the vertical rectus abdominis myocutaneous flap and gluteal flap, have been utilized for closure of big perineal defects after prolonged resections for primary or reoccurring rectal cancer or salvage surgery for anal cancer<sup>(42-45)</sup>. Because of the donor website morbidity, increased operative time, and greater expenses, it is questioned whether autologous tissue flaps ought to be performed as a regular in patients going through APR for rectal cancer. Pelvic floor restoration with making use of a biological mesh has been introduced recently and appears to be an attractive alternative for tissue aps based upon a recent systematic review<sup>(46)</sup>. However, a comparison in between main perineal injury closure and biological mesh-assisted closure has actually not yet been made. literature on biological mesh-assisted perineal closure after APR is scarce. On the other hand, the majority of the APR studies have a main oncological focus, whereas perineal injury recovery and perineal hernia development are frequently main result steps in biological mesh studies. This does not allow for an official contrast between primary perineal injury closure and biological mesh-helped closure based on literature information. although the pooled analysis recommends a reduced portion of perineal injury issues after biological mesh-assisted closure, RCTs are had to draw definitive conclusions. to date, 2 multicenter trials are being performed where pelvic floor reconstruction utilizing a biological mesh is compared with primary perineal wound closure .

Perineal wound issues are likewise most likely to be connected to the dead area in the hips with bacterial contamination. an omental plasty may solve this issue by filling of the pelvic cavity, enhancing the regional immune reaction, and promoting angiogenesis<sup>(47,48)</sup>. The application of an omental plasty has been recommended to improve primary perineal injury healing<sup>(49,50)</sup>. only 5 picked studies explained making use of an omental plasty without separate data on perineal injury recovery. the effect of this extra surgical procedure could therefore not be examined in the present meta-analysis.

In our organized evaluation, we found a rather high weighted pooled percentage of perineal hernia in patients undergoing pelvic flooring restoration with the use of a biological mesh. This contradictory findings is probably related to a more comprehensive description of perineal problems with more adequate follow-up in biological mesh research studies compared with oncological APR research studies utilizing primary perineal wound closure. In addition, the degree of the resection (only eAPR in biological mesh research studies) and a discovering curve effect of a new surgical technique may discuss the fairly high perineal hernia rate.

#### 4. CONCLUSION

Our organized evaluation demonstrates that neoadjuvant radiotherapy substantially increases perineal injury issues after APR, whereas the extralevator method seems to have less impact. Biological mesh-assisted perineal injury closure is an appealing method to enhance perineal wound healing, however we need to wait for results of ongoing randomized trials.

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