A systematic review and meta-analysis on omentoplasty for the management of abdominoperineal defects in patients treated for cancer

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Annals of Surgery. 2020 Apr;271(4):654-662. doi: 10.1097/SLA.0000000000003266. PMID: 30921047

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ABSTRACT

Objective

The objective of this systematic review and meta-analysis was to examine the effects of omentoplasty on pelviperineal morbidity following abdominoperineal resection (APR) in patients with cancer.

Background

Recent studies have questioned the use of omentoplasty for the prevention of perineal wound complications.

Methods

A systematic review of published literature since 2000 on the use of omentoplasty during APR for cancer was undertaken. Authors were requested to share their source patient data. Meta-analyses were conducted using a random-effects model.

Results

Fourteen studies comprising 1894 patients (n=839 omentoplasty) were included. The majority had APR for rectal cancer (87%). Omentoplasty was not significantly associated with the risk of pre-sacral abscess formation in the overall population (RR 1.11; 95% CI 0.79-1.56), nor in planned subgroup analysis (n=758) of APR with primary perineal closure for non-locally advanced rectal cancer (RR 1.06; 95% CI 0.68-1.64). No overall differences were found for complicated perineal wound healing within 30 days (RR 1.30; 95% CI 0.92-1.82), chronic perineal sinus (RR 1.08; 95% CI 0.53-2.20) and pelviperineal complication necessitating reoperation (RR 1.06; 95% CI 0.80-1.42) as well. An increased risk of developing a perineal hernia was found for patients submitted to omentoplasty (RR 1.85; 95% CI 1.26-2.72). Complications related to the omentoplasty were reported in 4.6% (95% CI 2.5-8.6%).

Conclusions

This meta-analysis revealed no beneficial effect of omentoplasty on pre-sacral abscess formation and perineal wound healing after APR, while it increases the likelihood of developing a perineal hernia. These findings do not support the routine use of omentoplasty in APR for cancer.

INTRODUCTION

The pelvic wound bed after abdominoperineal resection (APR) carries a high risk of morbidity.(1-3) This is likely related to the contaminated operative field and dead space formation with fluid accumulation, and may be further increased by extended resections and compromised perfusion post-radiotherapy. A randomized controlled trial showed that perineal complications within one year after APR with primary perineal closure may occur in up to 48%.(4) Patients frequently develop perineal wound dehiscence and infection, and often endure delayed healing. Secondary wound healing can take several months and may eventually result in a chronic perineal sinus.(5) Furthermore, patients may develop perineal pain and sitting problems, as well as a perineal hernia.(6, 7)

To improve perineal wound healing after APR, various reconstructive methods have been proposed. These include the use of a biological mesh and several tissue flaps, such as a pedicled omentoplasty (OP) or a vertical rectus abdominis muscle flap (VRAM).(8-10) The flaps serve to obliterate the often non-collapsible defect with healthy and well perfused tissue, which has been associated with reduced abscess formation and improved wound healing.(11, 12)

The omentum is supposedly an ideal option to prevent dead space formation after APR. It has a rich blood supply, expresses anti-inflammatory cytokines, often provides for abundant bulk and appears relatively easy to release.(13-16) Many surgeons therefore perform an OP as part of the APR procedure. In a recent nationwide study with variability in practice of applying OP, no improvement in perineal wound healing was observed, and the OP particularly seemed to increase the risk of perineal herniation.(6) These results challenge the value of OP for closure of the pelvic defect after APR. Therefore, the aim of this systematic review and meta-analysis was to assess the effects of OP following APR on pelviperineal morbidity and related problems in patients treated for cancer in the published literature since 2000.

METHODS

The study protocol was prospectively registered at PROSPERO (registration number: CRD42017073573) and followed Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidance.(17)

Search

The literature was systematically reviewed by searching in the PubMed-library for studies published between January 2000 and March 2017. The search was limited to publication

since 2000 to limit the influence of historical changes in surgical and peri-operative care, which better ties in to current practices. The search was rerun in June 2018 (Supplementary Digital Content 1). The search strategy only included terms relating to or describing neoplasms, surgical outcome and APR. Since most studies do not explicitly mention the use of OP in the title or abstract, this was not included as a search term. Additional articles were manually selected from the reference lists of the retrieved papers.

Eligibility

Original studies including patients undergoing APR for cancer and reporting on use of OP and perineal wound outcome were potentially eligible. Articles were restricted to the English language. Exclusion criteria were studies with no original data, individual case reports (<10 patients with OP), studies that did not report on at least one predefined outcome of interest, and studies that exclusively pertained to pelvic exenteration or benign disease.

Outcome parameters

The primary endpoint was incidence of pre-sacral abscess formation, as this was expected to be most consistently reported. Secondary endpoints were the rate of overall pelviperineal wound complications within 30 days, one year, and the total study period, wound healing time, specific pelviperineal morbidity (i.e. wound dehiscence, superficial wound infection, haemorrhage, perineal sinus), ileus (overall, and proportion requiring reoperation), perineal hernia (not specified), OP-related morbidity, operative time, and surgical perineal re-intervention. Pelviperineal complication included any pelvic or perineal wound event (including perineal hernia), and surgical perineal re-intervention any pelvic or perineal wound-related reoperation (including hernia repair). Perineal infection was categorized into superficial wound infection (including perineal abscess), and deep wound infection (i.e. pre-sacral abscess). Perineal haemorrhage included active perineal bleeding or hematoma (regardless of need for re-intervention). There was no definition given for pre-sacral abscess, perineal sinus and perineal hernia. Perineal hernia was based on the reporting of the source studies, and could vary from asymptomatic incidental CT finding to symptomatic perineal bulge requiring surgical repair.

Data collection and extraction

Two independent reviewers (RDB & CELK) scanned all abstracts identified by the search and cross-referencing. Full texts were retrieved for all studies that potentially met the inclusion criteria. Two reviewers (RDB & JAWH) further independently reviewed the eligibility of these studies in full text. Any disagreement on the eligibility of particular studies was resolved through consensus discussion with a third reviewer (PJT). Papers not meeting the inclusion criteria were excluded and listed with reason for omission (Figure 1). All authors

were contacted on three separate occasions to share either the source individual patient data or aggregate data, reported separately for OP and non-OP.

Data extraction included general study information, participant demographics, operative details, perineal wound outcome, length of follow-up, and information for assessment of the risk of bias. Any disagreement was solved by consensus discussion, if necessary with a third reviewer (PJT). In case of missing data, the study authors were contacted to request additional information.

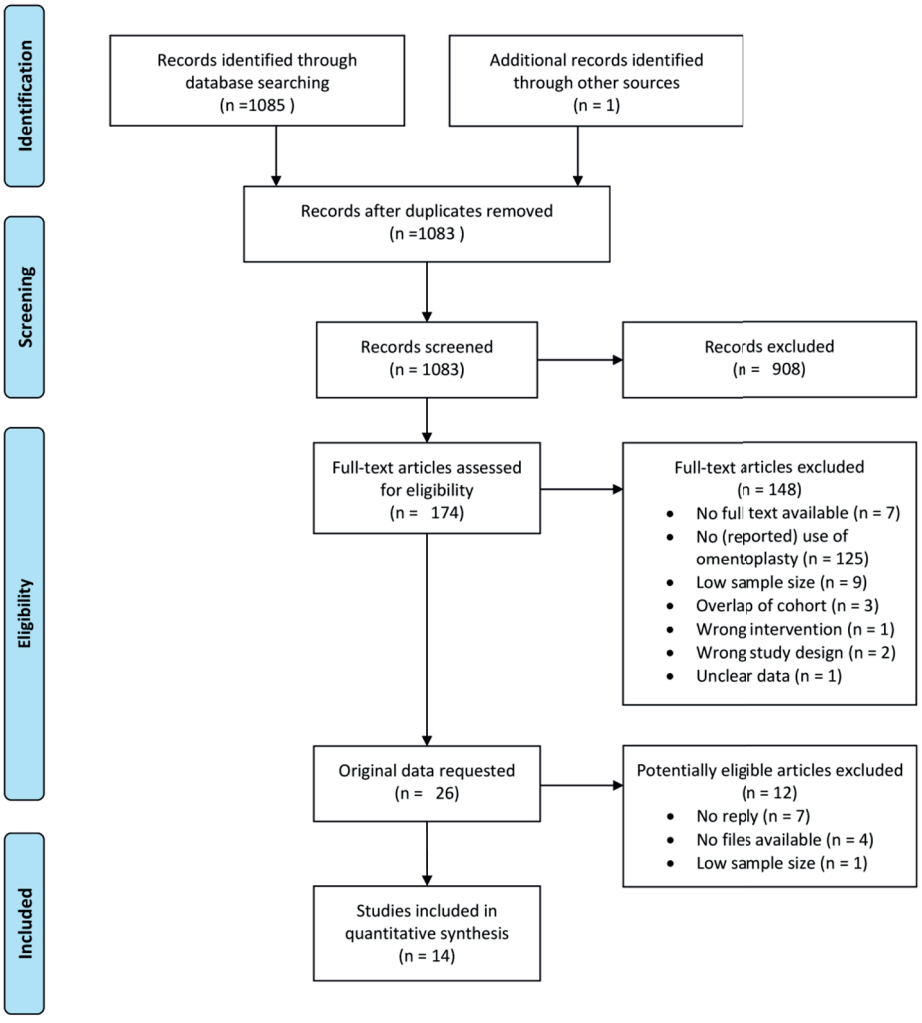

Figure 1. PRISMA flow diagram depicting the search strategy and study selection process.

The received source patient data was preferably used, and may slightly differ from the original publication. If this was not available, data from the original publication was used. The cohort of Musters et al. was updated using original patient files.(5) From the initial 104 patients of the BIOPEX study, 99 were entered in the analyses because of missing outcome data due to study exclusions.(4)

Assessment of risk of bias in included studies

Two reviewers (RDB & JAWH) independently assessed the risk of bias in the included studies using the Newcastle-Ottawa Scale (NOS) for non-randomized studies.(18, 19)

Data synthesis

All outcome measures were quantitatively summarized. If at least three comparative studies (≥10 cases in both groups) provided data on a study parameter, data were pooled in meta-analysis using Review Manager (RevMan 5; Cochrane Collaboration). Studies without a control (<10 cases of non-OP) were pooled in proportional meta-analysis using RStudio (version 3.5.1). Pooled estimates of effect were calculated along with corresponding 95% confidence interval (CI), using a random-effects model. The method as proposed by Wan et al. was used to approximate the estimation of the sample mean and standard deviation in case the median and interquartile range was given.(20) Dichotomous data were summarized by risk ratios (RR), and continuous data were presented as mean differences (MD). Heterogeneity between studies was perceived considerable when $I^2 \geq 75\%$.(21) Two-sided p-values <0.05 were considered statistically significant. Funnel plots were generated to assess for publication bias. The evidence along with the quality of the data were summarized in a GRADE summary of findings table.

Analysis of subgroups

In order to decrease potential bias introduced by diverse indication and surgical methods, a planned subgroup analysis was performed for patients that underwent APR with primary perineal closure for non-locally advanced rectal cancer. The additional exclusion criteria for the purpose of this subgroup analysis were reconstructions using a mesh and/or flap, other pelvic malignancies, pT4 stage, and adjacent organ resection. We also performed a planned subgroup analysis only in patients who received pre-operative radiotherapy.

RESULTS

Literature search and selection

The results of the literature search are displayed in Figure 1. After deduplication, the combined search yielded 1081 articles, of which 26 were identified as potentially eligible.

After contacting the authors, individual patient data were provided in six(4-6, 22-24) and aggregate data in four.(25-28) An additional of four studies with full text of the original paper only were included.(9, 10, 29, 30) Eleven studies without separate data for OP(31-41), and one study that eventually appeared to have included only one patient with OP(42) were excluded.

Study characteristics

General study descriptions are demonstrated in Table 1. Eleven studies had a control group (i.e. ≥10 cases of non-OP).(2, 4, 6, 9, 10, 22-24, 26, 28, 30) The quality of the included studies was moderate to good (range 5-9; Supplementary Table 2; Supplemental Digital Content 2). The 14 included studies covered a total of 1894 patients, of whom 839 underwent OP.

Table 1. Study descriptions of the included studies.

Study (Author)	Year	Country	Design	Quality*	Disease	Patients (N=1894)	OP (N=839)	Non-OP (N=1055)
De Broux *et al.*	2005	France	Retrospective cohort study	5	Rectal cancer	92	92	0
Lefevre *et al.*	2009	France	Retrospective cohort study	7	Anal cancer	95	52	43
Hultman *et al.*	2010	USA	Retrospective cohort study	5	Rectal cancer and anal cancer	70	29	41
Kirzin *et al.*	2010	France	Retrospective cohort study	6	Rectal cancer	109	19	90
Oida *et al.*	2012	Japan	Retrospective cohort study	8	Rectal cancer	45	20	25
Dumont *et al.*	2012	France	Retrospective cohort study	6	Rectal cancer, anal cancer and other	132	101	31
Hawkins *et al.*	2014	USA	Retrospective cohort study	8	Rectal cancer	251	109	142
Musters *et al.*	2014	Netherlands	Retrospective cohort study	9	Rectal cancer	128	50	78
Hardt *et al.*	2016	Germany	Retrospective cohort study	6	Anal cancer	17	16	1
Hellinga *et al.*	2016	Netherlands	Retrospective cohort study	5	Rectal cancer, anal cancer and other	24	20	4
Jones *et al.*	2017	United Kingdom	Prospective cohort study	6	Rectal cancer and anal cancer	266	42	224

Table 1. Study descriptions of the included studies. (continued)

Study (Author)	Year	Country	Design	Quality*	Disease	Patients (N=1894)	OP (N=839)	Non-OP (N=1055)
Musters *et al.*	2017	Netherlands	Prospective cohort study[a]	9	Rectal cancer	99	61	38
Blok *et al.*	2018	Netherlands	Retrospective cross-sectional cohort study	9	Rectal cancer	477	172	305
Baloch *et al.*	2018	Sweden	Retrospective cohort study	8	Rectal cancer, anal cancer and other	89	56	33

** Newcastle-Ottawa Quality Assesment Scale; OP: Omentoplasty a: randomized controlled trial of biomesh versus primary perineal closure, in which omentoplasty was at the discretion of the operating surgeon*

Pooled baseline characteristics of the two groups are demonstrated in Table 2. The indication for APR was predominantly rectal cancer (87.2%). The number of patients receiving neo-adjuvant radiotherapy was 82.5% in the OP group and 74.4% in the non-OP group. Similar proportions of adjacent organ resection were performed (21.4 % versus 18.2%) with slightly less additional reconstructive procedures in the OP group (17.8 % versus 27.5%). Median operative time was median 19 minutes longer for APR with OP, but not significantly different from the non-OP group. Median follow-up duration of the included studies ranged from 12-62 months (overall weighted mean 36.6 months). Supplementary Table 3 (Supplemental Digital Content 3) shows the baseline characteristics and operative details for each of the included studies.

Study endpoints

Supplementary Table 4 (Supplemental Digital Content 4) shows the outcomes for each of the included studies. The main findings of the study are summarized in Table 3. Visual inspection of the funnel plots for the main outcomes of interest did not suggest presence of significant publication bias (Supplementary Figure 1; Supplemental Digital Content 5).

Pre-sacral abscess

Twelve studies recorded the incidence of pre-sacral abscess formation.(4-6, 10, 22-29) The overall weighted mean proportion of pre-sacral abscess formation following OP was 8.7% (95% CI 6.1-12.3%). Considering nine comparative studies(4-6, 10, 22-24, 26, 28), pre-sacral abscesses similarly occurred after OP and non-OP (RR 1.11; 95% CI 0.79-1.56; $I^2 = 0\%$) (Figure 2.A). The risk of pre-sacral abscess was also similar in the predefined subgroup of APR with primary perineal closure for non-locally advanced rectal cancer (RR 1.06; 95% CI 0.68-1.64; $I^2 = 0\%$)(Figure 2.B).(4-6, 23, 24) Similarly, there was no reduced risk of developing

Table 2. Pooled baseline characteristics of study population with (OP) and without omentoplasty (Non-OP)

		All patients (N= 1894)		Non-locally advanced rectal cancer and primary perineal closure (N= 758)*	
		OP (N=839)	Non-OP (N=1055)	OP (N= 281)	Non-OP (N= 477)
Age	Years (Median [IQR])	64.3 [61.9 - 66.6]	64.0 [61.7 - 66.2]	64.9 [62.5 - 67.3]	66.2 [64.2 - 68.1]
Gender	Male	438 (52%)	659 (62%)	204 (73%)	321 (67%)
	Female	280 (33%)	355 (34%)	77 (27%)	156 (33%)
	NR	121 (14%)	178 (17%)	0 (0%)	0 (0%)
Disease	Rectal cancer	693 (83%)	959 (91%)	281 (100%)	477 (100%)
	Anal cancer	99 (12%)	52 (5%)	0 (0%)	0 (0%)
	Other malignant disease	18 (2%)	3 (0%)	0 (0%)	0 (0%)
	NR	29 (3%)	66 (6%)	0 (0%)	0 (0%)
Neoadjuvant therapy	None	104 (12%)	174 (16%)	18 (6%)	50 (10%)
	Short course RTx (25Gy)	93 (11%)	114 (11%)	86 (31%)	168 (35%)
	Long course RTx (40-60Gy)	78 (9%)	34 (3%)	15 (5%)	22 (5%)
	CRTx	319 (38%)	360 (34%)	147 (52%)	220 (46%)
	NR	245 (29%)	373 (35%)	0 (0%)	0 (0%)
Type of resection	APR	594 (71%)	793 (75%)	281 (100%)	477 (100%)
	APR with MVR	154 (18%)	175 (17%)	0 (0%)	0 (0%)
	Total pelvic exenteration	8 (1%)	1 (0%)	0 (0%)	0 (0%)
	NR	83 (10%)	86 (8%)	0 (0%)	0 (0%)
Perineal closure	Primary suturing	690 (82%)	765 (73%)	281 (100%)	477 (100%)
	Muscle flap reconstruction	42 (5%)	127 (12%)	0 (0%)	0 (0%)
	Mesh closure	107 (13%)	163 (15%)	0 (0%)	0 (0%)
	NR	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Follow up time	Months (Median [IQR])	36.6 [24.6 - 48.6]	36.6 [22.7 - 50.5]	37.9 [19.3 - 56.5]	36.8 [19.6 - 53.8]

OP: Omentoplasty; IQR: Interquartile range; NR: Not reported; RTx: Radiotherapy; CRTx: Chemoradiotherapy APR: Abdominoperineal resection; MVR: Multivisceral resection; Percentages might not add up due to rounding

pre-sacral abscesses after OP when only analysing the patients who have been treated with pre-operative radiotherapy (RR 0.94; 95% CI 0.61-1.45; I^2 = 0%).(2, 4, 6, 23, 24)

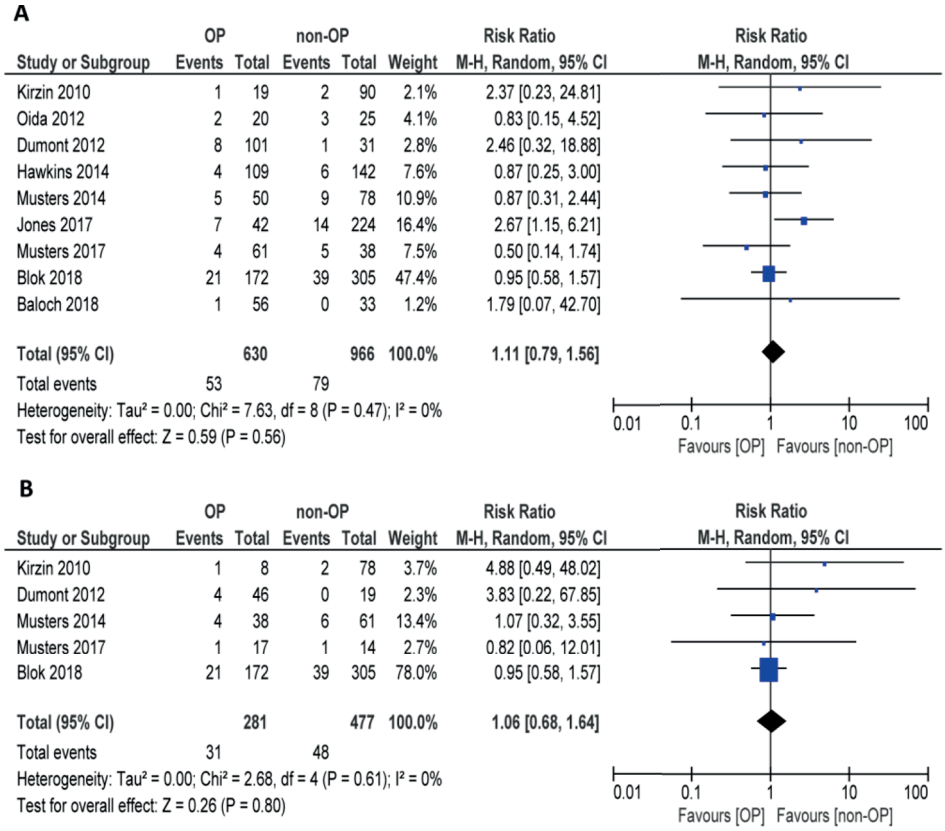

Figure 2. Meta-analyses comparing pre-sacral abscess formation between patients with and without omentoplasty in **A)** all patients who underwent APR for malignancy, and **B)** patients who underwent APR with primary perineal closure for non-locally advanced rectal cancer.

Perineal wound healing

Eight studies recorded the primary perineal wound healing.(2, 4, 24-29) The overall weighted mean cumulative proportion of complicated wound healing at 30 days following OP was 50.6% (95% CI 35.5-65.6%). In five comparative studies(2, 4, 24, 26, 28), the rate of complicated wound healing within 30 days was not significantly different after OP and non-OP (RR 1.30; 95% CI 0.92-1.82; I^2 = 74%). In subgroup analysis of APR with primary perineal closure for non-locally advanced disease, the association of OP with 30-day wound complications remained non-significant (RR 1.28; 95% CI 0.64-2.56; I^2 = 73%).(2, 4, 24) There was no reduced risk of pelviperineal morbidity within one year (RR 1.18; 95% CI 0.80-1.74; I^2 = 80%)(2, 4, 22, 24, 28) or within the total study period (RR 1.09; 95% CI 0.83-1.44; I^2 = 69%)(2, 4, 9, 10, 22-24, 28, 30) for patients submitted to OP.

Time to complete healing was not uniformly reported with regard to patient population (e.g. all patients or only those with dehiscence) and measuring unit (e.g. days or weeks) (Supplementary Table 4; Supplemental Digital Content 4). The included studies demonstrated no significant difference in time to achieve perineal wound healing in terms of mean number of days (MD 24 days in favour of non-OP; 95% CI minus 11 to 59; I^2 = 80%) (23, 24, 26, 30), or the proportion of patients in whom the perineal wound was healed within 3 months (RR 1.01; 95% CI 0.92-1.10; I^2 = 0%).(4, 6, 22, 23)

Table 3. GRADE Summary of findings table of the effects of omentoplasty for filling of the pelvic cavity following abdominoperineal resection

Patient population: Patients who underwent abdominoperineal resection for malignant disease

Intervention: Omentoplasty

Comparison: No omentoplasty

Outcomes	Relative effect	95% CI	I^2	No. of participants (studies)	Quality of the evidence (GRADE)
Complicated wound healing < 30 days	RR 1.30	0.92-1.82	74%	853 (5)	⊕⊕⊕⊕ High
Any complicated wound healing < follow-up	RR 1.09	0.83-1.44	69%	1033 (9)	⊕⊕⊕⊕ High
Superficial perineal infection	RR 0.85	0.45-1.62	78%	1100 (8)	⊕⊕⊕⊖ Moderate
Pre-sacral abscess	RR 1.11	0.79-1.56	0%	1596 (9)	⊕⊕⊕⊕ High
Perineal dehiscence	RR 1.21	0.96-1.53	54%	1621 (9)	⊕⊕⊕⊖ Moderate
Perineal haemorrhage	RR 1.39	0.29-6.58	25%	307 (3)	⊕⊕⊖⊖ Low
Persistent perineal sinus	RR 1.08	0.53-2.20	56%	1370 (8)	⊕⊕⊕⊖ Moderate
Perineal hernia	RR 1.85	1.26-2.72	0%	1584 (9)	⊕⊕⊕⊖ Moderate
Ileus	RR 0.90	0.62-1.31	0%	789 (6)	⊕⊕⊕⊖ Moderate
Reoperation for pelviperineal complication	RR 1.06	0.80-1.42	0%	1401 (9)	⊕⊕⊕⊕ High

GRADE Working Group grades of evidence

High quality: further research is very unlikely to change our confidence in the estimate effect

Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate

Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate

Very low quality: we are very uncertain about the estimate

RR: risk ratio; CI: confidence interval; I2: test for heterogeneity

Specific pelviperineal complications

The pooled proportions of specific pelviperineal complications following OP are demonstrated in Supplementary Figure 2 (Supplemental Digital Content 6). After OP, the overall weighted mean incidence of wound dehiscence was 32.2% (95% CI 22.6-43.5%)(2, 4, 6,

9, 22-24, 26-29), which was 20.0% (95% CI 11.4-32.9%) for superficial perineal infection (2, 4, 9, 10, 23-29), 4.1% (95% CI 1.6-10.5%) for haemorrhage(2, 9, 24), and 8.0% (95% CI 5.1-12.4%) for perineal sinus.(2, 4, 6, 9, 22-24, 28, 29) There were no statistically significant differences among patients with and without OP in terms of perineal wound dehiscence (RR 1.21; 95% CI 0.96-1.53; I^2 = 54%)(2, 4, 6, 9, 22-24, 26, 28), superficial perineal infection (RR 0.85; 95% CI 0.45-1.62; I^2 = 78%)(2, 4, 9, 10, 23, 24, 26, 28), pelviperineal haemorrhage (RR 1.39; 95% CI 0.29-6.58; I^2 = 25%)(2, 9, 24), or chronic perineal sinus (RR 1.08; 95% CI 0.53-2.20; I^2 = 56%)(2, 4, 6, 9, 22-24, 28) (Supplementary Figure 3, Supplemental Digital Content 7).

Ileus

Twelve studies recorded the incidence of ileus.(2, 4, 6, 9, 10, 23-29) In the OP-group, the overall weighted mean proportion of ileus was 7.8% (95% CI 4.2-14.2%)(2, 4, 9, 10, 23-26, 29), and 3.8% (95% CI 2.3-6.2%) required reoperation for ileus.(2, 4, 6, 25, 27-29) Considering eight comparative studies, overall incidence of ileus was not significantly different with or without OP (RR 0.90; 95% CI 0.62-1.31; I^2 = 0%)(2, 4, 9, 23, 24, 26), nor the proportion of ileus requiring reoperation (RR 1.19; 95% CI 0.58-2.44; I^2 = 0%). (2, 4, 6, 28)

Perineal hernia

Twelve studies evaluated the incidence of perineal hernia.(2, 4, 6, 9, 22, 24-30) The overall weighted mean proportion of perineal hernia was 8.9% (95% CI 5.7-13.7%) in those undergoing OP. Nine comparative studies recorded the incidence of perineal hernia.(2, 4, 6, 9, 22, 24, 26, 28, 30) The risk of perineal hernia was significantly increased in those submitted to OP compared to non-OP (RR 1.85; 95% CI 1.26-2.72; I^2 = 0%)(Figure 3.A). This association remained similar in those who underwent APR with primary perineal closure for non-locally advanced disease (RR 1.83; 95% CI 1.17-2.87; I^2 = 0%)(Figure 3.B).(2, 4, 6, 24)

Omental flap complications

Among eight studies, the weighted mean proportion of OP-related complications was 4.6% (95% CI 2.5-8.6%).(2, 4, 9, 10, 25, 27-29) Specific complications of the OP included signs of inflammation of the omentum (n=1), partial omental necrosis (n=1), total omental infarction (n=1), perineal dehiscence with omental protrusion due to necrosis of the OP (n=4), haemorrhagic shock due to bleeding of the gastro-epiploic artery (n=1) and internal herniation of small bowel underneath the OP (n=1).

Surgical re-intervention

In twelve studies on OP, the overall weighted mean proportion of pelviperineal complications necessitating surgery (including hernia repair) was 12.6% (95% CI 9.0-17.4%)(2, 4,

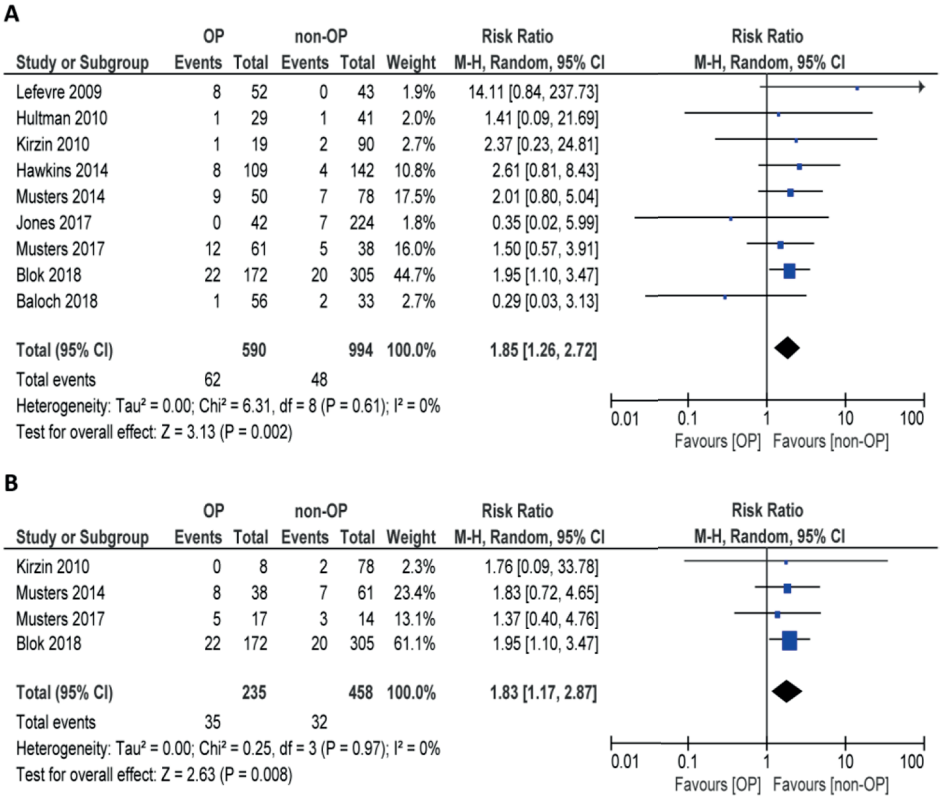

Figure 3. Meta-analyses comparing perineal hernia development between patients with and without omentoplasty in **A)** all patients who underwent APR for malignancy, and **B)** patients who underwent APR with primary perineal closure for non-locally advanced rectal cancer.

6, 9, 10, 22, 23, 25, 27-30), without significant difference between OP and non-OP (RR 1.06; 95% CI 0.80-1.42; I^2 = 0%).(2, 4, 6, 9, 10, 22, 23, 28, 30) Hernia repair tended to be more frequent in the OP group (RR 1.71; 95% CI 0.87-3.35; I^2 = 0%).(2, 4, 6, 28) Problems related to the OP itself were reason for reoperation in 3.8% (95% CI 1.9-7.6%). (2, 4, 9, 25, 27, 28)

DISCUSSION

In the current literature review with mainly source patient data, we found no evidence to suggest that OP reduces pelviperineal abscess formation, nor that OP enhances perineal wound healing considering any other endpoint, or that OP reduces the risk of small bowel obstruction. Similarly, no beneficial effect of OP was found in planned subgroup analysis of patients that underwent APR with primary perineal closure for non-locally advanced can-

cer, thereby likely reducing the risk of allocation bias. Furthermore, OP itself is associated with a small risk of complications and appears to be associated with perineal herniation.

The absence of any beneficial effects of OP as found in the present meta-analysis is in contrast to literature on autologous tissue flaps for perineal wound closure following APR.(11, 43) In particular, the use of a VRAM flap is well established.(8, 30, 44) However, studies directly comparing muscle flaps and OP are scarce. A retrospective single institutional study by Lefevre et al.(30) which was included in the present review – found that VRAM flap closure was associated with less perineal morbidity, reduced healing time and no perineal herniation (0% vs 15.4%; P=0.0072) if compared to primary layered closure with OP. There are several potential explanations as to why OP is not associated with such favourable outcomes. Probably, the omentum is more likely to leave residual dead space, especially with thin patients. Furthermore, OP might have less robust blood supply after full mobilization, and compromised perfusion of an OP is sometimes difficult to recognize intra-operatively. An OP with partial necrosis of the most distal parts, which are subsequently placed in the perineal wound, will likely counterbalance any beneficial effect in other patients. But in our opinion, the most crucial difference between OP and VRAM flap reconstruction is the filling of anal dead space. The muscle, fascia, subcutaneous fat and skin of a VRAM flap are perfectly suited for reconstruction of the pelvic floor and perineal defect, while an OP only consists of loose fatty tissue that does not provide any strength. OP mainly fills the pre-sacral space, but the excised anal canal and sphincter complex seems to be the critical wound bed. The small bowel can fill the pre-sacral space in the absence of an OP, as will occur after VRAM flap reconstruction.

Incidence of perineal hernia was around 10%, and is likely to even be an underestimation of the true incidence because of the retrospective design of most included studies. In meta-analysis, perineal hernia correlated significantly with the use of OP. This finding has recently been demonstrated in a nationwide study(6), but was felt to be counterintuitive by some surgeons, and probably best explained by wider resections in the OP-group. But this phenomenon may also be explained by the properties of an OP. As previously mentioned, the fatty and non-fibrous omentum is not providing any strength to the neo-pelvic floor, and even puts continuous pressure on the perineal skin in a standing position. It is understandable that, in case of a bulky OP with a long vascular pedicle, such redundant bulk of fat is more likely to descend below the level of the pelvic floor than a few loops of small bowel that are often restricted by a certain mesenteric length. The omental fat is certainly more likely to result in perineal bulging than VRAM flap closure where muscle and fascia is added to the neo-pelvic floor.(30)

Two systematic reviews on the value of OP after APR have been published previously, both in contradiction with the current meta-analysis.(45, 46) Compared to the review of Nilsson et al.(46), only one study(29) is overlapping, and only three(9, 10, 29) out of 14 studies are overlapping with the review by Killeen et al.(45) Most of the older studies that were included in both previous reviews, concern a small sample size and diversity regarding patient population and surgical methods, with only few comparative series. In addition, the rather historical studies have restricted generalizability, especially considering the less frequent use of pre-operative radiotherapy. Strengths of the current review are restricted inclusion of publication since 2000, more comparative studies, and the use of primary source patient data, even if the original publication was not intended to study the effect of OP. Furthermore, benign pathology such as IBD was excluded, in contrast to the previous reviews. This resulted in more homogeneous patient populations with higher internal and external validity than previous systematic reviews published on the subject.(45, 46) These methodological issues may explain the contradictory findings.

The main limitation of our study is the potential for a certain degree of allocation bias. In the absence of randomized controlled trials, it could be that surgeons selectively applied OP in those with a larger empty space after resection, and therefore an a priori greater risk of wound complications and hernia. To reduce potential confounding, a subgroup analysis was performed by excluding extended resections and additional reconstructive procedures. Even then, however, the potential for allocation bias cannot be excluded. A second limitation is that the definition of outcome variables in the source studies may be variable. In particular, the lack of a clear definition for pre-sacral abscess and perineal hernia (i.e. symptomatic perineal bulge or asymptomatic radiological finding) could potentially have influenced our results. However, reporting of perineal hernia was predominantly based on retrospective analysis of patient records, most likely not including small and asymptomatic radiological hernias . Also, total number of events were used for meta-analysis of perineal hernia, not properly taking into account the development of perineal hernia over time and differences among studies regarding duration of follow-up.

Based on the available literature, OP does not seem indicated for decreasing perineal wound complications after APR for cancer, nor does biological mesh closure.(4) Tissue transfer seems to have the greatest potential, but high quality studies comparing muscle flap closure to other methods of perineal wound closure are warranted. Although VRAM flap closure has been effectively used in selective populations(8), there remains the issue of donor and recipient site morbidity.(43, 47) A smaller flap without donor site problems such as the perineal turnover flap(48) seems attractive. We are currently evaluating the effectiveness of a modified gluteal turnover flap(49) for routine use after APR, and we

consider larger fascio-cutaneous gluteal or VRAM flaps only for the wider perineal defects with a high risk of sinus formation.

Conclusions

In this systematic review and meta-analysis, that is reflecting current surgical practice of patients who are submitted to APR for malignant disease, we found no evidence to support the use of an OP for reducing pelviperineal morbidity. Additionally, use of OP has an added risk of OP associated complications, and seems to be associated with the long-term likelihood of developing perineal hernia.

Acknowledgement

The authors would like to thank Faridi S. van Etten (clinical librarian) for her help with developing the search strategy. We also appreciate the assistance of Susan van Dieren (clinical epidemiologist), who aided in the statistics of the study. Further, the authors greatly appreciate the efforts of multiple authors who provided additional information and discussed their data with us.

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LIST OF SUPPLEMENTAL DIGITAL CONTENT

Supplemental Digital Content 1.docx; Supplementary Table 1. Electronic search strategy in the PUBMED-library.
Supplemental Digital Content 2.docx; Supplementary Table 2. Quality assessment of the included studies by the Newcastle Ottawa Scale.
Supplemental Digital Content 3.docx; Supplementary Table 3. Baseline characteristics and operative details for each of the included studies.
Supplemental Digital Content 4.docx; Supplementary Table 4. Outcomes for each of the included studies.
Supplemental Digital Content 5.docx; Supplementary Figure 1. Funnel plot analyses for the detection of publication bias.
Supplemental Digital Content 6.docx; Supplementary Figure 2. Pooled proportions of the outcome measures in the presence of an omentoplasty.
Supplemental Digital Content 7.docx; Supplementary Figure 3. Meta-analyses of pelviperineal morbidity and ileus comparing patients with and without omentoplasty in all patients and in a subgroup of patients who underwent APR with primary perineal closure for non-locally advanced rectal cancer.