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**Rectal cancer and Fournier’s gangrene - current knowledge and therapeutic options**

Bruketa T *et al*. Rectal cancer and Fournier’s gangrene

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**Abstract**

Fournier’s gangrene (FG) is a rapidly progressive bacterial infection that involves the subcutaneous fascia and part of the deep fascia but spares the muscle in the scrotal, perianal, and perineal region. The incidence increased dramatically while the reported incidence of rectal cancer-induced FG is unknown but is extremely low. Pathophysiology and clinical presentation of rectal cancer-induced FG *per se* does not differ from the other causes. Only rectal cancer-specific symptoms before a presentation could lead to the diagnosis. The diagnosis of rectal cancer-induced FG should be excluded: in every patient with blood on digital rectal examination; when urogenital and dermatologic causes are excluded; when fever or sepsis of unknown origin with perianal symptomatology. Therapeutic options are more complex than in other forms of FG. First, the causative rectal tumor should be removed. The survival of patients with rectal cancer resection is reported as 100% while with colostomy is 80%. The preferred method of rectal resection was not defined. Second, oncologic treatment should be administered but the timing should be adjusted to the resolution of the FG and sometimes to the healing of plastic reconstructive procedures that are commonly needed for the reconstruction of large perineal, scrotal and lower abdominal wall defects.

**Key words:** Rectal cancer; Fournier's gangrene; Necrotizing fasciitis; Necrotizing soft tissue infections; Proctologic examination; Surgical treatment; Oncologic treatment; Reconstructive surgery

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**Core tip:** The reported incidence of Fournier’s gangrene (FG) increased dramatically while the reported incidence of rectal cancer-induced FG is unknown but is extremely low. Therapeutic options are more complex than in other forms of FG. First, the causative rectal tumor should be removed - survival with rectal cancer resection is reported as 100% while with colostomy only is 80%. Second, timing of the oncologic treatment should be adjusted to the resolution of the FG and sometimes to the healing of plastic reconstructive procedures commonly needed for the reconstruction of large perineal, scrotal and lower abdominal wall defects.

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**Introduction**

There has been confusion in the literature as to the precise definition of necrotizing fasciitis (NF) and Fournier’s gangrene (FG), which has been compounded by the use of multiple terms. Even though NF was actually first described by Hippocrates in the 5th century BC as a complication of erysipelas (Many were attacked by the erysipelas all over the body when the exciting cause was a trivial accident flesh, sinews, and bones fell away in large quantities there were many deaths)[1], the description of the disease has been attributed by many to Avicenna (1025)[2] and Baurienne (1764)[3]. When NF involves the male genitalia, it is known as FG after Jean Alfred Fournier in 1843 described it and Jones in 1871 coined the term hospital gangrene[4]. In 1952 Wilson coined the term NF to describe the disease process that can occur in other parts of the body, in either gender, but which, when affecting the perineum, still merits the eponym FG[5].

Criteria for NF include (1) fascial necrosis; (2) spreading cellulitis with undermining of fascial planes; and (3) systemic toxicity with altered mental state and hyperthermia. Some add (4) multiorgan failure as a criterion. NF is classified into four types. Type 1 is due to a mixture of aerobic and anaerobic organisms usually following an abdominal or inguinal operation or is associated with diabetes mellitus. It is the most common, accounting for 80% or more of all the necrotizing soft tissue infections (NSTIs), including FG[6]. Type 2is due to Group A *Streptococcus* infectionsynergistic with a second organism (*Staphylococcus aureus*, coliforms, *Bacteroides* spp.) observed in the limbs[7]. Type 3 stems from Gram-negative marine bacteria. Type 4 is a fungal infection occurring mostly in immunocompromised persons.

When referring to FG there are two important issues. First, it is important to define FG precisely because sometimes authors attribute other forms of infection to FG that requires only simple drainage of pus and not extensive debridements[8]. In such cases, prognosis is excellent, and the inclusion of these patients in FG group leads to wrong conclusions. Second, diagnostic, therapeutic, and prognostic parameters, with longer follow-up should be written in future reports, to have complete picture of FG, especially rectal-cancer induced FG, which is extremely rarely published.

**PUBMED AND GOOGLE SCHOLAR SEARCH**

A Pubmed and Google Scholar search were conducted using the keywords “Fournier's gangrene”,“Necrotizing fasciitis”, “Rectal cancer”, and “Rectal tumor”. Inclusion criteria were restricted to all case reports and case series where the rectal cancer was confirmed as a cause of FG. Of the 27 articles dating from 1988 to 2014, 23 were available as fulltext and were relevant to our review.

**Incidence**

The overall (reported) incidence of FG increased dramatically in the 20th century. From 1764 to 1978 there were 386 reported cases; from 1950 to 1999, 1726 cases[9]. The incidence is rising due to an increase in the mean age of the population, increased numbers of patients with comorbidities, widespread use of immunosuppressive therapy or suffering from human immunodeficiency virus (HIV) infection, especially in Africa[10,11]. The overall incidence is 1.6/100000 males and represents less than 0.02% of hospital admissions[10]. The real incidence could be underestimated because most cases with grave prognosis were not published.

***Anorectal causes***

Anorectal pathology is the most common cause in both males and females (Table 1). The incidence varies significantly, mostly between 20% and 60% depending on the (sub)population analyzed. The most common causes are perianal/ischiorectal abscess and hemorrhoidectomy (Table 2). Other common causes are rectal injury and perianal fistula (Table 2); less common include sigmoid/rectal carcinoma, colorectal anastomotic dehiscence, appendicitis, perforated sigmoid diverticulitis, rectal biopsy, artificial sphincter or even anal dilation.

***Rectal cancer-induced FG***

The incidence of rectal cancer-induced FG is unknown. The first known case (of a famous person) with FG was that of Roman Emperor Galerius. He suffered from the diabetes and died of FG (in advanced stage worms were found in perineal and scrotal area). Eusebius that described the case claimed that bowel cancer was the underlying cause[44]. Rectal cancer is the third most common cancer in the United States[45] with 40000 patients diagnosed each year. Fortunately, there are several explanations for the low incidence of rectal cancer-induced FG. One is rectal cancer presentation before the potential development of FG and simple diagnosis. When the upper rectum is involved, patients can present with bowel obstruction before the potential development of FG. In addition, up to 26% of obstructive large bowel perforations are proximal to the obstructing (non-perforating) tumor presenting as acute abdomen, not FG. In addition, screening programs result in earlier stage rectal cancer diagnosis. We collected 23 cases with proven rectal cancer-induced FG (Table 3) while there are several more published[69] which were unavailable for analysis. The average age of patients with rectal cancer-induced FG was 60 years (range 28-80) with a male: female ratio of 21:2. The incidence of rectal cancer-induced FG in all-cause FG ranged from 1.47% to 16.6% and in the anorectal group varied significantly from 3.85% to 100% (Table 1). These percentages should be interpreted with caution because the studies included different etiologic groups of patients.

**Risk factors**

***All-cause FG***

Predisposing factors for all-cause FG are poor perfusion (peripheral vascular disease), hypertension, renal insufficiency, trauma, diabetes mellitus, malnutrition, smoking, obesity, immunocompromised status, intravenous drug abuse, malignancy and spinal cord injury[1]. Alcoholism and diabetes mellitus are the most common in western countries with rates of 25%-50% and 10%-60%, respectively[70–73]. Old age is not a predisposing factor; however, elderly patients with poor self-care and poor nutritional status are more susceptible[1]. Female to male ratio varies significantly (Table 1). The lower incidence in women is ascribed to better drainage of the perineal region through vaginal secretions[9,48]. In addition, the reported ratio depends on the type of clinic in which the data are collected, namely urology, surgery or gynecology. Reports from urology clinics tend to contain fewer female patients while the incidence of females is higher in reports from general surgery clinics.

***Anorectal causes of G***

From the published data, it is not possible to define specific risk factors for this group. General risk factors could be applied here. Proportion of anorectal causes range from 0% to 92.6% (average 40%) (Table 1).

***Rectal cancer-induced FG***

Seven of 23 articles (Table 3) mentioned general risk factors for rectal cancer-induced FG; the most common being diabetes mellitus. A specific risk factor is rectal cancer perforation. The risk of rectal cancer perforation aside of its growth is neoadjuvant or therapeutic chemoradiotherapy. Colorectal carcinoma constituents 9.2% of all colorectal perforations[74]. Of all colorectal carcinomas, 5.9% perforate and of these 5.8% are located in the rectum[75]. In 1977, 50% of perforated colorectal cancers were at rectosigmoid junction[76]. The site of perforation of the primary colorectal tumor is related to the primary tumor site in 50%[77]. One should be cautious with interpretation because ulceration at the site of a primary tumor (with or without chemoradiotherapy) may be a non-specific finding as ulceration, and deep necrosis are typical features in malignancies overall. Rectal cancer perforation as an adverse effect of preoperative (chemo)radiotherapy is extremely rare[78,79]. With increased use of bevacizumab, monoclonal immunoglobulin G1 antibody directed against VEGF, gastrointestinal perforation, as a side effect, is observed in 1.7% of patients. Only 4.2% of these were from the rectal cancer[80]. In a study by Hurwitz *et al*[81] gastrointestinal perforation rate was 1.5% in the group with previously untreated metastatic colorectal cancer. There are no data about perforation site.

**Pathophysiology**

FG exists due to synergism between low aggressive multiple aerobic and anaerobic organisms that are normally present within the distal rectum and perianal area. Aerobes cause platelet aggregation and accelerate coagulation by fixing complement, and produce heparinase[82]. The presence of sialic acids on the cell walls of the *Streptococcus* spp. and *E. coli* helps to inactivate the alternate complement pathway[83]. Microthrombosis of nutrient vessels reduces local blood supply causing dermal necrosis and allows the growth of facultative anaerobes and microaerophilic organisms such as *E. coli*. *Bacteroides* spp. that inhibits phagocytosis of many aerobes[84]. These produce the relatively insoluble gases composed of hydrogen, hydrogen sulphide, nitrogen and nitrous oxide, causing subcutaneous gas collections. Whether subcutaneous emphysema is merely the manifestation of a perforated rectal cancer or from bacterial gas production can be difficult to determine. The synergistic activity of aerobes and anaerobes leads to the production of various exotoxins and enzymes like collagenase, heparinase, hyaluronidase, streptokinase, streptodornase. This leads to digestion of fascial barriers, thus fueling the rapid spread of the infection and hemolytic anemia due to streptococcal hemolysins[83,85]. It does not appear that the origin of the infection (rectum, urinary, dermal) has any impact on the specificity of the species cultivated[73].

***Urogenital origin***

The infection originates from the urogenital triangle, usually secondary to urethral instrumentation. If the source is penile, then after the tough fibrous tunica albuginea is penetrated, the infection spreads to involve Buck’s fascia[86] which initially limits the infection to the ventral aspect of the penis. If the infection is not initially treated and Buck’s fascia is penetrated, the infection may progress along the Dartos fascia[87,88]. The Dartos fascia of the penis is a direct extension of Colles’ scrotal fascia, which is the continuation of the Scarpa’s fascia of the anterior abdominal wall. Thus, the progression of the infection can spread freely to the scrotum and the Scarpa’s fascia of the abdominal wall[86]. The scrotum readily develops dermal gangrene because it has virtually no subcutaneous fat[89]. If Colles’ scrotal fascia is penetrated, the infection can spread to the buttock, thigh, back and ischiorectal space. Perineal fascia is attached to the perineal body and urogenital diaphragm posteriorly and the pubic rami laterally, thus limiting progression in these directions. Laterally and inferiorly it connects with the fascia lata of the lower limbs. Posteriorly it is limited by the levator ani muscle. If the anal sphincter is damaged, infections gain access to the retroperitoneum through pararectal spaces.

***Anorectal origin***

If infection originates from an anorectal source (anal triangle), it penetrates the muscles of the anal sphincter to reach Colles’ fascia[90]. It penetrates Colles’ fascia and progress anteriorly along the Dartos fascia to involve the scrotum and penis. There is some evidence to indicate that Colles’ fascia is not a continuous layer but rather a condensation of fibrous tissue with interstices that could allow the spread of a perirectal process involving the scrotum and penis[86]. If the sphincteric apparatus is damaged, the infection can spread to the rectum into the presacral space, the retrovesical space, and the pelvirectal tissue. This can involve the retroperitoneal space to the level of the upper abdomen. Ultimately, the infection can penetrate into the peritoneal cavity. Therefore, anorectal sources of infection usually start perianally, and this variation in initial clinical presentation can serve as a guide to localizing the foci of infection[3]. Infection can pass superiorly along the Scarpa’s fascia to involve the anterior abdominal wall. If the Colles’ fascia is interrupted, the infection can spread to the ischiorectal fossa and subsequently to the buttocks and thighs.

There are three different etiopathogenetic paths of infection with rectal perforation. First is iatrogenic retroperitoneal rectal perforationwithout the presence of rectal carcinoma. This mechanism is found during rectal instrumentations, barium enemas, and diagnostic/therapeutic colonoscopy. The second mechanism is external rectal trauma sometimes with foreign body retained through the rectal wall. The third mechanism is true spontaneous perforation of rectal cancer that can develop into two clinical forms. More commonly it presents as ischiorectal and/or gluteal abscess or rarely in a form of FG. Tumor infiltration (with or without necrosis) of the rectal wall and surrounding tissues spreads the infection. Infection is much more fulminant then in iatrogenic extraperitoneal rectal perforation[91–93]. This is due to pre-procedural bowel preparation, with or without prophylactic antibiotics, which significantly reduces the incidence and severity of the infection.

Whatever the cause of FG, testicular involvement is rare because of the separate blood supply to the testes and the testicles are always spared if the disease affects the subcutaneous tissue only[94]. If necrotic testicles are found, an intra-abdominal process, which leads to thrombosis of the testicular artery, should be strongly suspected[50].

**Clinical presentation**

***Local findings***

It is difficult to determine the exact time point at which the disease progresses from a primary infection to an FG. Clinical presentation of perianal or scrotal FG has many similarities. When the disease progresses slowly, patients are often unable to remember a specific date of symptom onset or sometimes report a date more recent than the actual date. In this way, they attempt to avoid giving the impression that they were reluctant to seek medical help or that they underestimated their disease. Most patients seek medical attention an average of 5d after the onset of symptoms[70]. Where mentioned, in rectal cancer-induced FG, duration of symptoms lasted 2-14 d (Table 3).

The course of the disease can be divided into two phases that are characterized by different rates of disease progression. A first phase, stable and sometimes long, during which the body's immune system prevents local inflammation from spreading, is followed by a second phase during which infection progresses rapidly to the fulminant illness. It begins with a prodromal period of genital discomfort and pruritus followed by sudden onset of perianal or perineal pain out of proportion to the physical findings[1]. As the FG progresses, the pain is replaced by numbness and subsequent anesthesia caused by damage to cutaneous nerves[95]. Irrespective of the bacterial species, the initial bacterial growth takes place in the subcutaneous tissues, *i.e.*, the subcutaneous fat, superficial fascia and the superficial layer of the deep fascia. The skin remains intact initially, and the extent of the subdermal gangrene may not be apparent[96]. Later, skin develops patchy necrosis and becomes gangrenous. The swelling, shiny scrotum skin is typical early symptom of scrotal infection. Due to lack of subcutaneous fat in the scrotum, necrosis of Dartos fascia leads to the of exposure of the testes that may be coated with a thick layer of creamy pus. Sometimes small skin ulcers drain thin, reddish-brown, foul-smelling fluid (“dishwater fluid*”*). Odor characteristic of anaerobic infection may be present. Surrounding these draining wounds are variable amounts of skin necrosis. Induration or distinct margins are absent, with the diseased area gradually fading into normal skin. A black spot or dusky area in the perineal skin surrounded by erythema is considered pathognomonic of FG[66]. Crepitus and subcutaneous gas (gaseous emphysema) indicate the presence of dead tissue[97]. Crepitus in all-cause FG is found in 19%–64% of patients[98,99], and depends on the duration of FG and the underlying cause. There are no data about the incidence of crepitus in rectal cancer-induced FG. It commonly occurs in the first 48-72 h[100–102]. Some patients have blisters and bullas of adjacent tissues, initially filled with serous, then hemorrhagic fluid[103–105]. Lymphangitis and lymphadenitis are rare[106,107]. FG progresses at the speed of 2-3 cm2/h[40,108].

Initial localization of pain, edema, and redness could lead to the underlying group of etiologies. If initial presentation involves scrotum and penis or only penis urogenital pathology could be the cause[17]. All-cause FG starts as scrotal edema (Table 1) therefore group of causes cannot be defined only due to scrotal edema. Gangrene extension to the perineal/perianal region in delayed presentation complicates the possibility of identification of the cause. The scrotum should be checked for generalized crepitus, edema, erythema, and tenderness, superficial ulcerations, odor or discharge. Both testicles should be palpated and compared. Penis should be checked for lesions and discharge. The patients should be asked about recent urinary catheterization. Prostate infiltration by the rectal tumor can present with prostatic symptoms and can be misleading.

The most common initial localization of rectal cancer-induced FG was scrotum (Table 3). When scrotal edema develops in patients with anorectal pain, rectal bleeding, tenesmus or alteration of bowel habits and unintentional weight loss, rectal cancer should be suspected. Cachexia, weight loss, anemia, rectal bleeding, constipation, and diarrhea were present in this group (Table 3). Urinary retention was present in one patient. There are several mechanisms and risk factors for this presentation. Old age is a risk factor for urinary retention and benign prostatic hyperplasia. Also perianal/perineal pain plus infection that disturbs sympathetic and parasympathetic neuronal pathways in surrounding area causes urinary retention that can mislead to the conclusion of the urogenital origin of FG.

***Systemic findings***

Systemic findings can also be misleading. Patients may have a fever, malaise for a few days[109], nonspecific abdominal pain[110], general symptoms of infection without symptoms from the perineal area[111,112]. The septic state develops with the rapid development of severe toxemia causing pyrexia with or without hypothermia, tachycardia, hypotension, and reduced urine output[95]. Sepsis may occur in just a few hours progressing to organ failure and death[95]. The clinical picture is similar regardless of the bacterial species involved. All patients with fever or sepsis of unknown origin require a thorough genital, perineal and proctologic examination.

**Differential diagnosis**

Differential diagnosis includes two groups of diseases. First group consists of other forms of NSTIs also called infectious gangrene or gangrenous cellulitides(Table 4[96,113–116]) and the other consists of diseases that resemble gangrenous/necrotic infections. These are not progressive bacterial infections, but rather presentations of systemic or localized diseases or immunocompromized host.

**Diagnosis**

***Fournier gangrene per se***

The diagnosis is usually a clinical one. Early clinical recognition of FG is difficult, as the disease is often indistinguishable from cellulitides/abscesses early in its evolution (Table 4). To aid in diagnosis, a risk score was developed - Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score. A score of ≥ 6 raises the suspicion of NF, and a score of ≥ 8 is strongly predictive of the disease.

Laboratory findings define the disease severity, septic state, and metabolic derangements. A full blood count, C-reactive protein (CRP), urea, creatinine, glucose, calcium, potassium, sodium, coagulation studies, fibrinogen/fibrin degradation product levels, and acid-base status should be checked. Diabetics may present with ketoacidosis[117]. A mid-stream urine sample excludes/confirms urinary tract infection. One should be cautious because it can also be present despite causative rectal tumor. Hypocalcemia due to bacteria lipase is an important indicator of the early stage[118] and develops from extensive fat necrosis[119]. Total protein and albumin levels show obligatory hypoalbuminemia, especially in the advanced presentation. Full blood count, calcium, and CEA marker are rarely mentioned in articles with rectal cancer-induced FG. CRP was noted in 26% of these cases and ranged from 149 to 424 mg/L (Table 3). Leukocytes were noted in 57% and ranged 10000/mm3-36800/mm3 with one patient with 2700mm3 due to sepsis (Table 3)

The following two clinical courses should increase the likelihood of FG: (1) infectious process that does not respond well to antibiotics, and (2) the septic symptoms disproportionate to scrotal cutaneous manifestations in the early stage of infection[3].

The finger test is diagnostic. This is a bedside procedure where under local anesthesia a 2-cm incision is made over most prominent cutaneous changes down to the deep fascia and a gentle probing maneuver with the index finger is performed at the level of the deep fascia. The lack of bleeding, presence of characteristic dishwater pus, and easy blunt finger dissection of subcutaneous tissue off the fascia are features of a positive test[120].

Tissue biopsies and pus (during finger test and intraoperatively) define causative microorganisms and possible underlying pathology. The histopathological features of FG are necrosis of the superficial fascia with blood vessel thrombosis and suppuration[106,121]. Other consistent features include severe subcutaneous fat necrosis, severe inflammation of the dermis and subcutaneous fat, vasculitis, often with endarteritis, and local hemorrhage[106,121]. In the early stage, the epidermis shows no major changes[121].

***Underlying cause***

Digital rectal examination was performed in 70% of rectal cancer-induced FG cases and was positive in 75%, performed mostly preoperatively (Table 3). Macroperforation can be confirmed or ruled out in palpable tumors. Impalpable perforation does not exclude microperforation.

Rectoscopy (as bedside or intraoperative procedure) is mandatory in the following situations: (1) blood (any form) on digital rectal examination; (2) history and other/previous diagnostic modalities refer to rectal carcinoma; (3) urogenital and dermatologic causes excluded; (4) bacteria highly specific for (intestinal) rectal malignancy such as *Clostridium septicum*[122]; and (5) fever or sepsis of unknown origin with perianal symptoms/signs. Rectoscopy was performed in 52% of rectal-cancer induced FG with equal frequency preoperatively and during the initial operation (Table 3).

Gas may be detected on plain X-ray, indicating the presence of dead tissue[97]. X-rays were done in only 13% of rectal cancer-induced FG (Table 3).

Gas within the scrotal wall on ultrasound may be seen prior to clinical crepitus. Reactive unilateral or bilateral hydroceles may be present. If testicular involvement occurs, there is likely an intraabdominal or retroperitoneal source of infection. Ultrasound is also useful in differentiating FG from incarcerated inguinoscrotal hernia, the data unknown for the rectal cancer-induced FG.

Imaging modalities define the cause and the disease extent. CT has greater specificity than radiography or ultrasonography for defining the cause and the disease extent[87,88]. CT can demonstrate asymmetric fascial thickening, any coexisting fluid collection or abscess, fat stranding around the involved structures, and subcutaneous emphysema. In rectal cancer-induced FG, abdominal CT was performed in 56% of cases. Of these, tumor and air were detected in 61.5%, only air in 7.7%, only tumor in 23%. In 7.7%, no pathology was found. The finding of rectal tumor does not mean it is the cause of FG. Perforation or infiltration of the rectal tumor is highly probable when increased soft tissue density with abscess and/or gas bubbles is present around the tumor. In 43.5%, the abscess was detected: one retroperitoneal (intraoperative finding), four ischiorectal (one on CT and three intraoperatively), one in mesorectum (on CT), one perirectal (intraoperatively). In three cases, the location was not defined.

MRI gives greater soft tissue detail and fistulous tracts than CT[123] but is mostly unavailable in emergency settings.

**Treatment**

Proctologic examination under general anesthesia identifies the cause of the disease and determines its extent. Proposed diagnostic/therapeutic algorithm for rectal cancer-induced FG is presented in Figure 1.

***Rectal cancer treatment modalities***

**Colostomy:** Colostomy has been used for fecal diversion in cases of severe perineal involvement in all-cause FG with: (1) anal sphincter involvement; (2) fecal incontinence; and (3) continuous fecal contamination of the wound’s margins.

Rectal diversion decreases the number of germs in the perineal region and improves wound healing. The primary colostomy rate is 16-17%, whereas the secondary colostomy rate is 35%-40%[124,125]. In an anorectal female group, colostomy rate was 83.7%, with a primary colostomy in 37.5% and a secondary colostomy in 50%[29]. Colostomy rate in the anorectal group varies from 50% to 100% (only four articles have adequate data) (Table 1).

A transverse loop colostomy is preferred because it yields solid and formed stools with little contamination of the surrounding skin. The abdomen above the umbilicus is an ideal because FG often extends into the lower abdominal wall[126]. Necrosis around the stoma causes stomal detachment necessitating stomal translocation. In addition, colostomy should not be brought through the rectus muscle until the plastic surgery team has selected the possible reconstructive option. Most commonly vertical rectus abdominis myocutaneous flap (VRAM) with skin from the supraumbilical area provides excellent soft tissue bulk to obliterate perineal dead space[127–129]. The stool and urinary diversion ostomies can be brought out through one rectus muscle only after elevation of the contralateral VRAM[130].

Colostomy, as the only (mentioned) treatment of rectal cancer-induced FG, was performed in 43% of cases, with mortality of 20%. Three important parameters from published articles are not known: (1) rectal cancer operability and whether the colostomy was definitive surgical treatment; (2) long-term follow-up; therefore additional procedures that could be performed at later date are unknown; and (3) the location of colostomy.

The therapeutic algorithm is not defined if rectal cancer infiltrates prostate. Should colostomy be made first, followed by chemoradiotherapy and as a final act abdominoperineal resection (APR)[55], or should the APR be made as the first and definitive operation. If patient presents with multiple bilobar liver metastases colostomy could be the first line therapy.

**Rectal diversion device(s):** The Flexi-Seal® Fecal Management System by Convatec is a silicone catheter that protects the wounds from fecal contamination. It is an excellent alternative to colostomy for a shorter period (several weeks). The device avoids complications related to stomas, including better psychological recovery and may have an economic benefit. Unfortunately, recommendations from the manufacturer contraindicate its use when (perforated) rectal cancer with FG or any anorectal cause with FG is present[131]. On the contrary, Ozkan *et al*. recommended its use in FG with excellent results[32].

**Rectal cancer resection:** Rectal carcinoma is different from most other, even anorectal causes of FG, because elimination of systemic risk factors and purulent collection(s) does not eliminate the source of infection. Perforation of rectal cancer *per se* produces infection; therefore resection of the perforated rectal tumor is mandatory (see Prognosis). If the tumor did not perforate then the other causes should be ruled out. In this situation, initial resection of the rectal cancer is not mandatory. The most experienced surgeon available should perform the operation.

Localization of rectal cancer was described as lower or upper rectum (imprecise localization) in 13% and distance from anocutaneous line was noted in 30%, ranging from anocutaneous line to 10 cm (Table 3). APR as the initial operation was performed in 13% of cases; colostomy as an initial procedure with delayed APR in 26% of cases (Table 3). Latter option could be for the patients with poor operative risk, presence of the septicemia, old age or hemodynamically unstable patients. These factors eliminate the possibility of aggressive approach and at the first instance necrotic and infected tissue is removed and a major surgery postponed till the patient’s condition improve[51]. There are two advantages of this approach: (1) subsequent colonoscopy with pathohistological diagnosis of the rectal tumor; and (2) detection of synchronous colorectal tumors eliminating the need for subsequent resections. Unfortunately, when rectal cancer-induced FG is present delay of up to 7 d is intolerable due to rapid progression of FG and the need for rapid elimination of infective source. The patients should be warned about possibility of permanent stoma.

In high rectal cancers the dilemma is whether to do anterior rectal resection, Hartmann’s procedure or APR. Hartmann’s procedure adds safety due to fecal diversion and as primary treatment was performed in 8.7% of cases (Table 3). The problem could be the revascularization of the rectal stump due to extensive debridement of the perirectal area. Therefore even in high rectal cancer associated with FG, APR have the advantage of eliminating all infective focuses in the perineal/perianal region. The perineum is not closed primarily, but packed with several roll gauzes. When the spread of FG is stopped and the hemostasis is achieved with packs then vacuum assisted closure (VAC) minimizes skin defects and speeds tissue healing. The location of the perineal wound makes it difficult to maintain an adequate seal due to the irregular surfaces surrounding the gluteal folds and perineum. Enemas could be applied before changing the VAC dressings in patients without diverting colostomy. VAC dressings are changed every 72 h or when the progression of gangrene is found. Ozkan *et al*[32] recommend lower limit of pressure (without explanation), which was originally recommended to be between 50 and 125 mmHg.

Currently, extralevator *APR* (eAPR) is recommended for elective low rectal cancers[132]. It consists of wider excisions with *en bloc* resection of the distal rectum, sphincter complex, and levator muscles, resulting in a cylindrical specimen. This reduces the rate of positive resection margins and tumor perforation in distal rectal cancer, and improves oncological outcome, especially in perforated forms, as in FG. Wider excisions and increased use of neoadjuvant chemoradiotherapy have significantly increased perineal wound healing problems, in up to 59%[133,134]. Furthermore, perineal hernia is more likely – found in up to 20%[135]. Clinical outcome of biological meshes during eAPR appeared comparable to flap assisted perineal closure in a non-randomized studies based on systematic review[136]. Perineal hernias after biological mesh closure following eAPR were 8.2%[135,137–140]. One of the assumptions for successful use in FG is that gangrene (mostly) does not affect muscles; therefore mesh can be securely sutured to the muscles surrounding the defect after eAPR. The unsolved issue is the timing of application of biological mesh in FG patients.

***Extensive debridement***

Current estimates of all-cause FG mortality are 21% (range 7% to 75%) similar to 22% mortality from the preantibiotic era[141]. This suggests that initial therapy needs to be more aggressive and the first operation more extensive and definite. This also suggests that antibiotic therapy is not the main therapy. If in doubt cut it out is a truism in FG[66]. Intraoperative lack of resistance of normally adherent fascia to blunt dissection is confirmation of NF[7,119]. Debridement should be stopped when the separation of the skin and the subcutaneous tissue is not performed easily because the cutaneous necrosis is not a good marker. Surgical reexamination of the infected area and detachment of the necrotic tissue is advocated within 24 and should be carried out repeatedly. In all-cause FG an average of 3.5 procedures is required[142]. Most studies on anorectal etiology declare multiple procedures without absolute numbers. This is also true for rectal cancer-induced FG (Table 3). Duration of the hospitalization is unknown for the anorectal group. Duration of hospitalization for the rectal cancer-induced FG was noted in 30% of cases, ranging 23-130 (average 47) d.

The crucial significance of testicular infarction, implying thrombosis of the testicular artery, must be recognized as an absolute indication for laparotomy and retroperitoneal exploration. Posterior peritoneum may need to be incised before necrotic retroperitoneal tissues are exposed.

Hemorrhage or perioperative blood loss is inevitable due to (1) extensive debridement; (2) possible DIC; and (3) rectal resection. In addition, microcytic anemia can be present preoperatively due to bleeding rectal tumor.

***Antibiotic therapy***

The optimal approach to empiric antibiotic therapy for FG is uncertain; data are limited since most clinical trials exclude FG patients. The optimal duration of antibiotic treatment has not been defined. Antibiotics should be continued until no further debridements are needed, and the patient’s hemodynamic status and temperature has normalized; this duration must be tailored to individual patient circumstances or laboratory parameters such as leukocyte count or CRP level. High, intravenous doses should be used. Antibiotics should be adjusted to culture results. Most common initial (empiric) combinations used for all-cause FG are: (1) penicillin G or ampicillin, aminoglycoside or 3rd generation cephalosporin plus metronidazole or clindamycin[143]; (2) benzylpenicillin plus clindamycin plus gentamicin. If penicillin-allergic, meropenem plus clindamycin plus gentamicin. Review the need for gentamicin daily[144]; (3) meropenem plus clindamycin[145]; (4) clindamycin plus ciprofloxacin plus metronidazole[146]; and (5) for suspected Vibrio spp. include a tetracycline and 3rd generation cephalosporin (*e.g.*, doxycycline plus ceftazidime); ciprofloxacin may be an alternative[147,148].

***Nutritional support***

Due to extensive debridement physiologic changes are similar to extensive and deep burns. Patients with infected wounds or sepsis have increased requirements for nutrients and often have a reduced food intake. Early nutritional support had shorter duration before split thickness skin grafting than the conventional support significantly[149]. Catabolic effect of primary malignancy and/or cachexia could be present.

Nasogastric tube is placed when mechanical ventilation is required and when patients are unable to eat a satisfactory diet. Total parenteral nutrition (TPN) is used only if patients are unable to be fed enterally. Enteral nutrition is provided with high protein formulas. Attempts to estimate nutrient requirements based on any formula will inevitably lead to over- or under-feeding. Indirect calorimetry (IC) remains the most precise method to determine energy requirements. When IC is not available, provide calories at 25 kcal/kg per day or about 124% of estimated basal needs[150,151]. Energy expenditure should be measured by IC 2-3 times a week. Respiratory therapists measure oxygen consumption, production and resting energy expenditure and respiratory quotient in the early morning before patients had begun daily activities. Due to clinical status (*i.e.*, symptoms consistent with sepsis syndrome), patients are generally sedated, intubated, and receiving analgesics during IC. Resting energy expenditure is recorded when measurements are stable for at least 10 min. Patients on TEN or TPN had feedings continued at a steady rate throughout each measurement; patients on oral diets are measured before breakfast, after an overnight fast.

***Adjunctive therapy***

Underlying risk factors and metabolic derangements should be corrected. Honey, Royal Jelly, hyperbaric oxygen therapy, sodium hypochlorite, lyophilized collagenase, growth hormones, protein synthesis inhibitors, intravenous immunoglobulins are all adjunctive methods but without definitive proof of their positive therapeutic effect.

***Reconstructive surgery***

There are two main timing options for reconstructive surgery: (1) at the time of initial admission[21]; or (2) after the acute process has fully resolved. Reconstructive surgery is considered when an extensive healthy granulation tissue formation on the wound base is present. Secondary healing or delayed primary closure is applied for small residual defects (< 10 cm2)[16]. Eventually, testes can be covered with remaining scrotal skin or implanted in the subcutaneous tissue of the thigh or abdomen if viable.

To improve healing of the large perineal wound, sutured perineal pedicled retrocolic omentoplasty can be added to the procedure of APR[152,153]. The great omentum is pediculized on the left gastroepiploic artery and tightly sewn to the subcutaneous fatty tissue of the perianal skin. Although a high level of evidence is lacking, the procedure adds well vascularized, non-irradiated tissue to the pelvic cavity[154]. The well-vascularized muscle flap demonstrates greater resistance to bacterial inoculums and in wounds with some degree of contamination[155]. In the only study with follow-up of all-cause FG, during the first 12 months after hospital discharge, 12% of patients required inpatient hospital treatment for fistulas and needed revision surgery for new inflammatory processes[16]. In elective settings, after APR, VRAM and gluteal flap, have been used for closure of large perineal defects[128,156–158]. The problem arises when large areas are debrided eliminating the possibility for the use of standard flaps. In addition, if adjuvant chemoradiotherapy is indicated the questions are: (1) should the flaps be used; and (2) the timing of flap application. Also, due to the donor site morbidity, increased operative time, and higher costs, it is questioned whether autologous tissue flaps should be applied when VAC and skin grafting is available.

***Adjuvant chemoradiotherapy***

Due to the extremely small number and emergent presentation, there are no studies and recommendations when to start this form of therapy after complex surgical treatment of rectal cancer-induced FG. Only two articles mentioned adjuvant chemoradiotherapy after initial colostomy - an insufficient pool of data for making conclusions[52,68]. If oncologically indicated it should be offered when all wounds healed completely. If flaps were used consultation with plastic/reconstructive surgeon is advisable.

**Prognosis**

***All-cause Fg***

The mortality from all-cause FG has dropped significantly in the last century. In 1871, Jones claimed 46% mortality for all NSTIs. Unfortunately, mortality has changed little since Meleney in 1924, first recognized the need for early surgical intervention[159]. Currently, the survival rate is in the range of 60% to even 100% (Table 1). Since many studies were conducted on males, the difference in male-female survival is unknown.

There are several issues here. First, mostly all-cause FG survival or mortality is reported. Second, reports are from different decades. Third, specific underlying cause is not always presented, and prognosis could be etiology dependent. Fourth, non-catastrophic soft tissue infections are sometimes defined as FG declaring better prognosis falsely. Fifth, when true FG is present, the underlying cause is sometimes not attributed correctly due to the confounding factors[160].

Poor prognostic factors include age over 60, peripheral vascular disease, poor nutritional status[1], sepsis[89], positive blood cultures[89], and delayed presentation/treatment[161]. The duration of symptoms is prognostic, and none of the patients admitted within 48 hours of symptom onset died[1,38]. Female pelvic anatomy has been claimed to be better for drainage of secretions through the vagina[162]. On the other hand, some suggested that it is a disadvantage related with rapid dissemination of the disease[163,164]. Other poor prognostic parameters include high serum creatinine, lactate, sodium and calcium or low bicarbonate[165,166], low magnesium at admission[167] and renal function impairment on admission[12,168,169]. Increased serum calcium may be due to renal failure, bacteremia, or TPN. Lactate level > 4.0 mmol/L is an independent predictor of mortality[170]. High neutrophil-lymphocyte ratio and the platelet-lymphocyte ratio values were associated with significant increases in the number of debridements, hospital stay duration, cost, and mortality rate[23]. Influence of diabetes mellitus[12,25,171–174] on mortality is controversial, but the extent to the abdominal wall has been reported to be directly related to mortality[1,12,175,176]. The involved body surface area (BSA) and the number of debridements did not predict the outcome in some series[71,172,174]. In contrast, BSA ≥ 15 cm2 had a mortality of 75%[24]. Therefore, this issue remains controversial[166,168,172,174].

Mean age, race, the prevalence of comorbid conditions and number of debridements were similar in both genders. However, twice as many women required mechanical ventilation and dialysis, with longer hospital stay and mortality, but without statistical significance[10]. Table 1 shows the average duration of hospitalization in all-cause FG of 24 d (range 1 to 278 d).

Of all the anaerobic species isolated in all-cause FG, none was present as the sole organism. No differences in clinical course, morbidity, or mortality were demonstrated with different bacteria(s) isolated[177–179].

Prognostic indices for mortality predictions such as Fournier’s Gangrene Severity Index (FSGI) are still controversial[24,180,181]. Many studies show significant mortality with FSGI >9 and 100% mortality with FSGI >11[38,172,182]. Some claim usefulness in predicting survival but not the length of hospital stay[142]. Of the nine parameters of FSGI, temperature, heart rate and respiratory rate were considered to be the most important[1]. APACHE II score correlated with the prognosis with a significant increase in mortality with a score over 25[183]. Other indices include age-adjusted Charlson Comorbidity Index (ACCI)[184] and the surgical Apgar Score (sAPGAR)[185], which are easily calculated at the bedside but the prognostic power is controversial[186].

***Anorectal causes of Fg***

The disease usually behaves more aggressively, produces severe systemic toxicity, and is associated with higher mortality than FG from other causes[73,99,161,187]. The survival of female patients is 71%[29]. Survival varied from 0% to 85.7% and was presented in only four articles (Table 1). The real incidence and prognosis of any specific cause cannot be calculated from the available data.

One of the inaccuracies with previously mentioned indices is that these do not evaluate the influence of the underlying cause on prognosis, duration of hospitalization, number of debridements or other parameters. It was previously stated that different primary locations and causes (could) have different prognoses. Yilmazlar *et al*. modified FGSI adding the dissemination score (plus age) making the Uludag FSGI (UFGSI) for all-cause FG[43].

***Rectal cancer-induced FG***

Rectal cancers that spontaneously perforate without the development of FG seem to be much more aggressive than rectal cancer in general, as a significantly larger proportion of these patients have metastatic disease at the time of diagnosis (64% *vs* 29%). Survival in patients with locally contained perforated rectal cancer is very much dependent on the presence of metastatic disease. In the absence of the latter, if a wide margin clear of all macroscopic tumor is achieved, the survival curve approximates that of patients with a non-perforated tumor[188].

Duration of hospitalization cannot be obtained for disease-specific or even etiology-group-specific FG (Table 1). Duration of hospitalization of rectal cancer-induced FG ranges 23-130 d. Unfortunately, only 30% of cases have these data (Table 3). None of the articles presented BSA and correlation with survival could not be made (Table 3).

FSGI was calculated in only one of 23 rectal cancer-induced FG cases and no other scoring systems were used or have data for calculations (Table 3). The overall prognosis is as follows: survival 74%, mortality 13% and for 13% there was no data (Table 3).

There are many limitations of these studies for final conclusions. First, long-term follow-up is lacking. Therefore only prognosis of FG (due to rectal cancer), not the prognosis of rectal cancer itself after surviving FG, is known. Long-term survival is unknown because less than 50% of surviving patients had follow-up for one year or more (Table 3). Second, prognostic comparison between T4 rectal cancer, perforated rectal cancer, and rectal cancer-induced FG groups considering long-term survival cannot be made. Presumption is that the prognosis of rectal cancer-induced FG could be worse due to: (1) significant delay in starting adjuvant chemoradiotherapy in survivors; and (2) inflammation due to perforation of rectal cancer aids in spreading or promoting cancer cell dissemination. Third, analysis of the influence of the type of surgical procedure is insufficient due to the rarity of this pathology and (potentially) low rate of published cases that did not survive any form of surgical treatment. In the group that underwent APR, whether as initial operation (13%) or delayed after colostomy (26%), survival was 100%. Hartmann’s procedure as the initial operation was performed in 8.7% with the survival of 100% (Table 3). On the contrary, the survival with only loop colostomy was 80% (Table 3). The conclusions cannot be drawn because there is no possibility of comparison. Therefore, patients with the more advanced disease, poor general status, older age or hemodynamic instability could be offered only colostomy. Finally, it is important to emphasize that all patients that underwent rectal cancer resection survived.

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**Table 1 Anorectal causes of Fournier’s gangrene – incidence, colostomy rate, duration of hospitalization and survival**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Ref.** | **anorectal cause** | **male:female ratio** | **rectal cancer in all-cause group** | **Rectal cancer in anorectal cause group** | **colostomy (all-cause/rectal cause)** | **survival (all-cause/rectal cause)** | **the most common region** | **duration of hospitalization** |
| Benjelloun *et al*[12], 2013 | 70% | 44:6 | 0% |  | 10%/no data | 76%/no data | Scrotum | 21 |
| Bhatnagar *et al*[13], 2008 | 7.30% | Male only (110) | 0% |  | 4%/no data | 92.7%/no data | Scrotum | 19.3 |
| Cakmak *et al*[14], 2008 | 63.10% | 45:20 | 0% |  | 23.1%/no data | 70.3%/no data |  | 24.4 |
| Carrol *et al*[15], 1986 | 50% | 13:1 |  |  | 28.57%/no data | 79%/no data |  | 48 |
| Czymek *et al*[16], 2009 | 57.60% | 23:10 | 3% | 5.26% |  | 81.9%/no data |  |  |
| Efem *et al*[17], 1994 | 0% | Male only (20) | 0% |  |  |  | Scrotum |  |
| Eke *et al*[9], 2000 | 21% | 10:1 |  |  |  | 84%/no data |  | 2-278 |
| Eskitaşcıoğlu *et al*[18], 2014 | 20% | 19:1 | 2.50% | 50.00% | 15%/no dana |  | Scrotum | 34.78 |
| Fajdic *et al*[19], 2007 | 42.85% | Male only (7) | 0% |  | 14.3%/no data | 85.7%/no data | Perianal | 25.8 |
| Ghnnam *et al*[20], 2008 | 54.05% | Male only (74) | 0% |  | 1.4%/no data | 78.4%/no data |  | 9.2 |
| Rodríguez Hermosa *et al*[21], 2001 | 30% | Male only (10) | 0% |  | 30%/50% | 60%/75% | Scrotum | 27 |
| Jiménez-Pacheco *et al*[22], 2012 | 29.70% | Male only (37) | 0% |  |  | 95%/no data |  | 27.54 |
| Kahramanca *et al*[23], 2014 | 22.06% | 48:20 | 1.47% | 6.67% | 22.06%/no data | 92.65%/no data |  | 15.37 |
| Kara *et al*[24], 2009 | 33.30% | 10:5 | 0% |  | 53.3% no data | 80%/no data | Scrotum and perineum |  |
| Karbhari *et al*[25], 2014 | 20% |  | 0% |  |  | 80%/no data | Scrotum |  |
| Khan *et al*[26], 2009 | 21% | Male only (19) | 0% |  | 5.3%/no data |  |  | 26 |
| Khandelwal *et al*[27], 2013 | 24.60% | Male only (57) | 0% |  | 20.3%/no data | 68.5%/no data |  | 19.6 |
| Korkut *et al*[28], 2003 | 58% | 37:8 | 2.22% | 3.85% | 40%/no data | 80%/no data |  | 12 |
| Liang *et al*[29], 2008 | 87.50% | Female only (8) | 0% |  | 87.5%/85.7% | 75%/85.7% |  | 32.2 |

**Table 2 Anorectal causes of Fournier’s gangrene**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Ref.** | **Abscess** | **Hemorrhoidectomy** | **Hemorrhoids** | **Intestinal obstruction** | **Perianal fistula** | **RT for rectal carcinoma** | **Rectal carcinoma** | **Artificial sphincter** | **Anal fissure** | **Rectal injury** |
| Benjelloun *et al*[12], 2013 | 88.50% |  | 11.50% |  |  |  |  |  |  |  |
| Bhatnagar *et al*[13], 2008 |  | 75.00% |  | 25.00% |  |  |  |  |  |  |
| Cakmak *et al*[14], 2008 | 43.90% | 43.90% |  |  | 12.20% |  |  |  |  |  |
| Czymek *et al*[16], 2009 | 68.42% |  |  |  | 3.00% | 15.79% | 3.00% | 3.00% |  |  |
| Eskitaşcıoğlu *et al*[18], 2014 | 56.25% |  |  |  | 12.50% |  | 12.50% |  | 18.75% |  |
| Fajdic *et al*[19], 2007 | 33.30% |  | 33.30% |  | 33.30% |  |  |  |  |  |
| Ghnnam *et al*[20], 2008 | 90.00% | 10.00% |  |  |  |  |  |  |  |  |
| Rodríguez Hermosa *et al*[21], 2001 | 75.00% |  |  |  |  |  |  |  |  | 25.00% |
| Kahramanca *et al*[23], 2014 | 66.66% |  |  |  |  |  | 6.66% |  |  | 26.66% |
| Kara *et al*[24], 2009 | 60.00% |  |  |  |  |  |  |  |  | 40.00% |
| Khan *et al*[26], 2009 | 75.00% | 25.00% |  |  |  |  |  |  |  |  |
| Khandelwal *et al*[27], 2013 | 75.00% | 25.00% |  |  |  |  |  |  |  |  |
| Korkut *et al*[28], 2003 | 92.30% |  |  |  | 4.16% |  | 4.16% |  |  |  |
| Liang *et al*[29], 2008 | 100.00% |  |  |  |  |  |  |  |  |  |
| Oymacı *et al*[31], 2014 | 100.00% |  |  |  |  |  |  |  |  |  |
| Ozkan *et al*[32], 2014 | 62.50% |  |  |  |  |  | 25.00% |  |  | 12.50% |
| Singh *et al*[33], 2004 | 100.00% |  |  |  |  |  |  |  |  |  |
| Tan *et al*[36], 2006 | 40.00% | 40.00% |  |  |  |  | 20.00% |  |  |  |
| Unalp *et al*[38], 2008 | 100.00% |  |  |  |  |  |  |  |  |  |
| Villanueva Sáenz *et al*[40], 2002 | 88.00% |  |  |  | 8.00% |  | 4.00% |  |  |  |
| Walker *et al*[41], 1983 |  |  |  |  |  |  | 100.00% |  |  |  |
| Wang *et al*[42], 2012 | 91.00% |  |  |  |  |  | 9.00% |  |  |  |

RT: radiotherapy.

**Table 3 Case reports of Fournier’s gangrene as associated with perforated rectal cancer**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Ref.** | **Age/sex** | **Risk factors** | **duration of simptoms/****hospitalization** | **L/****CRP** | **starting point** | **DRE** | **MSCT (tumor, air)** | **rectoscopy** | **distance from AC border** | **microbiology** | **Operation** | **day of operation** | **outcome/survival** |
| Ash *et al*[46], 2005 | 33/m |   | 2/nd | 10/nd | scrotum |   | Yes (tumor, air) | No |   |   | colostomy | 1 |   |
| Carr *et al*[47], 2010 | 54/m | alcoholism |  nd/23 |  nd | scrotum, perineum, gluteus |   | Yes (tumor, no air) |   |   |   | APR | 1 | alive |
| Chan *et al*[48], 2013 | 78/m | smoker, hypertension, cerebrovascular accident, dyslipidemia | 5/nd | 36,8/nd | perineum, scrotum | Neg | Yes (tumor, air) | Yes | 10 cm | *E. coli* | colostomy | 5 | alive |
| Eke *et al*[49], 1999 | 65/m | diabetes |  nd/nd |  nd | penis |   |   |   |   | S. aureus | sigmoid colostomy |   | alive |
| Gamagami *et al*[50], 1998 | 45/m | diabetes | 4/nd |  nd | perianal | Pos |   | Yes |   | *E. coli*, Enterococi | loop colostomy/APR | 1/28 | alive/1 year df  |
| Gupta *et al*[51], 2010 | 55/m |   | 7/nd | 14,4/149 |   | Pos |   | Yes |   | *E. coli*, Bacteroides | colostomy |   | died |
| Highton *et al*[52], 2009 | 79/m |   | 2/nd |  nd | right thigh | Neg |   | Yes | upper | *E. coli*, anaerobes | end colostomy and mucosus fistula | 1 | alive |
| Katusic *et al*[53], 2010 | 65/m |   |  nd/23 |  nd | scrotum, perianal, right groin | Pos |   |   |   | *E. coli*, Pseudomonas | no colostomy |   | alive |
| Khalil *et al*[54], 2010 | 71/m | No  | 10/nd | 20/424 | right thigh | Neg | Yes (tumor, air) |   |   |   | Hartmann procedure |   | alive/6 year survival |

**Table 4 Classification, clinical aspects, anatomopathology and microbiology of necrotizing soft tissue infections**[96,113-116]

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Necrotizing fasciitis****Type 1** | **Necrotizing fasciitis****Type 2** | **Clostridium myonecrosis (gas gangrene)****Type 3** | **Fungal necrotizing fasciitis****Type 4** | **Clostridium fasciitis** | **Progressive bacterial****synergistic gangrene** | **Synergistic****necrotizing****cellulitis** | **Pseudomonas****gangrenous****cellulitis** | **Streptococcal myonecrosis****(nrcrotizing myositis)** |
| Pain | + / ++ | ++ / +++ | +++ | +++ | + | +++ | ++ / +++ | + / ++ | ++ / +++ |
| Anaesthesiaof lesions | In advanced stages | In advanced stages | - | - | - | - | - | - / + | - |
| Cutaneous signs | Edema, erythema, bullae, necrotic and ulcerated lesions | Edema, erythema, necrotic bullae | Pale, Yellow-brown discolourationof skin, Necrotico-hemorragic (brown) bullae | Edema, erythema | Minor edema, pale skin | Necrotic ulcer dusky margin anderythematous periphery at the margins of the wound | Cellulitis with foul-smelling,thick discharge from necrotic skin | Black/gray eschar.Dark dischargewith surroundingerythema, hemorrhagic bullae | Edema, copper coloured, blisters in advanced stage |
| Subcutaneous appearance of infection | Subcutaneous tissue and fascial necrosis | Subcutaneous tissue and fascial necrosis | Necrotic area composed of green-black patches.Serosanguinous. 'mousy'-smelling discharge, bluish muscles | Subcutaneous tissue, fascial and muscle necrosis |  | Subcutaneous tissue necrosis and gangrene | Dark pus or 'dishwasher' fliud |  | Seropurulent discharge |
| Systemic toxicity | + to +++ | + to +++(Toxic shock syndrome) | +++ | +++ | + | + | ++ to +++ | +++ | + to +++ (Streptococcal Toxic Shock Syndrome) |
| Fever | High | High | Moderate to high | High |  | Minimal or absent | Moderate | High |  |
| Progression | Moderate (3-14 d) | Very fast (1-3 d) | Very fast (1-3 d) | Very fast (1-3 d) | Moderate (> 3 d) | Moderate (3-14 d) | Moderate (3 to 14 d) | Moderate (3 to 14 d) | Fast (1-4 d) |
| Crepitus (gas) | - / + | - | +++ | ++ / +++ | ++ | - | + | - | - /+ |
| Deep fascias infection | - to ++ | + to +++ | +++ |  | + | - | - to ++ | - | - / + |
| Muscular infection | - / + (secondary) | - / + (secondary) | +++ |  | - | - | + to +++ | - | +++ |
| Site of entry, initiating factor | Wound, vascular lesion, surgery, local infection | Trauma, surgery, cutaneous lesion, burn, erysipelas, varicella | Non penetrating trauma, limb crushing, im. injection, sepsis | Trauma, surgery | Wound, surgery | Surgery | Prior local lesions, perirectal lesions | Trauma, surgery | Trauma, surgery, muscle strain |
| Risk factors | Diabetes mellitus | Vascular disease | Immunosuppression | Immunosupression | Diabetes mellitus |  | Diabetes mellitus | Immunosupresson | Immunosupression |
| Miocrobiology | Enterobacteraceae, Anaerobes, Streptococcus, Staphyloccocus | Group A Streptococcus,methicillin-resistant S. aureus (MRSA) | C. perfingensC. septicum / Vibrio spp. | C. albicansC. neoformans | C. perfingens, C. septicum | Staphylococcus aureus, microaerophilic streptococci, Enterobacteriaceae | Mixed aerobes and anaerobes | Pseudomonas aeruginosa | Group A Streptococcus |

***Fournier’s gangrene*** with suspected **rectal cancer**

Digital rectal examination

Negative

Perforated tumor

Non-perforated tumor1

Preoperative or intraoperative

rectoscopy2

Abdominopelvic CT scan

Fournier's gangrene not

due to rectal cancer

Confirmation/suspicion of

rectal cancer perforation3

±

Transversostomy/sigmoidostomy

Unstable patient

(Extralevator) abdominoperineal resection

Stabilization4

Stable patient

Hartmann's procedure

**Figure 1 Diagnostic-therapeutic algorithm for suspected/proven Fournier’s gangrene due to rectal cancer.** Perioperative management and necrosectomy are excluded which are standard procedures in Fournier’s gangrene treatment in all patients. 1Impalpable perforation does not exclude microperforation; 2(1)blood (any form) on digital rectal examination; (2) history and other/previous diagnostic modalities refer to rectal carcinoma; (3) urogenital and dermatologic causes excluded; (4) bacteria highly specific for (intestinal) rectal malignancy such as *Clostridium septicum*; and (5) fever or sepsis of unknown origin with perianal symptoms/signs; 3increased soft tissue density with abscess and/or gas bubbles around the tumor; 4After confirmation of rectal cancer, definitive oncologic operation is performed after stabilization and neoadjuvant chemoradiotherapy if indicated. Reconstructive surgery after consultation with plastic surgeon.