International Journal of Surgery 11 (2013) 514–517

Contents lists available at SciVerse ScienceDirect

International Journal of Surgery

journal homepage: www.theijs.com

Review

How should perineal wounds be closed following abdominoperineal resection in patients post radiotherapy – Primary closure or flap repair? Best evidence topic (BET)

A.M. Howell, O.A. Jarral, O. Faiz, P. Ziprin, A. Darzi, E. Zacharakis*

Department of Surgery and Cancer, Imperial College London, United Kingdom

ARTICLE INFO

Article history:
Received 10 February 2012
Received in revised form
3 April 2013
Accepted 14 May 2013
Available online 21 May 2013

Keywords:
Abdominoperineal resection
Rectal neoplasm
Anal neoplasm
Myocutaneous flap
Perineal wound healing

ABSTRACT

This best evidence topic was investigated according to a described protocol. The question posed was: should the irradiated perineal wound following abdominoperineal resection (APR) be closed with primary repair or a myocutaneous flap. Using the reported search 364 papers were found of which eight represented the best evidence to answer the clinical question. The conclusion drawn is that there is some limited evidence for recommending flap closure in abdominoperineal resection post radiotherapy. The best evidence available was from a systematic review of cohort studies and case series. Although no meta-analysis was performed, overall wound healing was improved using flap closure with a low frequency of flap necrosis. Other studies providing evidence were case–control series or cohort studies. Three papers prospectively compared vertical rectus abdominus muscle (VRAM) flap with primary closure; two of which demonstrated statistically significant improvement in complication rates with flap closure. Two retrospective case control series showed significant improvement in major wound complication rates in the flap group. Two studies retrospectively compared gracilis flap repair with primary closure and showed significantly lower incidence of major perineal complications.

Most studies suffered from significant limitations, small sample sizes and no direct comparisons between matched groups with respect to type of anatomic flap, wound size, tumour recurrence or radiation dose. Whilst there is evidence that myocutaneous flap closure following APR in radiotherapy patients can reduce wound related complications, prospective randomized controlled trials are warranted.

1. Introduction

This best evidence topic was generated according to the structure outlined in the International Journal of Surgery.[1]

2. Clinical scenario

At a regional cancer multi-disciplinary team meeting a colleague suggests that your irradiated patients undergoing abdomino-perineal resection (APR) would have better post-operative wound healing if myocutaneous flap repair was used instead of primary closure. You decide to assess the evidence base for this assertion.

3. Three-part question

In [patients undergoing APR with pre-operative radiotherapy], is [flap repair] or [primary closure] superior in terms of [wound healing].

4. Search strategy

Evidence was searched for using Medline (Pubmed) (1946–12 January 2012): Using the MESH search: ("Perineum"[Mesh]) AND "Surgical Flaps"[Mesh]. The papers were limited to English language and humans. Reference lists were searched for additional relevant research.

5. Search outcome

341 papers were extracted. 108 papers related to other surgical specialties and 179 were comments, case reports, case series or

* Corresponding author. Tel.: +44 2078866666; fax: +44 2078867950.
E-mail addresses: manoszacharakis@hotmail.com, e.zacharakis@imperial.ac.uk (E. Zacharakis).

1743-9191/$ – see front matter © 2013 Surgical Associates Ltd. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ijsu.2013.05.004

technical reviews and therefore excluded. 46 papers concerned either benign colorectal cases or solutions for wound closure other than myocutaneous flaps. Papers were excluded, if they did not directly compare primary closure with myocutaneous flap closure.[10,11,12]

6. Results

Eight studies provided the highest level of evidence to answer the question. These are shown in Table 1.

7. Discussion

Nisar et al.[2] performed a systematic literature search of peer-reviewed journals in English relating to anal or rectal oncological resections and myocutaneous flaps. 36 studies of various methodologies were identified. Five case-controlled studies were identified relating to vertical rectus abdominus muscle (VRAM) flaps. Two case controlled studies were shown using gracilis flaps. The review also included case series using gluteus maximus flaps. The review was comprehensive but limited by the calibre of studies available at the time of the search. No meta-analysis was performed and the oncological outcome was not reported. Case series as well as cohort and case-controls were included. 7 out of 300 patients suffered total flap loss after VRAM reconstruction and 8 out of 83 suffered cutaneous necrosis in the gracilis reconstruction group. However where the groups were controlled, improved overall wound outcomes were shown for flap repair.

Chan et al.[3] undertook a prospective controlled cohort study comparing 21 patients undergoing abdominoperineal excision for malignancy who had primary closure with 30 patients who had a myocutaneous flap repair (24 VRAM, 6 gracilis). The study was limited in that patients were placed in either group depending on surgeons' preference and therefore there were a higher proportion of patients receiving pre operative chemo-radiotherapy and a greater number of recurrent cancers in the flap group ($p = 0.011$). The study included patients undergoing total pelvic exenteration and abdominosacral resection. The study showed no major perineal complications in either group for unirradiated patients. The flap group had a lower overall rate of perineal complications however there was a higher rate of major complications requiring reoperation in the flap group with a 17% flap necrosis rate. Flap repair had a non-statistically significant shorter length of stay. Small sample size, lack of power calculation and the inclusion of non-irradiated patients in the control group limit this study.

Chessin et al.[4] conducted a prospective cohort study of 19 post radiotherapy APR patients who underwent VRAM flap repair and compared them to 59 patients who had primary closure in a historical control group. The groups were matched with respect to tumour stage. The primary end point was wound healing. The study showed significantly lower rates of perineal wound healing in the flap group compared with the primary closure group with comparable rates of general complications and complications related to the abdominal wound. In addition all wound complications in the flap group were minor. Limitations of the study include the bias related to using a historical control group. In addition patients in the VRAM flap group had increased factors associated with poor healing including lower tumour site and operation for tumour recurrence, however this may actually further support the use of VRAM flap for high risk patients.

Butler et al.[5] retrospectively reviewed a case series of all patients undergoing APR during a 12-year period and directly compared VRAM flap repair (35) with primary closure (76). Both groups were well matched in terms of patient characteristics and tumour stage but there were more recurrent tumours and anal SCC in the flap group. The study showed no difference between flap and primary closure for minor complications including perineal hernia, but showed significantly higher rates of severe complications in the primary closure group. One patient had complete flap necrosis, which was reconstructed with gracilis flaps. Abdominal wall complications were comparable. No oncological outcomes were reported.

Radice et al.[6] studied 95 patients over a 6-year period who underwent APR and radiotherapy for locally advanced or recurrent anorectal cancer. Patients were divided into three groups; primary closure (20), primary closure with pedicle omental graft (24) or immediate myocutaneous flap closure (13). Patients in the flap group had fewer wound complications, so much so that the author's practice was modified to selectively increase the number of flaps for high dose radiation wounds. 8 patients in the primary closure groups went on to have conversion to flap repair. The study was not powered for statistical significance and patients groups were not matched.

Shibata et al.[7] retrospectively reviewed 16 patients undergoing APR post irradiation for recurrent rectal carcinoma who had gracilis flap closure of the perineum. The wound outcomes were compared to 24 patients over a similar time period undergoing primary closure of the perineal wound for similar indications. Patient characteristics were comparable, however the flap group received statistically higher doses of radiation. Despite being higher risk-patients in the flap group had statistically lower incidence of major complications, defined as major abscesses requiring reoperation. Risk of minor complications such as persistent perineal sinus tracts and subcutaneous abscesses were comparable. Limitations of the study include short follow up- only 6 months with no comment on abdominal wound complications or perineal herniation.

Persichetti et al.[8] conducted a comprehensive study of 10 patients undergoing APR post neoadjuvant radiotherapy with gracilis muscle flap closure between 200 and 2005. This case series was compared to 25 patients who underwent primary repair at an earlier time 1997–2001, however all resections were performed by the same surgical team. The patients' postoperative complications were reviewed as well as objective markers of sepsis and blood loss. Blood loss between the two groups was comparable as were minor wound dehiscence, perineal hernias and seromas. Major complications requiring re-operation or persistent infection were statistically higher in the primary closure group.

Lefevre et al.[9] retrospectively compared 95 patients who underwent APR for anal squamous cell carcinoma most of who were post radio-chemotherapy and who had either VRAM flap or primary closure with omentoplasty. Flap closure patients were younger, and had more advanced cancer (ypT3-T4 67.6% vs. 38.4%). Perineal complications were significantly reduced in the VRAM group. Perineal wound dehiscence occurred in the primary closure group (11.5%) vs. 0 in the VRAM group ($p = 0.0214$). The rate of positive surgical margins was higher in the flap group but not statistically significant (26.1% vs.11.5%). 2 patients died within 2/12 post operatively in the VRAM flap group, one due to perineal sepsis. Long-term survival in the 2 groups was equivalent despite the more advanced stage of the VRAM group.

The level of evidence supporting myocutaneous flap repair of perineum for irradiated patients undergoing APR is consistent. However all studies have small sample sizes and with distinct differences between the flap and primary closure groups. For all study populations there were a greater number of recurrent cancer cases in the flap group, which will therefore most likely require more radical excision, which introduces bias when it comes to assessing wound healing outcomes. In fact these studies show surgeons practicing flap repair preferentially for higher risk patients. Not all studies included data on resection margins, or on

Table 1
Papers demonstrating best evidence.

Author, date and country of research	Patient group (APR = Abdominoperineal resection)	Study type and level of evidence	Outcomes	Key results	Comments
Nisar PJ et al.[2] 2008 UK	36 Trials; including 13 studies comparing primary closure to flaps. Combined VRAM flap closure = 300. Gracilis = 83.	Systematic review of cohort studies. Level IIA	Perineal wound outcomes including flap necrosis.	No meta-analysis performed. 7/300 flap necrosis (VRAM). 8/83 flap necrosis (gracilis).	Showed consistency in literature for improved perineal healing rates for myocutaneous flaps for studies that compared flaps with controls. Case series and comparisons of different types of flap with no controls were also included.
Chan S et al.[3] 2010 UK	51 patients undergoing APR. Primary closure = 21. Flap closure = 30 (24 VRAM, 6 Gracilis).	Prospective cohort study. Level IIIB	Major perineal wound complications requiring reoperation. Length of stay. Flap necrosis.	Flap = 17%, Primary closure = 14% ($p = 0.65$). Flap = 20 days, Primary closure = 15 days ($p = 0.36$). 17%	Two groups not standardised with respect to radiotherapy, therefore greater proportion of irradiated patients in flap group cf with primary closure group, presumably due to surgeon's bias.
Chessin DB et al.[4] 2005 USA	78 patients undergoing APR post radiotherapy. Primary closure = 59. Flap closure = 19 (VRAM).	Prospective cohort study. Level IIIB.	Perineal wound complications. Other complications including abdominal wall.	Flap 15.8%, Primary closure 44.1% ($p = 0.03$). Flap 42.1%, Primary closure 42.2% ($p = 0.8$).	Greater number of patients with anal squamous tumours, vaginectomy and recurrence in the flap group. However overall showed better outcomes for flaps.
Butler CE et al.[5] 2008 USA	111 patients undergoing APR post radiotherapy. Primary closure = 76, flap closure = 35 (VRAM).	Retrospective Case-control series. Level IV.	Major complications (perineal wound/flap dehiscence) Minor complications (Perineal/pelvic fluid collection requiring drainage). Perineal abscess. Abdominal wall complication.	Flap 9%, primary 30% ($p = 0.014$). Flap 3%, primary 25% ($p = 0.03$). Flap 9%, primary 37% ($p = 0.002$). No significant difference between two groups.	This retrospective study showed superiority of flap vs. primary closure in patients post radiation, with a statistically significant decrease in severe wound complications and no difference in long term abdominal wall complications (mean follow up 3.8 years).
Radice E et al.[6] 1999 USA	57 patients undergoing APR. Primary closure = 20. Primary closure and omental pelvic graft = 24. Flap closure = 13.	Prospective case–control series. Level IV.	Major complications (requiring reoperation). Acute (30 day) wound complications. Delayed wound healing.	Flap = 0%, Primary closure = 15%, omental graft 21%. Flap = 15% Primary closure = 35%, with omental graft 37%. Flap = 8%, primary closure = 15%, omental graft = 25%.	Groups not standardised with respect to tumour recurrence, with flap group having more radical surgery and chemo irradiation.
Shibata D et al.[7] 1999 USA	40 patients underwent APR Primary closure = 24. Flap closure = 16 (Gracilis).	Case-control series. Retrospective. Level IV.	Major complications (infection requiring readmission/reoperation). Minor complications (sinus, subcutaneous abscess).	Flap = 12%, primary closure = 46%; ($p = 0.028$). Flap = 25%, primary closure = 21%.	This retrospective study showed a possible advantage of gracilis flap over primary closure however radiotherapy dose not standardised.
Persichetti P et al.[8] 2007 Italy	35 patients undergoing APR. Primary closure = 25. Flap closure = 10 (gracilis).	Case control series retrospective study. Level IV.	Major complications (requiring reoperation). Mild – moderate complications (seroma, dehiscence, delayed healing). Length of stay.	Flap = 0, primary closure = 10 ($p = 0.03339$). No statistical difference between the two groups. No statistical difference.	This study focused on immediate and short-term postoperative outcomes. Used objective measures of sepsis: leukocyte count and temperature.
Lefevre JH et al.[9] 2009 France	95 patients underwent APR for anal cancer. Primary closure with omentoplasty = 27. Flap closure = 42(VRAM).	Case-control series. Retrospective. Level; IV.	Mortality. Major complication (requiring re-operation). Perineal dehiscence. Minor wound complications. 5 year survival. Disease free survival.	Flap = 2 (2.1%), primary closure = 0 ($p = 0.116$). Flap = 25.6%, primary closure = 17.3%, ($p = 0.3248$). Flap = 0%, primary closure = 11.5% ($p = 0.0214$). Flap = 26.8%, primary closure = 44.2% ($p = 0.097$). Flap = 58.1%, primary closure = 54.4% ($p = 0.6756$). Flap = 41.1%, primary closure = 48.9% ($p = 0.2756$).	Retrospective case–control series. 92% patients received pre-operative radiotherapy. Patients receiving flaps were younger with greater tumour stage and more likely to have had radiotherapy.

survival; which particularly for anal cancer salvage surgery, needs to be commented upon.[13]

Another question that these studies do not specifically address is how best to close the perineal wound after performing a cylindrical excision or extra-levator abdomino-perineal excision (ELAPE) in radical anorectal tumour surgery. One study suggested that this procedure produces better oncological outcomes for low rectal tumours however it was associated with increased perineal wound complications, compared to standard APR. This may be overcome with the use of myocutaneous flap closure.[14] New evidence is emerging about the benefits of using biological mesh reconstruction in order to augment closure and prevent perineal herniation post APR.[15,16] There is also work showing the superiority of omental flap closure.[12]

Randomised controlled trials to assess the benefits of flap closure are required. Patients should be stratified according to whether they underwent APR, versus ELAPE versus extended ELAPE. Primary closure versus myocutaneous flap repair and mesh repair compared to omental flap repair needs to be examined, with matched control groups with respect to tumour stage and radiotherapy regimes.

8. Clinical bottom line

With the limited evidence demonstrated thus far; myocutaneous flaps can be suggested for irradiated perineal defects; however which flap is superior and whether there is a role for flap repairs in non-irradiated or low risk patient groups can not be determined. The level of evidence is not high enough to demand a change in practice.

Ethical approval

Review paper (Best Evidence Topic) and therefore no ethical approval required.

Funding

No funding required or supplied.

Author contribution

AM Howell: data collection, analysis and write up: main author.
OA Jarral: data collection, manuscript editing.
O Faiz: manuscript editing, direction of investigation.
P Ziprin: manuscript editing, direction of investigation.
A Darzi: manuscript review and supervision.
E Zacharakis: study design, manuscript review and supervision.

Conflict of interest

None.

References

1. Khan OA, Dunning J, Parvaiz AC, Agha R, Rosin D, Mackway-Jones K. Towards evidence-based medicine in surgical practice: best BETs. *International Journal of Surgery* 2011;**9**:585–8.
2. Nisar PJ, Scott HJ. Myocutaneous flap reconstruction of the pelvis after abdominoperineal excision. *Colorectal Disease* 2009;**11**:806–16.
3. Chan S, Miller M, Ng R, et al. Use of myocutaneous flaps for perineal closure following abdominoperineal excision of the rectum for adenocarcinoma. *Colorectal Disease* 2010;**12**:555–60.
4. Chessin DB, Hartley J, Cohen AM, et al. Rectus flap reconstruction decreases perineal wound complications after pelvic chemoradiation and surgery: a cohort study. *Annals of Surgical Oncology* 2005;**12**:104–10.
5. Butler CE, Gundeslioglu AO, Rodriguez-Bigas MA. Outcomes of immediate vertical rectus abdominis myocutaneous flap reconstruction for irradiated abdominoperineal resection defects. *Journal of the American College of Surgeons* 2008;**206**:694–703.
6. Radice E, Nelson H, Mercill S, Farouk R, Petty P, Gunderson L. Primary myocutaneous flap closure following resection of locally advanced pelvic malignancies. *British Journal of Surgery* 1999;**86**:349–54.
7. Shibata D, Hyland W, Busse P, et al. Immediate reconstruction of the perineal wound with gracilis muscle flaps following abdominoperineal resection and intraoperative radiation therapy for recurrent carcinoma of the rectum. *Annals of Surgical Oncology* 1999;**6**:33–7.
8. Persichetti P, Cogliandro A, Marangi GF, et al. Pelvic and perineal reconstruction following abdominoperineal resection: the role of gracilis flap. *Annals of Plastic Surgery* 2007;**59**:168–72.
9. Lefevre JH, Parc Y, Kerneis S, et al. Abdomino-perineal resection for anal cancer: impact of a vertical rectus abdominis myocutaneus flap on survival, recurrence, morbidity, and wound healing. *Annals of Surgery* 2009;**250**:707–11.
10. Ferenschild FT, Vermaas M, Hofer SO, Verhoef C, Eggermont AM, de Wilt JH. Salvage abdominoperineal resection and perineal wound healing in local recurrent or persistent anal cancer. *World Journal of Surgery* 2005;**29**:1452–7.
11. Tei TM, Stolzenburg T, Buntzen S, Laurberg S, Kjeldsen H. Use of transpelvic rectus abdominis musculocutaneous flap for anal cancer salvage surgery. *British Journal of Surgery* 2003;**90**:575–80.
12. Hultman CS, Sherrill MA, Halvorson EG, et al. Utility of the omentum in pelvic floor reconstruction following resection of anorectal malignancy: patient selection, technical caveats, and clinical outcomes. *Annals of Plastic Surgery* 2010;**64**:559–62.
13. Sunesen KG, Buntzen S, Tei T, Lindegaard JC, Norgaard M, Laurberg S. Perineal healing and survival after anal cancer salvage surgery: 10-year experience with primary perineal reconstruction using the vertical rectus abdominis myocutaneous (VRAM) flap. *Annals of Surgical Oncology* 2009;**16**:68–77.
14. West NP, Anderin C, Smith KJ, Holm T, Quirke P. Multicentre experience with extralevator abdominoperineal excision for low rectal cancer. *British Journal of Surgery* 2010;**97**:588–99.
15. Martijnse IS, Holman F, Nieuwenhuijzen GA, Rutten HJ, Nienhuijs SW. Perineal hernia repair after abdominoperineal rectal excision. *Diseases of the Colon and Rectum* 2012;**55**:90–5.
16. Christensen HK, Nerstrom P, Tei T, Laurberg S. Perineal repair after extralevator abdominoperineal excision for low rectal cancer. *Diseases of the Colon and Rectum* 2011;**54**:717–27.