Prevention and Management of Nonhealing Perineal Wounds

Allen Kamrava, MD, MBA¹ Najjia N. Mahmoud, MD²

Address for correspondence Allen Kamrava, MD, MBA, LA Colon and Rectal Surgical Associates, 9400 Brighton Way, Suite 307, Beverly Hills, CA 90210 (e-mail: Allen.Kamrava@gmail.com).

Clin Colon Rectal Surg 2013;26:106-111.

Abstract

Keywords

- proctectomy
- ► Crohn perineum
- ► perineal wound
- surgical site infection

Complex perineal wounds are at risk for nonhealing. High-risk procedures include proctectomy for Crohn disease, anal cancer and radiated distal rectal cancers. A basic understanding of both patient and procedural risk factors is helpful in planning and executing operative procedures for these conditions and to minimize associated wound complications. Diabetes, obesity, and malnutrition may contribute to wound breakdown and failure to heal. Delaying operative intervention, adding nutritional supplementation, and employing intestinal diversion as well as myocutaneous flaps may help optimize conditions for wound healing.

Objectives: Upon completion of this article in the setting of Crohn disease, the reader should be able (1) to describe factors that increase the risk for postoperative perineal wound complications, (2) to discuss preoperative strategies aimed at minimizing the risk for postoperative perineal wound complications, and (3) to evaluate and manage postoperative perineal wound complications.

The treatment of complex perineal wounds starts with a good understanding of the etiology. Any perineal wound can harbor sepsis, subsequently dehisce, and become a chronic, long-term problem. Certain diseases and procedures are far more likely to result in wound infection and/or delayed wound healing, and a specific knowledge of this is important and necessary. Increased risk for perineal wound breakdown is typically due to either high-risk procedures that are associated with an increased risk of breakdown or patient comorbidities that potentiate these risks. Conditions involving high-risk perineal wounds include total proctectomy for Crohn disease (CD), total proctectomy for recurrent or residual anal cancer, and abdominoperineal resection after neoadjuvant chemoradiation for advanced distal rectal cancer. Risk of surgical site infection and nonhealing following these procedures is high, and patient comorbidities such as diabetes, obesity, and malnutrition seem to worsen outcomes. In this chapter, we will serve to discuss common causes of perineal wound complications as well as specific strategies for treatment and prevention. 1-5

Total proctectomy is performed appropriately for a variety of conditions, including severe, refractory anorectal CD unresponsive to medical management, as well as radiated anal and distal rectal cancers. Although the basic procedure (proctectomy with excision of surrounding anal margin dermis and epidermis) is common to all of these conditions, there are special considerations and circumstances that distinguish each of these.

The Perineal Wound

The perineal wound resulting from an abdominoperineal resection (APR) has always been considered troublesome. Miles' original description of the treatment of the perineal incision involved leaving it open to heal by secondary intention, a strategy resulting in a long-term chronic wound. Modern use of chemotherapy and postoperative radiation called for more reliable closure of the perineum to expedite post operative care. However, even when primary closure is instituted, high rates of both wound infection (11–16%) and delayed wound healing can be apparent. A recent study from the University of Pennsylvania examined the effect of surgical technique on perineal wound infection rates. In this study, 150 patients undergoing APR for both inflammatory

¹LA Colon and Rectal Surgical Associates, Beverly Hills, California

² Department of Surgery, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania

bowel disease (IBD) and cancer were evaluated. The overall rate of major wound infection was 30%. Lithotomy position for perineal dissection was found to be major risk factors for major perineal wound complications. Those patients who were turned to the prone position for perineal dissection and closure had a wound infection rate of 11 versus 36% for those dissected in the lithotomy position (p < 0.005). In this study, a statistically significant increase in perineal wound infection was also seen in patients treated with neoadjuvant radiation therapy (p = 0.027), those undergoing surgery for IBD (p = 0.018), and in cases with blood loss > 600 mL (p = 0.032). These results are similar to those in a large study of over 600 patients at the Cleveland Clinic where the total rate of nonhealing was 16.2%. Obesity, neoadjuvant chemoradiation, and intraoperative bleeding were all found to significantly elevate risk of perineal wound infection in this review.

Proctectomy in the setting of CD represents the highest risk of perineal wound infection across all indications. Patients are often ill and malnourished, and markedly immunosuppressed. Complex fistulizing disease can make wide margins necessary. Primary closure is typically difficult, if not impossible.

Tissue flap reconstruction is often necessary both for wound healing and tissue coverage. The goal of flap reconstruction is to use a nonirradiated, well-vascularized tissue to bridge a large defect. Data regarding use of myocutaneous flaps in the reconstruction of perineal wounds to aid healing and prevent wound complications are mostly retrospective. It is unclear that universal and consistent application of these techniques is necessary. However, in certain instances, selective use of flap reconstruction can be beneficial; preoperative determination of those wounds best managed with flap closure is essential to minimizing postoperative wound complications.

Risk factors that may make flap reconstruction a better choice include large defect size, reirradiated anal cancers, presence of infected tissue, need for exenteration, procedures that include partial vaginectomy, and patient conditions that increase risk for wound infection and primary nonhealing, such as malnutrition and prolonged immunosuppression. The use of neoadjuvant chemotherapy in an otherwise healthy patient is not a clear indication for use of flap closure if blood loss is low, good apposition of tissue is possible (prone positioning), and sepsis is nonexistent.

Flap choices most commonly include vertical rectus abdominis myocutaneous (VRAM), gracilis, and gluteal flaps. The choice of flap is partially dependent upon surgeon experience, patient positioning, and tissue defect. VRAM flaps have the most reliable blood supply and the advantage of the potential for a stable skin pedicle that can make large defect or vaginal reconstruction easier and tension free. The skin pedicle works well for posterior vaginal wall reconstruction and forms a stable "bridge" in those with large central or asymmetric perineal tissue losses. In a study of 18 patients who underwent VRAM following APR for recurrent anal cancer, four were treated with immediate reconstruction and healed uneventfully. The remaining 14 patients were closed primarily with major wound complications in five. ¹⁰ In another review, five of

eight patients operated upon for anal cancer with primary closure developed serious wound complications while 14 with VRAM closure had uneventful recoveries.¹¹

Gracilis flap closure is a good strategy for smaller wounds or wounds where VRAM flap coverage is unavailable (the patient has or needs bilateral ostomies, or has had multiple abdominal operations in the past). Although the muscle alone is typically used, a thigh skin pedicle can be harvested if needed. It suffers from a less-reliable blood supply and results in greater rates of tissue loss postoperatively. Even so, Shibata showed that use of gracilis flap closure resulted in a 50% reduction in the rate of wound failure following proctectomy for the treatment of recurrent rectal cancer. ¹²

Data regarding the use of gluteal advancement flaps is not as robust. These flaps can be used successfully in the closure of large tissue defects created by cylindrical APR.¹³ In a series reported by Baird, 15 of 16 patients achieved wound healing using this technique, though 7 patients did require local revision or ongoing local wound care to achieve complete healing.¹⁴

Numerous studies have evaluated the outcomes of primary closure of the perineal wound versus secondary delayed closure. Most reviews conclude that primary closure is significantly superior to secondary closure. 15–19 More rapid wound healing for resumption of oncologic care, improved quality of life, and less need for prolonged nursing assistance/wound care make primary closure a better choice. A prospective randomized trial that compared primary versus secondary closure techniques demonstrated a significant improvement in wound healing in the initial 3 postoperative months with primary closure of any type. 20 Although perineal wound infections were also higher in the primary closure group, they were generally under 20%.

Clearly, wound infection and nonhealing in proctectomy is multifactorial. Knowledge of risks and mitigation of risk factors play a very important role in the anticipation, prevention, and treatment of this complication. Myocutaneous flaps may be used selectively in those patients with risk factors for perineal wound dehiscence.

Operative Planning

It is estimated that \sim 14% of patients with CD will ultimately require proctectomy 12 for failure of both medical management and local surgical therapy. A complete proctectomy needs to be carefully timed and planned in these individuals who may be malnourished and immunosuppressed. Early studies demonstrated wound failure rates between 36.8 and 78.9%. $^{21-23}$ A more recent study by Yamamoto et al reported a 23% rate of failure for primary closure after proctectomy in the setting of CD. 24 These wounds pose an impressive challenge that often requires several treatment strategies based on patient factors to allow for successful healing. There are typically two scenarios that lead to proctectomy: fulminant or toxic colitis with extensive rectal involvement and refractory perianal sepsis with fistulization and anal stenosis. These conditions require different approaches.

A subtotal colectomy with an end ileostomy and a mucous fistula or a Hartmann closure of the rectal stump is

recommended in most patients with fulminant or toxic colitis and rectal involvement as most patients are extremely ill, malnourished, and steroid dependent; removing the abdominal portion of the colon alone results in rapid reversal of symptoms. Avoidance of proctectomy is feasible in the majority of these patients; attempts at proctectomy in these sick patients often result in excessive hemorrhage, damage to pelvic nerves and surrounding structures, and other technical misadventures. Uncertainty regarding the diagnosis (CD vs. ulcerative colitis) can also make proctectomy undesirable. The risk of perineal sepsis and wound dehiscence increases significantly in these critically ill patients. Need for expeditious colectomy is paramount; subsequent consideration of proctectomy or reconstruction can be done later when the patient is well nourished, pathology has been reviewed, and immunosuppression has been discontinued. In patients with CD with rectal involvement, further medical management of residual rectal disease may be favorable to proctectomy as long as symptoms are tolerable. Occasionally, treatment of the remaining rectum allows ileorectal anastomosis to take place. If not, a staged completion proctectomy in a healthy patient may serve to decrease risks of complications.

Patients with longstanding, complex perianal CD who require proctocolectomy are a far more common problem. These patients may need proctectomy secondary to advanced complex perianal fistulas or stenosis that has rendered the anus nonfunctional. Perianal sepsis created by abscesses or undrained fistulas or sinus tracts may increase the risk of perineal wound complications. In the setting of active perianal sepsis, it is advisable to proceed with abscess drainage first, seton placement if required, and delayed resection to allow the acute phase of infection to pass. Fecal diversion (diverting ileostomy/colostomy or Hartmann procedure) in severe cases may allow the disease to transition to a more quiescent state prior to proctectomy and may be a good stepwise strategy, along with abscess drainage, to allow resolution of the septic focus and general improvement of the patient's health and nutrition.

Special technical considerations that may be specific to CD exist because of its unique pathology. Fistulas, both transphincteric and supralevator, can complicate proctectomy by creating a fibrotic, inflamed field that makes native tissue apposition difficult. Rectal strictures, as well as patient factors including malnutrition and immunosuppression, are also potential complicating features of CD.

Though there is little data regarding the association of CD-related anorectal strictures with the outcomes of proctectomy, Linares et al reported their experience with 19 proctectomies in such patients. Nine patients had delayed healing and in three, healing was not complete by 12 months. ²⁵ In a review of patients with CD with rectal stricture compared with those that did not, Fields et al reported that 50% of patients with rectal stricture also had concomitant perirectal abscesses, whereas only 17.1% of those without rectal stricture ²⁶ were affected by undrained perianal sepsis. Given these findings, rectal stricture is more likely a marker for active perineal sepsis, which in turn is more likely to account for wound failure. In patients with a rectal stricture, a

thorough exam of the perirectal region to ensure adequate control of sepsis prior to radical resection may indirectly result in better overall wound healing.

Patient Factors

Patients with severe systemic disease may suffer from protein-calorie malnutrition characterized by weight loss and low albumin and prealbumin levels. These deficiencies are typically obvious and those patients with albumin levels below 3 g/dL may benefit from preoperative total parenteral nutrition. However, even despite advances in overall nutrition and health of chronically ill patients, microdeficiencies of certain vitamins can still hamper postoperative wound healing. In the setting of active and recurrent CD, food intake is typically overall decreased. A recent study demonstrated that even for patients in clinical remission, avoidance of major food groups continued, with 18 to 33% of patients with IBD avoiding grains, dairy, and/or vegetables.²⁷

Zinc, vitamin A, and vitamin C are all essential nutrients for wound healing. Glucocorticoids impair zinc absorption and increase vitamin C losses. Furthermore, zinc and vitamin A are lost in the stool during bouts of diarrhea and steatorrhea, respectively. Zinc losses are significantly higher in patients with fistulizing CD, despite a normal weight and even a normal albumin level. Ror patients on corticosteroids, vitamin A 10,000 to 15,000 IU/day has been recommended to enhance wound healing. Vitamin C supplementation is also recommended at a dose of 100 to 200 mg/day to enhance wound healing. The suggested dosing for zinc supplementation is 40 mg of elemental zinc (176-mg zinc sulfate) for 10 days; however, these doses should not be continued for more than 2 to 3 weeks as excess zinc may interfere with other metabolites and result in other mineral deficiencies.

There is abundant evidence in the literature that obesity is also a risk factor for wound infection after rectal resection.³¹ Nystrom and colleagues compared wound thickness to rates of postoperative infection in 189 colorectal operations; they found that for wounds > 3.5 cm, the rate of infection was 20% versus 6.8% for wounds that were < 3.5 cm in depth.³² The difficulty of managing a perineal wound is compounded in an obese patient, as access for wound care is more difficult and the larger wound takes longer to heal. In a retrospective review of 584 consecutive patients, Benoist et al reported a higher rate of complications in left-sided and pelvic resection in obese patients. They reported a mortality rate of 5% after proctectomy among obese patients versus 0.5% among nonobese patients. Forty-three percent of obese patients undergoing proctocolectomy required a blood transfusion, as opposed to 19% of nonobese patients (p < 0.02).³³

The detrimental effects of smoking on the healing of perineal wounds in the setting of CD are likely multifactorial. Smoking is a well-known risk factor for clinical relapse of CD, ^{34–36} as well as an independent risk factor for impaired wound healing. ^{37,38} For patients who are active smokers, abstention from smoking is advised for at least 4 to 6 weeks preoperatively to achieve a significant decrease in the rate of wound complications. ^{37,38}

Antitumor Necrosis Factor Therapies

A recent prospective database demonstrates that patients operated on within 3 months of infliximab administration did not experience an increased rate of intraoperative complications.³⁹ A retrospective review by Colombel and colleagues supports these conclusions.⁴⁰ A prospective study of 413 consecutive patients at Massachusetts General Hospital, 24% of whom had received infliximab treatment within 12 weeks of an operative procedure, found no significant difference in rates of postoperative complications in these patients versus patients that did not receive infliximab preoperatively.⁴¹ Although the literature fails to separately consider perineal wound complications, it seems reasonable to adhere to general guidelines for operative intervention and antitumor necrosis factor therapy when considering perineal reconstruction.

Evaluation and Treatment of Perineal Wounds

A subset of patients will inevitably present with perineal wound failures. The first consideration should always be whether treatment needs to be performed urgently. Sepsis clearly mandates immediate operative intervention to drain pus and obtain source control of the septic process. Patients who present nonurgently need a thorough evaluation of the wound to assess for the best treatment strategy.

Physical Examination

- 1. Wound size: Wound size may range from a superficial sinus to a complete dehiscence of the perineal wound.
- 2. Wound effluent: Purulent, serous, or feculent discharge should be noted.
- 3. Foreign body reaction: Foreign material and stitch granulomas need to be removed.
- 4. Tissue quality: Evaluate the viability of the perineal tissue. Ensure all fibrinous exudate is debrided and all nonviable tissue is resected to healthy tissue.

Although rare, conversion of a nonhealing wound or fistula to either squamous cell carcinoma or adenocarcinoma has been reported. Chronic, nonhealing wounds, or wounds that appear hard, ulcerated, or fungating should be biopsied. The use of examination under anesthesia is often needed to better explore the wound, debride necrotic tissue, and facilitate biopsy.

In deeper wounds that are difficult to fully evaluate due to extent or patient discomfort, the utilization of additional imaging (either computed tomography [CT] scan or magnetic resonance imaging [MRI]) may be helpful. Undrained collections, foreign bodies, and enterocutaneous fistulas can be detected and defined.

Treatment Strategies for Perineal Wound Complications

The initial management of nonseptic wound dehiscence is typically conservative. In general, this is comprised of wound care with dressing changes. If all sources of infection are controlled and all necrotic tissue is debrided, 89% of wounds will heal within 6 months. 47

The decision to proceed with simple dressing changes as opposed to more aggressive options depends upon the quality and size of the wound, patient comorbidities, and overall health. A large, clean wound in a radiated field can still take a significant amount of time to heal. Costs and inconvenience to the patient associated with this strategy need to be considered. Nonrandomized studies and case reports exist describing the use of negative-pressure vacuum-assisted wound closure systems for the primary treatment of infected or nonhealing perineal wounds. For some contaminated wounds or wounds in patients who cannot undergo simultaneous flap reconstruction, this may be an alternative to consider. In a larger wound, it may be used as a bridge to myocutaneous flap reconstruction.

Persistent perineal sinus is defined by Watts et al as persistence greater than 6 months postoperatively. ⁴⁹ Treatment options include serial debridement and curettage, lay open techniques with marsupialization, or wide excision with primary closure or tissue flap closure. The goal is to remove chronic fibrosis and establish conditions more likely to heal. Wide excision was described by Ferrari and DenBesten. In their series, they reported favorable results for wide excision, coccygectomy, and skin graft. ⁵⁰ Despite reports of favorable results, one must keep in mind that skin grafts in the perineal region are exposed to a difficult wound environment in the setting of high sheer forces and are typically not used routinely if other tissue coverage options are available.

Numerous studies demonstrate the benefit of myocutaneous flaps for management of non-healing perineal wounds.^{8,51–54} Kapoor et al demonstrated that selective use of flaps offers significant improvements in wound complication rates.⁸ As with the use of flaps for primary closure, gracilis flaps for the management of a nonhealing perineal wound may be slightly less successful than VRAM flaps (50-100% vs. 90%, respectively); however, gracilis flaps have the advantage of avoiding an abdominal incision. The same is true for gluteal rotational flaps. Rotational tissue flaps require a healthy, well-nourished patient and a clean wound bed free of sepsis with good granulation tissue to be successful. Tissue flaps should be considered in select patients with delayed closure or persistent sinuses. 51 Use of flaps for delayed wound healing is dependent upon the size and quality of the wound and the ability of the patient to medically tolerate additional procedures.

Conclusions

Perineal wounds after proctectomy can be a challenging issue for the clinician. Individuals with CD, recurrent anal or rectal cancer, and previous pelvic radiation are at increased risk for wound failure. Considerations regarding staged operative interventions as well as myocutaneous flaps may help prevent wound failure in these instances. Attention to patient nutrition and comorbidities can minimize the risk of infection and subsequent nonhealing as well. Patients with nonhealing wounds despite preventative measures should be examined

for foreign bodies, granulation tissue, and deep sinus tracts. If optimization of patient nutrition, drainage of septic foci, and local debridement and wound treatment fail to result in wound healing, then a myocutaneous flap should be considered.

References

- 1 Zorcolo L, Restivo A, Capra F, Fantola G, Marongiu L, Casula G. Does long-course radiotherapy influence postoperative perineal morbidity after abdominoperineal resection of the rectum for cancer? Colorectal Dis 2011;13(12):1407–1412
- 2 Bullard KM, Trudel JL, Baxter NN, Rothenberger DA. Primary perineal wound closure after preoperative radiotherapy and abdominoperineal resection has a high incidence of wound failure. Dis Colon Rectum 2005;48(3):438-443
- 3 El-Gazzaz G, Kiran RP, Lavery I. Wound complications in rectal cancer patients undergoing primary closure of the perineal wound after abdominoperineal resection. Dis Colon Rectum 2009; 52(12):1962-1966
- 4 Matsuda K, Hotta T, Takifuji K, et al. Long-term comorbidity of diabetes mellitus is a risk factor for perineal wound complications after an abdominoperineal resection. Langenbecks Arch Surg 2009;394(1):65-70
- 5 Turner II, Russell GB, Blackstock AW, Levine EA. Impact of neoadjuvant therapy on postoperative complications in patients undergoing resection for rectal adenocarcinoma. Am Surg 2004;70(12):1045-1049
- 6 Miles W. A method of performing APR for adenocarcinoma of the low rectum. Lancet 1908;2:1912
- 7 Showalter S, Kelz RR, Mahmoud NN. Effect of technique on postoperative perineal wound infections in abdominoperineal resection. Am J Surg 2012. Accepted
- 8 Kapoor V, Cole J, Isik FF, Sinanan M, Flum D. Does the use of a flap during abdominoperineal resection decrease pelvic wound morbidity? Am Surg 2005;71(2):117-122
- 9 Nisar PJ, Scott HJ. Myocutaneous flap reconstruction of the pelvis after abdominoperineal excision. Colorectal Dis 2009;11(8): 806-816
- 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 J Surg 2005;29(11):1452-1457
- 11 Tei TM, Stolzenburg T, Buntzen S, Laurberg S, Kjeldsen H. Use of transpelvic rectus abdominis musculocutaneous flap for anal cancer salvage surgery. Br J Surg 2003;90(5):575-580
- 12 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. Ann Surg Oncol 1999; 6(1):33-37
- 13 Anderin C, Martling A, Lagergren J, Ljung A, Holm T. Short-term outcome after gluteus maximus myocutaneous flap reconstruction of the pelvic floor following extra-levator abdominoperineal excision of the rectum. Colorectal Dis 2012;14(9):1060-1064
- 14 Baird WL, Hester TR, Nahai F, Bostwick J III. Management of perineal wounds following abdominoperineal resection with inferior gluteal flaps. Arch Surg 1990;125(11):1486-1489
- 15 Tompkins RG, Warshaw AL. Improved management of the perineal wound after proctectomy. Ann Surg 1985;202(6):760-765
- 16 Elliot MS, Todd IP. Primary suture of the perineal wound using constant suction and irrigation, following rectal excision for inflammatory bowel disease. Ann R Coll Surg Engl 1985;67(1):6–7
- 17 McLeod R, Cohen Z, Langer B, Taylor B. Primary perineal wound closure following excision of the rectum. Can J Surg 1983;26(2): 122-124

- 18 Marks CG, Ritchie JK, Todd IP, Wadsworth J. Primary suture of the perineal wound following rectal excision for inflammatory bowel disease. Br J Surg 1978;65(8):560-564
- Warshaw AL, Ottinger LW, Bartlett MK. Primary perineal closure after proctocolectomy for inflammatory bowel disease. Prevention of the persistent perineal sinus. Am J Surg 1977;133(4):414-419
- 20 Delalande JP, Hay JM, Fingerhut A, Kohlmann G, Paquet JC; French Association for Surgical Research. Perineal wound management after abdominoperineal rectal excision for carcinoma with unsatisfactory hemostasis or gross septic contamination: primary closure vs. packing. A multicenter, controlled trial. Dis Colon Rectum 1994;37(9):890-896
- 21 Keighley MR, Allan RN. Current status and influence of operation on perianal Crohn's disease. Int J Colorectal Dis 1986;1(2):
- 22 De Dombal FT, Burton I, Goligher JC. The early and late results of surgical treatment for Crohn's disease. Br J Surg 1971;58(11): 805-816
- 23 Ritchie JK. Ileostomy and excisional surgery for chronic inflammatory disease of the colon: a survey of one hospital region. Gut 1971;12(7):528-540
- 24 Yamamoto T, Bain IM, Allan RN, Keighley MRB. Persistent perineal sinus after proctocolectomy for Crohn's disease. Dis Colon Rectum 1999;42(1):96-101
- 25 Linares L, Moreira LF, Andrews H, Allan RN, Alexander-Williams J, Keighley MR. Natural history and treatment of anorectal strictures complicating Crohn's disease. Br J Surg 1988;75(7):653–655
- 26 Fields S, Rosainz L, Korelitz BI, Panagopoulos G, Schneider J. Rectal strictures in Crohn's disease and coexisting perirectal complications. Inflamm Bowel Dis 2008;14(1):29-31
- 27 Sousa Guerreiro C, Cravo M, Costa AR, et al. A comprehensive approach to evaluate nutritional status in Crohn's patients in the era of biologic therapy: a case-control study. Am J Gastroenterol 2007;102(11):2551-2556
- 28 Hwang C, Ross V, Mahadevan U. Micronutrient deficiencies in inflammatory bowel disease: from A to zinc. Inflamm Bowel Dis 2012;18(10):1961-1981
- Sinno S, Lee DS, Khachemoune A. Vitamins and cutaneous wound healing. J Wound Care 2011;20(6):287-293
- 30 Anstead GM. Steroids, retinoids, and wound healing. Adv Wound Care 1998;11(6):277-285
- Gendall KA, Raniga S, Kennedy R, Frizelle FA. The impact of obesity on outcome after major colorectal surgery. Dis Colon Rectum 2007;50(12):2223-2237
- 32 Nyström PO, Jonstam A, Höjer H, Ling L. Incisional infection after colorectal surgery in obese patients. Acta Chir Scand 1987;153 (3):225-227
- 33 Benoist S, Panis Y, Alves A, Valleur P. Impact of obesity on surgical outcomes after colorectal resection. Am | Surg 2000;179(4): 275 - 281
- 34 Duffy LC, Zielezny MA, Marshall JR, et al. Cigarette smoking and risk of clinical relapse in patients with Crohn's disease. Am J Prev Med 1990;6(3):161-166
- 35 Sutherland LR, Ramcharan S, Bryant H, Fick G. Effect of cigarette smoking on recurrence of Crohn's disease. Gastroenterology 1990;98(5 Pt 1):1123-1128
- 36 Cottone M, Rosselli M, Orlando A, et al. Smoking habits and recurrence in Crohn's disease. Gastroenterology 1994;106(3):
- 37 Goertz O, Kapalschinski N, Skorzinski T, et al. [Wound healing complications in smokers, non-smokers and after abstinence from smoking]. Chirurg 2012;83(7):652–656
- 38 Sorensen LT, Karlsmark T, Gottrup F. Abstinence from smoking reduces incisional wound infection: a randomized controlled trial. Ann Surg 2003;238(1):1-5
- 39 Kasparek MS, Bruckmeier A, Beigel F, et al. Infliximab does not affect postoperative complication rates in Crohn's patients undergoing abdominal surgery. Inflamm Bowel Dis 2012;18(7):1207-1213

- 40 Colombel JF, Loftus EV Jr, Tremaine WJ, et al. Early postoperative complications are not increased in patients with Crohn's disease treated perioperatively with infliximab or immunosuppressive therapy. Am J Gastroenterol 2004;99(5):878-883
- 41 Kunitake H, Hodin R, Shellito PC, Sands BE, Korzenik J, Bordeianou L. Perioperative treatment with infliximab in patients with Crohn's disease and ulcerative colitis is not associated with an increased rate of postoperative complications. J Gastrointest Surg 2008;12(10):1730-1736, discussion 1736-1737
- 42 Sarani B, Orkin BA. Squamous Cell CA arising in an unhealed wound in Crohn's disease. South Med J 1997; 90(9):940-942
- 43 Buchman AL, Arment ME, Doty J. Development of squamous cell CA in chronic perineal sinus and wound in CD. AM J. Gastro 1991;86:1829-1832
- 44 Ky A, Sohn N, Weinstein MA, Korelitz BI. Carcinoma arising in anorectal fistulas of Crohn's disease. Dis Colon Rectum 1998;41 (8):992-996
- 45 Smith R, Hicks D, Tomljanovich PI, Lele SB, Rajput A, Dunn KB. Adenocarcinoma arising from chronic perianal Crohn's disease: case report and review of the literature. Am Surg 2008;74(1):
- 46 Iesalnieks I, Gaertner WB, Glass H, et al. Fistula-associated anal adenocarcinoma in Crohn's disease. Inflamm Bowel Dis 2010; 16(10):1643-1648

- 47 Wiatrek RL, Thomas JS, Papaconstantinou HT. Perineal wound complications after abdominoperineal resection. Clin Colon Rectal Surg 2008;21(1):76-85
- 48 Cresti S, Ouaïssi M, Sielezneff I, et al. Advantage of vacuum assisted closure on healing of wound associated with omentoplasty after abdominoperineal excision: a case report. World J Surg Oncol
- 49 Watts JM, de Dombal FT, Goligher JC. Long-term complications and prognosis following major surgery for ulcerative colitis. Br J Surg 1966;53(12):1014-1023
- 50 Ferrari BT, DenBesten L. The prevention and treatment of the persistent perineal sinus. World J Surg 1980;4(2):167–172
- Menon A, Clark MA, Shatari T, Keh C, Keighley MR. Pedicled flaps in the treatment of nonhealing perineal wounds. Colorectal Dis 2005;7(5):441-444
- 52 Galandiuk S, Jorden J, Mahid S, McCafferty MH, Tobin G. The use of tissue flaps as an adjunct to pelvic surgery. Am J Surg 2005;190 (2):186-190
- 53 Anthony JP, Mathes SJ. The recalcitrant perineal wound after rectal extirpation. Applications of muscle flap closure. Arch Surg 1990;125(10):1371-1376, discussion 1376-1377
- Hurst RD, Gottlieb LJ, Crucitti P, Melis M, Rubin M, Michelassi F. Primary closure of complicated perineal wounds with myocutaneous and fasciocutaneous flaps after proctectomy for Crohn's disease. Surgery 2001;130(4):767-772, discussion 772-773

