Case series of Fournier's gangrene: Affected body surface area — The underestimated prognostic factor

CrossMark

Henrique Morais[*], Jessica Neves, Hugo Maciel Ribeiro, Marta Ferreira, Narcisa Guimarães, Nuno Azenha, Raquel Dias, Alice Fonseca, Lucilia Conceição

Department of Surgery, Hospital Distrital da Figueira da Foz, 3094-001, Figueira da Foz, Portugal

HIGHLIGHTS

- Fournier's gangrene is a devastating disease that challenges the modern medicine.
- Predicting the outcome may be a crucial step in his management.
- Current scores are not always effective.
- Affected body surface area is a key factor in patients outcome.
- Current scores may be improved with the inclusion of affected body surface area.

ARTICLE INFO

ABSTRACT

Objectives: Identifying the factors affecting the outcome of patients with Fournier's Gangrene and assaying the accuracy of the Fournier Gangrene Severity Index (FGIS), the Uludag score (UdS), affected Body Surface Area (BSA) and the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) model as prognostic tools.

Materials and methods: Retrospective study involving all patients with Fournier's gangrene treated in our Hospital between January 2008 and December 2015. The epidemiological, clinical, biochemical and management data of these patients was obtained and analyzed.

Results: The series includes 19 patients, 14 male and 5 female, with a median age of 70 (62; 78,5) years. The mortality rate was 21%. From the data analyzed, only the affected BSA (BSA>3.25%) was associated with mortality (p = 0.016). None of the established scores (FGSI; UdS; LRINEC) proved to be a useful tool for predicting mortality. The combination of affected BSA and FSGI (FGSI≥9 or BSA>3.25%), (p = 0.004) and the combination of the affected BSA and the LRINEC model (LRICEC≥8 and BSA>3.25%), (p = 0.004) led to a major improvement in these scores.

Conclusions: Affected BSA is a useful prognostic factor in Fournier's gangrene. The existing prognostic scores can be improved with the introduction of this factor.

1. Introduction

Fournier's gangrene is a life-threatening condition that can be defined as a necrotizing fasciitis of the perineum and genital area. It has the ability to spread to the adjacent areas, namely the abdominal wall and the retroperitoneal area. It was first described in 1764 by Baurienne [1], but was named after the description made in 1883 by French Venereologist Jean Alfred Fournier [2]. Despite the insight into physiopathological mechanisms thereof, technological progress and the improvement of clinical practice, mortality remains dramatically high [3], around 20–30% without a clear decreasing trend.

Fournier's gangrene is a surgical emergency and its early recognition, prompt and aggressive treatment remain the cornerstones of management.

The factors affecting the outcome of these patients remained unclear until the study by Laor et al. in 1995 [4]. Their work led to the Fournier's Gangrene Severity Index — FGSI, which is a score calculated from clinical and laboratory data at admission (heart and

respiratory rate, temperature, leukocyte count, hematocrit and serum sodium, potassium, creatinine and bicarbonate). A score >9 is associated with a 75% probability of death and a score ≤9 with a survival probability of 78%.

Affected body surface area (BSA) is one of the ongoing trends in the search for prognostic factors in Fournier's Gangrene. However, there is no consensus regarding his prognostic value. Some reports show that patients with higher affected BSA are more likely to succumb to the disease [5–8] and more likely to need multiple debridements. These findings led Yilmazlar et al. in 2007 [9] to propose a modification of the FGSI score, the Uludag score (UdS) which adds age and extension by anatomical regions. The authors stated that patients with a score ≥9 were 13.64 times more likely to die [10].

The Laboratory Risk Indicator for Necrotizing Fasciitis [11] (LRINEC) is a validated model, based on laboratory blood tests (leukocyte count, hemoglobin and serum sodium, creatinine, glucose and C-reactive protein) for diagnostic purposes, allowing an earlier establishment of necrotizing fasciitis diagnosis. A score ≥8 is a strong predictor of the disease. Some works validated its prognostic capability in Fournier's gangrene [12–14], but the optimal cut-off value remains undefined.

The aim of this paper is to identify the factors affecting the outcome of patients with Fournier's gangrene and to determine the accuracy of FGSI, UdS, affected BSA and the LRINEC model as prognostic tools in our population.

2. Materials and methods

This is a retrospective study from a single center. The study was registered with the Research Registry under the single identifying number researchregistry1656. Our work follows the PROCESS guidelines [15] for reporting case series in surgery.

This case series is based on the data of all patients diagnosed with Fournier's gangrene who were treated and followed in the Department of General Surgery, at Figueira da Foz District Hospital (community hospital), in Figueira da Foz (Portugal), between January 2008 and December 2015. Due to the retrospective nature of the study, and once assured the confidentiality of the data, the approval by the Hospital Ethical Committee is unnecessary.

Inclusion criteria: Necrotizing fasciitis evolving the anterior and/ or the posterior perineum. Exclusion criteria: Necrotizing fasciitis secondarily affecting the perineum. The diagnosis was established exclusively on the basis of clinical criteria. A total of 19 patients meeting these criteria were found.

Data concerning medical history, signs and symptoms upon admission, etiological factors, physical examination, laboratory data, microbiological studies, the timing and extent of surgical debridement, antibiotic therapy, timing and need for further surgical debridements and timings for reconstruction was collected.

Patients were divided in two groups: survivors and non-survivors.

The FGSI, UdS and LRINEC scores were calculated based on admission data. The affected body surface area (BSA) was calculated based on the nomograms routinely used to assess the extent of burn injuries. These nomograms were modified for use in Fournier's gangrene [5]: penis, perineum and scrotum each account for 1% of the affected BSA, ischiorectal fossa accounts for 2.5% as shown in Fig. 1.

2.1. Treatment considerations

After the diagnosis fluid resuscitation was promptly initiated with crystalloid fluids, the Foley catheter was placed to monitor resuscitation and to minimize perineal contamination. Urine
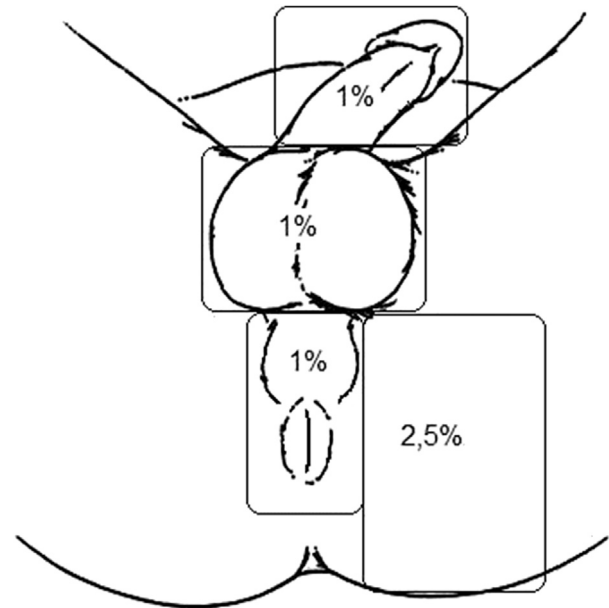

Fig. 1. Adapted nomogram for determining affected BSA.

samples for cultures were obtained. Empiric antibiotherapy was started, in two cases with penicillin and aminoglycosides, in one with third generation cephalosporin and metronidazol, and in the rest with carbapenems. The regimen was later reviewed taking in account culture results.

Ultrasound assessment was carried out when the exact location of fluid collections and their extent was uncertain. Color Doppler was used to assess the testicular blood flow.

Surgical debridement took place in the operating theater and was performed by a senior surgeon or a surgery resident supervised by at least one senior surgeon. The debridement was aggressive, seeking to remove all contaminated and nonviable tissue. Samples for bacteriological cultures were routinely obtained. All wounds were washed intra-operatively with H_2O_2 and left open, drainage tubes were placed where there was a subcutaneous tunnel between two incisions. The decision to perform simultaneous colostomy was not systematic and was dependent on the extent of posterior perineum involvement. Additional debridements were performed following clinical criteria.

The dressings were changed once or twice daily, depending on the degree of exsudation; in the beginning, in all cases, with Dakin's solution and then following the surgeon's preference.

Some survivors needed reconstruction surgery, which was performed only after the infection was fully managed.

2.2. Statistical analysis

Data was analyzed using IBM SPSS Statistics 22® (IBM, Armonk, USA). The categorical variables are displayed as frequencies and percentages, the continuous variables are shown by median and Q1-Q3 quartiles (median [Q1; Q3]). Missing data was excluded. For categorical variables Chi Square and Fisher exact test were performed, for continuous variables the Mann−Whitney U test was applied. The interquartile range (IQR) was determined in continuous variables of interest and median + IQR was set as cut-off. Statistical significance was established at $p < 0.05$.

3. Results

The suspected etiological factor for Fournier's gangrene was: perianal abscess in 5 cases (26.3%); urinary infection in 4 cases (21%); genital infection, trauma and surgical wound account in 1 case each. The etiology could not be determined in 7 patients (36.8%).

More than one germ was isolated in 9 patients (47.4%), 7 survivors and 2 non-survivors. The most common isolated germ was *E. Coli* in 7 patients *(*36,8%*)*, followed by *Proteus* spp, *S. Aureus* and *E. faecalis,* accounting for 3 cases *(*16,8%*)* each. There was no microbiological isolation in 4 patients (21%), all of whom survived.

The mortality rate was 21%. Median length of stay was 32 (14; 58) days for the survivors, the non-survivors deceased a median of 9 (6.5; 21) days after admission. Among the survivors the need for reconstructive procedures, other than simple closure, was established in 8 patients (53.3%). These procedures were performed a median of 29.5 (20; 35) days after admission, increasing the length of stay from a median of 14 (10.5; 28) to a median of 46 (35; 61) days.

None of the established predicting scores for the Fournier's gangrene was statistically associated with the mortality in our patients (see Table 3). For the BSA a cut-off value of 3.25% was set following statistical principles (median + IQR). The modification of this scores allowed us to determine that the formula "LRICEC≥8

Table 1
Clinical features at admission.

	Survivors (n = 15)	Non-survivors (n = 4)	p value
Gender (M/F)	12/3	2/2	0.272
Age (yr)	70 (62.5; 78)	72.5 (49; 84.5)	0.764
Charlson Comorbidity Index	4 (3; 6.5)	5 (2.5; 7)	0.885
Evolution time (from onset of symptoms until surgery) (days)	4 (3; 5)	4.5 (2; 10.5)	0.775
Heart rate (bpm)	88 (81; 105.5)	96 (87; 120)	0.394
Systolic BP (mmHg)	115 (109; 121.5)	111.5 (93.5; 158)	0.960
Diastolic BP (mmHg)	63 (61; 77)	56 (49.5; 83.5)	0.192
Body temperature (°C)	38 (36.75; 38.7)	37.3 (36.4; 37.95)	0.367
Affected BSA (%)	1 (0.75; 1.75)	4 (2.375; 5)	0.103
Extensive perineal disease (both *perinea*)	5	2	0.475
Extra-perineal disease	4	3	0.117
Re-operation	6	3	0.303
Colostomy	4	0	0.530

Table 2
Biochemical features at admission.

	Survivors (n = 15)	Non-survivors (n = 4)	p value
WBC count (G/L)	17.4 (12.45; 20.4)	18.9 (13.1; 29.75)	0.764
Hemoglobin (gr/dl)	12.4 (10.5; 13.4)	9.3 (7.4; 12.85)	0.317
Hematocrit (%)	36.9 (32.7; 39.55)	33 (23.8; 42.9)	0.920
Platelet count (G/L)	259 (215.5; 311)	210.5 (102; 359.5)	0.549
ALT(U/L)	27 (24; 95.5)	18.5 (13.5; 22.5)	0.045
LDH (U/L)	371 (343; 405)	485 (373; 559.5)	0.258
Alkaline Phosphatase (U/L)	121 (70; 132)	230 (147.5; 274.5)	0.047
Blood glucose level (mg/dl)	178 (145; 227.5)	264.5 (117.5; 536.5)	1
Urea (mg/dl)	24 (18; 34.5)	22.5 (16.5; 43)	0.764
Creatinine (mg/dl)	1 (1; 1.5)	1 (0.5; 1.5)	0.561
Serum Sodium (mmol/L)	135 (133; 136)	131.5 (127; 133)	0.075
Serum potassium (mmol/L)	4 (4; 5)	4 (4; 4.5)	0.679
C-reactive protein (mg/L)	281 (208.5; 333)	261.5 (199.5; 414.5)	1

Table 3
Performance of the different prognostic models.

	Survivors (n = 15)	Non-survivors (n = 4)	p value
FGSI≥9	1	2	0.097
UdS≥9	6	2	1
LRINEC≥8	9	4	0.255
BSA> 3.25%	1	3	0.016
FGSI≥9 or BSA> 3.25%	2	4	0.004
FGSI≥9 and BSA> 3.25%	0	1	0.211
LRINEC or BSA> 3.25%	10	4	0.530
LRICEC≥8 and BSA> 3.25%	0	3	0.004

and BSA> 3.25%" predicted mortality in 75% of the patients, with a false positive rate of 0%. On the other hand, the formula "FSGI≥9 or BSA> 3.25%" predicted the mortality in all cases, but with a higher false positive rate (33.3%).

4. Discussion

Several definitions for Fournier's gangrene have been submitted [16–18]. In our report we used a broader definition. All cases with perineal involvement were included, even where anterior perineum and genitalia were completely spared. Although we believe this definition is the most accurate, this led to the incorporation of cases that were excluded from other reports, which should be taken into consideration when comparisons are made.

Some drawbacks can be identified in this study. It is retrospective. The number of patients is limited, which impacts the statistical analysis leading to the use of less powerful statistical tests and preventing a multivariate statistical analysis. The diagnosis was established solely on a clinical basis, so there is no histopathological diagnostic evidence.

Of the epidemiological, clinical and biochemical data analyzed (Table 1 and 2), only ALT reached a marginal statically significant result (p = 0.045), with non-survivors having a lower ALT. Since both medians (survivors and non-survivors) are in the normal range of values, we lend no meaning to this finding.

Additionally, we did not find a link between the affected body area (anterior versus posterior perineum) and the results (see Table 2).

As shown in Table 3, the established scores for predicting mortality (FGSI and UdS) were not useful. The LRINEC model's applicability as a mortality predictor was also tested and did not show better results. Unlike those scores, the affected BSA produced interesting findings; when we compared the affected BSA of survivors and non-survivors (Table 1) we did not find any statistically significant results, whereas when we applied a cut-off point (Table 3) the differences were statistically significant. Even though this cut-off was adjusted to our population, the results are clear and show that 75% of the patients with BSA >3.25% (BSA > median + IQR) died. This suggests that other factors aside, the more extensive the disease the worse the outcome. Although we cannot confirm that extreme BSA is an independent prognostic factor, due to our sample size, that conclusion is in line with other publications [5–8].

we tried to determine whether the inclusion of the affected BSA to the existing scores would improve their performance.

When we added the BSA to the FSGI score ("FGSI≥9 or BSA>3.25%") we found a clear increase in the sensitivity of the score, from 50% to 100%, without any decrease in specificity. The same conclusion cannot be drawn from "FGSI≥9 and BSA>3.25%", perhaps because the conditions are too restrictive. Even so, we can conclude that affected BSA improves the FGSI prognostic

capabilities.

Although the UdS was not a useful prognostic tool on our population, our results with FGSI allow us to infer that the UdS is an improvement in the right direction of the FSGI score. It could be refined by including affected BSA, instead of affected anatomical regions currently used.

The LRINEC score was built and refined to be a diagnostic tool not a prognostic one; therefore, we expect it to be highly sensitive, but with low specificity. In our series the LRINEC score was not a useful prognostic tool, but the impact of the BSA on the LRINEC model is absolutely clear. On the one hand the "LRICEC≥8 or BSA>3.25%" score, which is no more than a simple extension of the LRINEC inclusion criteria, is not a useful tool due to the low specificity (28.6%). On the other hand, the "LRICEC≥8 and BSA>3.25%", which is a restriction of the LRINEC criteria by affected BSA, show a huge improvement in the LRINEC score performance, with a specificity of 100% and a sensitivity of 75%. We may thus conclude that the affected BSA improves the LRINEC model performance as a prognostic tool, which may be the factor that definitively transforms this score into a prognostic one.

5. Conclusion

Affected BSA is a useful prognostic factor in Fournier's gangrene but, more importantly, it improves the FGSI and LRINEC prognostic capabilities. This is the first time, as we are aware, that someone identifies the affected BSA as a refinement factor of the FGSI and LRINEC. Unfortunately the ideal weight of the affected BSA and the optimal cut-off point could not be determined; additional studies with larger populations are required. Meanwhile, we suggest the use of affected BSA, FGSI and LRINEC as minimum parameters to assess the prognosis of Fournier's gangrene.

Ethical approval

None.

Sources of funding

The investigators.

Author contribution

Henrique Morais - Conception and design of the study, acquisition of data, analysis and interpretation of data, drafting the article, revising it critically for important intellectual content, final approval of the version to be submitted.

Jessica Neves; Hugo Maciel Ribeiro; Marta Ferreira; Narcisa Guimarães - Analysis and interpretation of data, revising it critically for important intellectual content, final approval of the version to be published.

Nuno Azenha; Raquel Dias; Alice Fonseca; Lucilia Conceição - Revising it critically for important intellectual content, final approval of the version to be published.

Conflicts of interest

None.

Trial registry number

None.

Guarantor

The corresponding author is the guarantor of submission.

Research registration unique identifying number (UIN)

researchregistry1656.

References

[1] H. Baurienne, Sur une plaie contuse qui s'est terminée par le sphacele de tout le scrotum, J. Med. Chir. Pharm. 20 (1764) 251—256.
[2] J.A. Fournier, Gangrène foudroyante de la verge, Semin. Med. 3 (1883) 345—348.
[3] W. Pawłowski, M. Wronski, I.W. Krasnodebski, Fournier's gangrene, Pol. Merkur Lek. 16 (97) (2004) 85—87.
[4] E. Laor, L.S. Palmer, B.M. Tolia, R.E. Reid, H.I. Winter, Outcome prediction in patients with Fournier's gangrene, J. Urol. 154 (1995) 89—92.
[5] L.S. Palmer, H.I. Winter, B.M. Tolia, R.E. Reid, E. Laor, The limited impact of involved surface area and surgical debridement on survival in Fournier's gangrene, Br. J. Urol. 76 (1995) 208—212.
[6] J.P. Spirnak, M.I. Resnick, N. Hampel, Fournier's gangrene. Report of 20 patients, J. Urol. 131 (1984) 289—291.
[7] A. Tuncel, O. Aydin, U. Tekdogan, Fournier 's gangrene severity index score, Eur. Urol. 50 (2006) 838—843.
[8] C.O. Yeniyol, T. Suelozgen, M. Arslan, Fournier 's gangrene: experience with 25 patients and use of Fournier 's gangrene severity index score, Urology 64 (2004) 218—222.
[9] T. Yilmazlar, E. Ozturk, A. Alsoy, H. Ozguc, Necrotizing soft tissue infections: APACHEII score, dissemination, and survival, World J. Surg. 31 (2007) 1858—1862.
[10] T. Yilmazlar, O. Isik, E. Ozturk, A. Ozer, B. Gulcu, I. Ercan, Fournier's gangrene: review of 120 patients and predictors of mortality, Ulus. Travma Acil Cerrahi Derg. 20 (5) (2014) 333—337.
[11] C.H. Wong, L.W. Khin, K.S. Heng, K.C. Tan, Low CO. The LRINEC (Laboratory Risk indicator for necrotizing fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections, Crit. Care Med. 32 (7) (2004) 1535—1541.
[12] O. Bozkurt, V. Sen, O. Demir, A. Esen, Evaluation of the utility of different scoring systems (FGSI, LRINEC and NLR) in the management of Fournier's gangrene, Int. Urol. Nephrol. 47 (2) (2015) 243—248.
[13] A. Kislaoglu, B. Ozogul, S. Kara, A. Bayramoglu, N. Aksungur, S.S. Atamanalp, Fournier's Gangrene: relation of disease outcomes with LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score and necrotic area width, Acta Medica Mediterr. 31 (2015) 17.
[14] M. Kincius, T. Telksnys, D. Trumbeckas, M. Jievaltas, D. Milonas, Evaluation of LRINEC scale feasibility for predicting outcomes of Fournier gangrene, Surg. Infect. Larchmt 17 (4) (2016) 448—453.
[15] R.A. Agha, A.J. Fowler, S. Rajmohan, I. Barai, Orgill DP and the PROCESS group. The PROCESS statement: preferred reporting of case series in surgery, Int. J. Surg. 36 (Pt A) (2016) 319—323.
[16] R.J. Yaghan, T.M. Al-Jaberi, I. Bani-Hani, Fournier's gangrene: changing face of the disease, Dis. Colon Rectum 43 (2000) 1300—1308.
[17] C.F. Kuo, W.S. Wang, C.M. Lee, C.P. Liu, H.K. Tseng, Fournier's gangrene: ten-year experience in a medical center in northern Taiwan, J. Microbiol. Immunol. Infect. 40 (2007) 500—506.
[18] M. Sroczyński, M. Sebastian, J. Rudnicki, A. Sebastian, A.K. Agrawal, A complex approach to the treatment of Fournier's gangrene, Adv. Clin. Exp. Med. 22 (2013) 131—135.