Fournier's gangrene : What are the prognostic factors? Our experience with 40 patients

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La gangrene de Fournier : Quels sont les facteurs pronostics ?
Notre experience a propos de 40 patients

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RÉSUMÉ

Prérequis : La gangrène de Fournier (GF) est un état infectieux grave et fulminant infestant les organes génitaux externes et le périnée. Et, malgré un traitement approprié, le taux de mortalité reste élevé en cas de GF.

But : Etudier les facteurs de survie des patients atteints de GF et évalué l'intérêt de l'étude de l'index de sévérité de la gangrène de Fournier (ISGF).

Méthodes: Entre 1995 et 2010, 40 patients atteints de GF ont été traités dans notre institution. Ils ont tous bénéficié d'une triple antibiothérapie à large spectre, une large excision et un nettoyage exhaustif de la plaie. Ils ont ensuite subi des greffes cutanées ou une fermeture secondaire en cas de nécessité. Les données ont intéressé la démographie de patients, les antécédents médicaux, les facteurs prédisposant, des agents étiologiques, les signes et la symptomatologie clinique des patients à leur admission, leur examen physique, ainsi que les données biologiques et bactériologiques. Le délai et l'importance de l'excision des lésions nécrotiques ainsi que leur résultats ont également été examinés. L'étendue des lésions cutanées malades a été calculée à partir de nomogrammes de la surface corporelle.

Résultats: Tous nos 40 patients inclus dans cette étude étaient des hommes, leur âge moyen était de 52,75 ans (21-75 ans). Douze (30%) avaient une GF en rapport avec une pathologie anorectale. Chez 6 patients (15%) aucun facteur étiologique n'a pu être identifié. Le diabète sucré s'avérait être un facteur prédisposant chez 13 patients (32,5%). Le délai moyen de consultation était de 8,72 jours (extrêmes: 3 à 30). Tous nos patients ont eu une excision du tissu nécrotique. Une orchidectomie a été réalisée dans 7 cas (17,5%). La greffe de peau a été faite chez 6 patients (15%). Le taux global de mortalité était de 17,5%, due à l'acidose métabolique grave et à la septicémie. Nous avons comparé dans deux groupes: ceux qui sont décédés (n = 7) et ceux qui ont survécu (n = 33). Les paramètres biologiques à leur admission qui semblent corréler de façon statistiquement significative avec le pronostic étaient l'hématocrite (p= 0,003) et la natrémie (p = 0,05). L'étendue de la surface cutanée affectée chez les patients décédés n'était pas significativement différente de celle chez ceux qui ont survécu (4,07% et 3,14%, p=0,4). La moyenne de l'ISGF (sans compter le taux sérique de bicarbonate) pour les survivants était de 9,1 comparé à 6,8 pour les décédés (p = 0,16).

Conclusion: La GF est une infection fulminante rapidement progressive. Notre étude montre que l'hématocrite et la natrémie ont une valeur pronostique à l'inverse de l'ISGF qui ne semble pas avoir de valeur pronostique.

Mots-clés

Gangrène de Fournier, fasciite nécrosante, idiopathique, étiologie, traitement, évolution, mortalité, Pronostic.

SUMMARY

Background : Fournier's gangrene (FG) is a serious, extensive fulminant infection of the genitals and perineum. Indeed, despite antibiotics and aggressive debridement, the mortality rate of FG remains high.

Aim: Through our experience, we intent to identify effective factors in the survival of patients with FG and we try to determine how the Fournier's gangrene severity index score (FGSIS) is accurate.

Methods: Between 1995 and 2010, 40 patients with Fournier's gangrene were treated in our institution. All of them were treated with broad-spectrum triple antimicrobial therapy, broad debridement and exhaustive cleaning. Then they underwent skin grafts or delayed closure as needed. Data were collected on demographics, medical history, predisposing factors of FG, etiological infection agents, admission signs and symptoms, physical examination, admission laboratory studies and bacteriology. Timing and degree of surgical debridement as well as outcomes were also reviewed. The extent of disease was calculated from body surface area nomograms.

Results: All the 40 patients included in this study were males; their mean age was 52,75 years (21-75 years). Twelve patients (30%) had FG secondary to anorectal pathological conditions. No etiologic factors of FG were found in 6 patients (15%). Diabetes mellitus as predisposing factor was found in 13 patients (32.5%). The mean hospital stay was 8.72 days (range, 3 to 30). All the patients underwent surgical debridement. Orchidectomy was done in 7 cases (17.5%). Skin grafts were applied to 6 patients (15%) and the remaining wounds, once cleaned, were approximated. The overall mortality rate was 17.5% (7 patients) due to severe metabolic acidosis in relation to diabetic decompensation and sepsis.

We individualized two groups: those who died (n = 7) and those who survived (n = 33). We evaluated the admission laboratory parameters that are significantly correlated with outcome included hematocrit (p=0.003) and serum sodium (p=0.05). The extent of body surface area involved among patients who died was not found significantly different statistically between the two groups (4.07% and 3,14%, p=0,4). The mean FGSIS (without counting bicarbonate serum level) for survivors was 9.1 compared with 6,8 for nonsurvivors (p=0.16).

Conclusion: FG is a rapidly progressive, fulminant infection's condition. Hematocrit and serum sodium levels were found to be the only prognostic factors. It doesn't seem that the FGSIS has a prognostic value.

Key-words

Fournier's gangrene, necrotizing fascitis, idiopathic, etiology, treatment, outcome, mortality, prognosis.

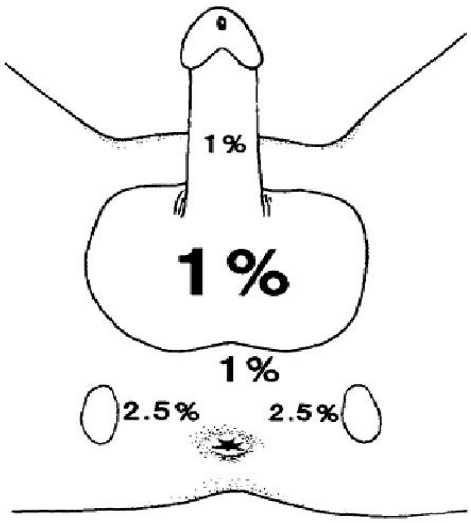
Fournier's gangrene (FG) is a rare but extremely serious necrotizing fasciitis of the genitourinary tract (1). Despite antibiotics, aggressive debridement and modern intensive care techniques, the mortality rate from FG remains still high at between 30% to 50% (2-6). The factors affecting survival or death from FG are not clearly identified, measured and analyzed in the literature even with the Laor study (2) in 1995. We reviewed our experience on 40 patients who were treated for FG and intent to determine these prognostic factors and to identify the effective factors in the survival of the disease.

METHODS

All our patients diagnosed with FG were admitted to our Department of Urology, between January 1995 and January 2010. Their medical records were collected in details, they were related to demographics, medical history, admission symptoms, physical examination and laboratory results: age, aetiology, existence of co-morbidities, predisposing factors, duration between the onset of symptoms and surgery, culture findings, and clinical outcome. The general conditions of patients were studied, with special emphasis on their body temperature, heart and respiratory rates, and blood pressure. Biochemical (serum creatinine, and albumin), hematologic (hematocrit,white blood cell count, platelet count and prothrombin ratio), and bacteriologic study results were also noted at admission. Presence of confusion, hypotension (systolic BP<80mmHg), leukocytosis (>15,000), and fever (>38°C) were considered as sepsis criteria.

The antibiotic therapy used and the timing of debridement were all recorded. The extent of surgical debridement was calculated from modified body surface area nomograms routinely used to assess the extent of burn injuries: the penis, scrotum and perineum accounted for 1% surface area each, each ischiorectal fossa 2.5% and so forth (Figure 1).

Figure 1 : Percentage allocation of perinael surface area



The surface area was evaluated according to the operative photos, schemas and surgeon description. We used the Fournier's gangrene severity index (Table 1) created by Laor et al (2) in 1995. According to this score, 9 parameters were measured in every case and the degree of deviation from normal was graded from 0 to 4. The individual values are summed to reach the FGSI score (FGSIS). These parameters are temperature; heart rate; respiratory rate; serum sodium, potassium, creatinine, and bicarbonate levels; hematocrit and leukocyte count (Table 1). In our series, bicarbonate level was not available in almost all cases. Thus FGSIS was calculated without this parameter.

Table 1 : Répartition des patientes selon les signes fonctionnels

VARIABLE	+4	+3	+2	+1	0	+1	+2	+3	+4
Temp: (^{0}C)	>41	39-40.9	-	38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	<29.9
Pulse rate	>180	140-179	110-139	-	70-109	-	55-69	40-54	<39
Respiratory rate (b/min)	>50	35-49	-	25-34	12-24	10-11	6-9	-	<5
Serum Na^+ (mmol/l)	>180	160-179	155-159	150-154	130-149	-	120-129	111-119	<110
Serum K^+ (mmol/l)	>7	6-6.9	-	5.5-5.9	3.5-5.4	3-3.4	2.5-2.9	-	<2.5
Serum Creatinine (mg/100ml)	>3.5	2-3.4	1.5-1.9	-	0.6-1.4	-	<0.6	-	-
Haematocrit (%)	>60	-	50-59.9	46-49.9	30-45.9	-	20-29.9	-	<20
WBC (total / mm^3 x1000)	>40	-	20-39.9	15-19.9	3-14.9	-	1-2.9	-	<1
Serum Bicarbonate (mmol/l)	>52	41-51.9	-	32-40.9	22-31.9	-	18-21.9	15-17.9	<15

Table 2 : Predisposing medical or surgical illnesses

Condition	No. Survived	No. Died	Total
Diabetes mellitus	9	4	13
Peripheral vascular disease	2	1	3
Hepatic dysfunction	1	0	1
Cardiac disorders	2	0	2
Spermatic cord / Testis trauma	2	0	2
Hypertension	2	0	0
Urethral involvement/ manipulation	3	1	4
Malignancy and chemotherapy	1	1	2
Hemorrhoidectomy	0	3	3
Vitiligo	1	0	1
Acute pancreatitis	0	1	1
Stroke	2	0	2
Paraplegia due to spinal trauma	2	1	2
Recent uretritis	1	0	1

Data were evaluated stratified by whether the patient survived or died. Mortality was defined as disease-related death during the hospital stay and survival was measured in days. Statistical analyses were carried out by using the statistical packages for SPSS 15.0 for Windows (SPSS, Chicago, IL, USA) with $p < 0.05$ considered significant.

RESULTS

All patients included in this study were males. Their mean age was 52.75±10.8 years (ranges 21-75 years). All of them were from a low socioeconomic class with poor hygiene standards, and 6 of them had a long history of active alcoholic abuse. Thirteen patients (32.5%) were diabetics (Table 2).

Two patients were operated of bladder tumor and two for uretral stenosis. Four of the patients had two or more predisposing disorders for FG. No definite predisposing factor was reported in 12 patients (30%). Twelve patients (30%) had FG secondary to perineal conditions (perianal abscess (n=2) and periurethral abscess (n=10)). Twenty one patients (52.5%) developed FG secondary to urogenital infections (scrotal abscess in 17 patients, penile trauma in 2 patients and after endoscopic urethrotomy for urethral stenosis in two patients) and secondary to tourniquet penis strangulation in the last case. No etiologic factors for FG were found in 6 (15%) patients and they were classified as idiopathic FG. The mean duration from the onset of symptoms to hospital admission was 8.72 ± 2.09 days (range: 3-30 days). The diagnosis of FG was clinical. Patients consulted for varying signs and symptoms:

- Swelling and redness in the perineal area: 12 patients (30%).
- Scrotal swelling and erythema in all cases.
- Genitoscrotal pain: 31 cases (77.5%)
- Purulence or wound discharge in almost all cases: 36 patients (90%).
- Fever greater than ≥ 38°C: 18 patients (45%)
- Indurations, necrosis, gangrenous patches of the skin (Figure 2): 8 patients (20%)

Figure 2: Necrosis and cutaneous gangrenous patches in the penis

- Crepitation or fluctuance: 14 patients (35%).
- Lower urinary tract symptoms: 7 patients (17.5%).

In addition, five patients had severe metabolic acidosis, 13 patients were admitted with sepsis (45%) and two patients were unconscious on presentation.

Infection was located in the scrotum (n=31), the penis (n=17), the perineum (n=12) and the inguinal region (n=12). It was extended to the lower abdomen (n=15) and there was extension to unilateral or bilateral femoral regions in two patients. Bacteriologic studies were done in five cases only and revealed Escherichia coli (n=4) and coagulase-negative staphylococcus in one case. No anaerobic cultures were performed.

Before surgery, all patients underwent aggressive fluid resuscitation and were treated with parenteral broad-spectrum triple antimicrobial agents, using metronidazole (n=32), cephalosporin of the first and the third generation (8 and 3), fluoroquinolone (n=5), an aminoglycoside such as gentamicin

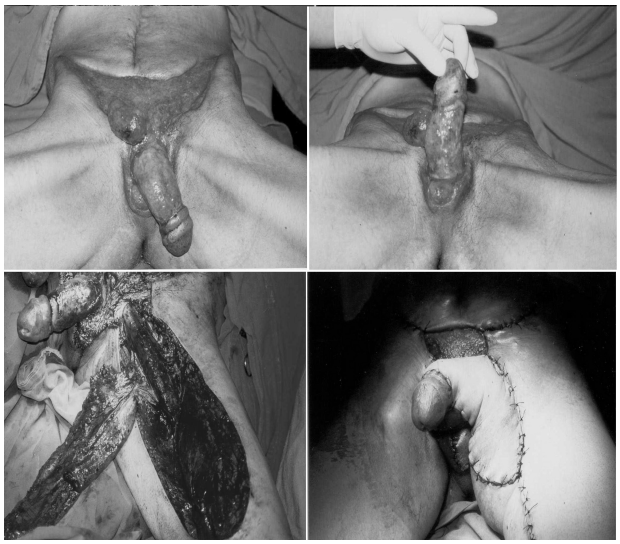
sulfate (n=25) and amikacin in one case, colistin (n=3) and beta-lactamin (n=20). They received hemodynamic support when required, mechanical ventilation, continuous monitoring, and inotropic support were applied when necessary. All patients underwent aggressive and extensive surgical debridement (Figure 3).

Figure 3: Large debrided and denuded areas reaching the left axilla

The areas of debridement were initially irrigated by hydrogen peroxide, then saline, and packed with dressings soaked in povidone-iodine. After the initial surgery, the wound was closely monitored, adequate nutrition was ensured to support wound healing and early enteral feeding was considered. The wounds were cleaned with hydrogen peroxide, hypertonic saline (10% sodium chloride solution) and povidone -iodine 2 times a day. Patients underwent repeated debridement, two or more days after the first and further necrotic tissues were debrided when needed under local or no anesthesia. Because of necrosis, orchidectomy was necessary in 7 patients (bilateral in one case) and penis amputation in one case. Urinary diversion was made via suprapubic cystostomy in 12 patients and transurethral catheter in 6 patients. One patient underwent diverting colostomy to avoid fecal contamination. Once cleaned, twelve patients were managed by local advancement. Skin grafting was reserved only for cases with lost skin without available local skin cover (n=6) (Figure 4). Multiple free split-thickness patch skin grafts "in mosaic" were harvested from the ventral aspect of the thigh and applied to 3 patients (16%) and rotational flaps in 3 cases. The 22 remaining patients underwent delayed closure once their wounds were clean and viability established. Only 4 patients had their testes reimplanted into the groin with scrotal reconstruction (Figure 4).

One patient developed perineal fistula four months later and was treated successfully by endoscopic urethrotomy and transurethral stenting. Seven patients (17.5%) died because of septicemia and severe metabolic acidosis.

Figure 4: Postoperative view: skin grafting with testes reimplantation



They were over 50 years of age in 5 cases and four of them had diabetes.

Of the evaluated 40 patients, 7 died (17.5%) and 33 survived (92.5%). The difference in age between those who survived (mean age/ 52.24 years, range 21 to 75) and those who died (mean age 55,14 years, range 35 to 67) was not statistically significant (p=0,96). The most common co-morbidity was diabetes mellitus; 9 survivors (27.3%) and 4 who died (57.1%) were diabetic. The difference was not statistically significant (p=0.58).

The difference in the duration of symptoms before presentation was not statistically significant between patients who survived (9.1 (3-30) days) and those who died (6.8 (3-15) days (p=0.16).

The mean extent of the body surface area involved in the necrotizing process in patients who survived and those who died was 3.14% and 4.07%, respectively (p=0.43).

The number of surgical debridements did not seem to influence patient outcome (p=0.39); up to four times debridement procedure were performed in two patients. As it can be seen in Table 3, the statistically significant parameters for a bad prognosis and death were as follows: low hematocrit (p=0.003) and sodium (p=0.05) levels.

None of the following parameters seems to influence the patient's outcome: late consulting (p=0.94), high creatinine (p=0.79), leukocyte and platelet count (p=0.10 and 0.44 respectively) levels, and low potassium (p=0.55), low prothrombin ratio (p=0.16) and high glycemia (p=0.33) levels at admission evaluation.

The mean admission FGSIS for survivors and those who died was 6.4 and 7.57 respectively (p=0.2) (without serum bicarbonate level). Of the nine parameters, only hematocrit and serum sodium levels affected the outcome. With a FG severity index value of 9 or 8 as a threshold, we didn't find any prognostic interest of the FGSIS.

DISCUSSION

FG is a serious infectious condition, thus, its diagnosis must be done early. According to this study, only low levels of hematocrit and serum sodium were found to be prognostic factors after surgical debridement and under antibiotherapy. It doesn't seem that the FGSIS and the other parameters of this score have a prognostic value. FG is defined as a fulminant form of infective necrotizing fascitis of the perineal, genital or perianal regions, which commonly affects men, but can also occur in women and even children (3). It is a relatively rare condition and its true incidence is unknown. A meta-analysis was able to identify about 1726 cases published from January 1950 to September 1999 (4). The greatest number of cases occurs between the ages of 20 and 50 years (4) (15 cases in our series). But, the reported age of patients with the disease has progressively increased in the published data. In 1984 Spirnak et al. (5) reported 54.6 years old. Laor et al (2) in 1995 reported an average age of 61 years. The mean age of our patients was 52.7 years.

This entity is a synergistic gangrene secondary to a polymicrobial flora with a poorly defined portal of entry (6). Recent studies suggest that the periurethral glands may be the primary source of the infecting organisms (7). The cutaneous manifestations are merely the tip of iceberg as the infection spreads along the dartos fascia planes, the scrotum and penis, Colles' fascia of the perineum, and Scarpa's fascia of the abdominal wall (8). The extent of the involved area may reach the abdominal wall, axilla, and thighs (1).

It is believed, actually, that systemic conditions such as diabetes mellitus, alcoholism, smallpox, measles, paralysis or neurological deficit, paraplegia, cirrhosis and debilitated and immunosuppressed individuals are predisposed to the development of this entity (5,8-11). Although one study reported that diabetes is not a prognostic factor in the outcome (12). The findings from the present study support these results because 32.5% of our patients were diabetics but no significant difference of co- morbidities was observed between groups either who survived or died. Several local predisposing factors have been reported, including perianal disease, urethral stricture, local trauma, and malignancy (13, 14).

Most of the patients presented within the first week of initiation of symptoms. No significant difference of timing of presentation was observed between survival and dead groups ($p=0.94$).

FG shows vast heterogenicity in clinical presentation, from an insidious onset and slow progression to rapid onset and fulminant course; the latter being the more common. It starts with a prodromal period of genital discomfort or pruritus, followed by genital erythema, pain, swelling, and crepitation, revealing subcutaneous gas formation of the perineal and/or genital regions. There is often crepitus and areas of gangrene or blister formation on the skin (1, 15).

Both anaerobic and aerobic (Gram-negative enteric bacilli and Gram-positive cocci (16, 17) organisms isolated from wound cultures have been quoted as an important bacteriologic principle in FG (2). Paty and Smith (14) found E. coli, Bacteroides, and streptococci to be the most common organisms. Laor and Yeniyol (1, 2) concluded that the most common organisms were E. coli and Streptococcus species, followed by Staphylococcus and Enterococcus which were more commonly isolated than Bacteroides (2).

The management of this infectious entity should be critical and aggressive:

- Triple broad-spectrum antibiotics active against both aerobic and anaerobic microorganisms must be immediately administered parenterally.
- Debridements and excision of all frankly necrotic tissue or that with doubtful viability.

Surgical debridement plays the key role (16) and its aim is to remove all non-viable tissues, halt progression of infection and alleviate the systemic toxicity. Appropriate medical and surgical treatment is mandatory to limit severe sloughing and sepsis (8). A minority of patients require split-thickness skin grafts on denuded areas. Skin grafts were applied on denuded clean areas in 6 of our patients with excellent results. The remaining patients had wound healing by delayed closure.

Testes and spermatic cords are generally not affected by the disease, since they maintain an adequate and independent blood supply (18). In a recent study by Ayan et al., who retrospectively reviewed records of 41 patients with FG, bilateral orchidectomy were done in four patients (9.7%) and unilateral orchidectomy in five patients (12.1%) due to necrosis (19). In a review by Smith et al., orchidectomy was performed in 21% patients; in most cases, the indications of orchidectomy were preexisting epididymorchitis or scrotal abscess (3).

In our study, 7 patients underwent orchidectomy because of gangrenous testis damage and 4 needed subcutaneous testicular repositioning.

Colostomy is sometimes needed to decrease fecal contamination, especially so in the presence of infective sphincteric destruction or rectal perforation (13, 20, 21). It was done once in our series since the perianal area was extensively involved in the gangrene.

Appropriate urinary diversion can usually be accomplished by a Foley's catheter unless urethral disruption or stricture coexists. Suprapubic cystostomy was performed in 12 patients because of the urethral extension of the gangrene or urethral injury.

Adjuvant therapy such as the irrigation of wounds with hydrogen peroxide to generate nascent oxygen to destroy the anaerobic organisms or the use of hyperbaric oxygen have all been tried with justifiable results (22). Even unprocessed honey dressings were applied on the wounds for a period of 10 days as reported by Hejase et al (10).

Since the initial reports (5, 8, 23), FG seems to be less and less fulminant (5, 13). But even with appropriate treatment approaches, mortality is high as 4 to 67% (11, 24, 25). Mortality rates would be due to the rapid progression of the disease associated with sepsis and the presence of other co-morbid conditions. In our study, the overall mortality rate was 17.5%. Such a high ratio means that this disease is still serious and fatal in Tunisia.

In published reports, the factors affecting survival or death from FG were not clearly identified until the study of Laor and colleagues in 1995 (2), in which measurable pathophysiologic data between survivors and non survivors of FG were compared.

Clayton et al. (13) found that patients who survived were significantly younger statistically than those who died of FG (52 and 69 years old, respectively). Although age did not seem to correlate directly with mortality in our series (p=0.88), in the older population, a debilitated state has a negative impact on survival. These patients generally do not take care of themselves, do not eat well, do not live in hygienic conditions, and tend to ignore accompanying illnesses, which go untreated, and, thus, their prognosis is worse.

In addition, some particular diseases, such as cardiac failure, hypertension and renal insufficiency have an adverse effect on survival. Diabetes mellitus did not seem to affect the outcome (14) as in our study.

Many authors find higher mortality rate in patients presenting late to hospital (26, 27).

In our series, most of patients consulted within the first week and the area involved with FG was small (≤5% in 75% of cases), which enabled us to start effective surgical debridement and medical therapy of both fasciitis and the predisposing illnesses in time.

When we considered the admission biological parameters, we found that those who died had lower leukocyte and platelet counts, creatinine, prothrombin ratio, and hematocrit; and greater sodium, potassium and glycemia levels than did the survivors. However, the differences in all these parameters were not statistically significant. Only lower hematocrit and serum sodium levels have prognostic values.

Yeniyol et al (1) found that those who died had greater leukocyte counts, urea, creatinine, alkaline phosphatase, and lactate dehydrogenase levels, and lower hematocrit, bicarbonate, sodium, potassium, total protein, and albumin levels than did the survivors. The differences in all these parameters were statistically significant. Lower serum albumin and total protein levels both reflect debilitation and a bad prognosis and were directly related to mortality.

Laor et al.(2) stated that patients who survived had significantly greater hematocrit, serum calcium, albumin, and cholesterol levels and lower blood urea nitrogen and alkaline phosphatase levels compared with the admission laboratory results. Clayton et al. (13) found that only blood urea nitrogen greater than 50 mg/dL was statistically significant for mortality.

However, because these clinical and laboratory parameters, taken individually, do not seem to be enough sensible to measure in the clinical situation, Laor et al. (2) created the FGSIS. They found that the mean FGSIS for survivors was significantly lower than for nonsurvivors and correlated with the death rate. They concluded that when an FGSIS of 9 is used as a threshold parameter to predict the outcome, those with a score greater than 9 had a 75% probability of death, and an index score of 9 or less was associated with a 78% probability of survival (2). In our study, we did not find the same data. Certainly we didn't include the "bicarbonate level" as a parameter in the score, but more studies are needed to better evaluate this score.

The mean extent of body surface area involved in the necrotizing process in our patients was not statistically different between those who survived and those who died, suggesting that the extent of disease is not predictive of outcome (p=0.43). We find it difficult to discount the importance of this parameter. It is conceivable that if this difference were maintained in a larger sample size, statistical significance would be reached. Although Clayton et al.(13) and Laor et Yeniyol (1, 2) suggested that the extent of disease was not predictive of outcome as in our series, Spirnak et al.(5) associated the greater mortality rate for patients who underwent more frequent operations due to greater extent of the disease.

We didn't found that the extent of body surface area involved in the necrotizing process or the number of operations were related to mortality (p=0.4 and 0.39 respectively).

This, may be because they did not survive longly enough for a possible other debridements. Aggressive surgical debridement always suggests a positive effect on survival (2, 5).

CONCLUSION

FG is a serious infectious disease. Deviation from a metabolic balanced status at presentation may be the most important general parameter that predicts outcome especially hematocrit and serum sodium. We are not sure that the FGSIS can be used to evaluate the therapeutic options and to predict the outcome.

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