# Risk Factors and Interventions: Fournier Gangrene in a Tertiary Hospital: A 10-year Experience

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## ABSTRACT

**Objective.** The study aimed to describe the patient demographic characteristics, clinical factors, surgical interventions, and quality of care parameters in non-survivors and survivors of Fournier's gangrene (FG).

**Methods.** A total of 131 cases of Fournier's gangrene (FG) were included in a retrospective chart review in the Philippine General Hospital over 10 years using the Department of Surgery research database. We collected data for various direct and derived variables from the identified population. The primary outcome was mortality rate, while other factors studied were genital and colorectal manipulation, bowel diversion, laboratory parameters (white blood cell count, creatinine, hemoglobin).

**Results.** The mortality rate was 15%. Diabetes mellitus was common comorbidity among patients with Fournier's disease. The following were statistically more common in the non-survivor group: female sex, concomitant bowel diversion surgery. Admission data in the non-survivor group showed a lower serum hemoglobin, a higher serum creatinine, and an increased percentage of patients with an abnormal white blood cell count; these did not statistically differ between cohorts, however. The median time to first antibiotic infusion was six hours. The median time to surgery was 13 hours.

**Conclusions.** Among patients with Fournier's gangrene, the proportion of women and those undergoing bowel diversion was higher in those who did not survive. The time of infusion of antibiotics or time to surgery did not differ significantly between survivors and non-survivors.

*Key Words: Fournier's gangrene, fasciitis, necrotizing fasciitis, gangrene*

## INTRODUCTION

Fournier's Gangrene (FG) is a necrotizing fasciitis of the perineal area signified by the presence of erythema, induration, necrosis, and crepitus. Most commonly, systemic signs and symptoms of overwhelming infection are present, such as fever, hypotension, and leukocytosis. It is a relevant disease entity as it affects a significant number of the productive adult population, with the biggest age distribution in 50- to 59-year-old men, followed by men younger than 40 years old.[1]

A worldwide review by Eke in 2000 reported 1726 published cases, over 50 years.[2] FG is also predominantly a disease in low socioeconomic classes where poor health-seeking behaviors result in delayed patient management, increased severity of the disease at the first consult, and increased rates of mortality.[3] In contemporary series, the mortality rate of FG is still high at 20-50%.[4]

The established mainstay of management is wide excision and broad-spectrum antibiotic therapy.[3] There is conflicting

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evidence, however, as to which patient factors and novel interventions impact survival. For example, most studies cite the amount of debridement as a negative prognostic factor[5,6] but some do not.[2] Many other such differences exist. Some[7] cite male gender as a risk factor for mortality, while others[8] cite female gender.

A 2014 study, Lin hypothesized that by selecting the most significant parameters that differentiate survivors from non-survivors, a better risk-stratification of FG could be achieved.[9] Similarly, in choosing significant factors that affect mortality in the Philippine setting, a better understanding of FG prognosis can be gleaned; patients and practitioners may be advised accordingly. Extrapolating Western data to a Philippine setting is difficult. Therefore, there is a need to establish local data to better inform management protocols.

There is a paucity of local data on FG. Four studies reported a wide range of local mortality rates from 0 to 27[5,10-13] comparable to worldwide statistics. In all studies, diabetes mellitus was identified as the most commonly occurring comorbid condition. All studies consistently stated that broad-spectrum antibiotics and wide excision surgery are the mainstays of therapy. These local studies, however, did not assess other patient prognostic factors and timing of initiation of treatment as potential risk factors for mortality.

The study aims to describe and compare the patient demographics, clinical factors, surgical interventions, and quality of care parameters for non-survivors and survivors of FG in the Philippine General Hospital (PGH) over 10 years.

## MATERIALS AND METHODS

This is an observational retrospective cohort study of patients with a diagnosis of FG admitted to the PGH from January 1, 2009, to December 31, 2018.

A search for eligible patients was done using the Integrated Surgical Information System using the diagnosis query function where admitting or final diagnosis was "Fournier's gangrene." The patients' charts and their information in available hospital electronic information systems were reviewed. The following variables were collected for each patient: date of birth, age, gender, comorbidities, date/time of admission, date/time of surgery, date/time of first antibiotic infusion, hemoglobin on admission, white blood cell count on admission, creatinine level on admission, HIV status, diagnosis of diabetes mellitus, history of urogenital or colorectal manipulation, discharge outcomes and mortality. HIV unknown status was indicated for those who opted out of testing.

The following derived data were calculated from different timings of events noted in the patient records: (1) Door-to-needle time: duration in hours from the time of admission to time of the first infusion of antibiotics; and (2) Door-to-knife time: duration in hours from the time of admission to time of surgery.

Descriptive statistics were used to summarize the demographic and clinical characteristics of the patients. Frequency and proportion were used for categorical variables, median and interquartile range for non-normally distributed continuous variables, and mean and SD for normally distributed continuous variables. Independent sample T-test, Mann-Whitney U test, and Fisher's exact test were used to determine the difference in means, ranks, and frequencies, respectively, between non-survivors and survivors. Odds ratio and corresponding 95% confidence intervals from binary logistic regression were computed to determine significant factors for mortality. All statistical tests were two-tailed. Shapiro-Wilk was used to test the normality of the continuous variables. Missing variables were neither replaced nor estimated. Null hypotheses were rejected at a 0.05 α-level of significance. STATA 13.1 was used for data analysis.

The study protocol was approved by the University of the Philippines Research Ethics Board (UPM-REB) and implemented following the principles of Good Clinical Practice and the Declaration of Helsinki.

## RESULTS

A total of 131 patients diagnosed with FG were included in the study. The number of cases increased over the study period (Table 1). The mean age of the population was 47.59 years (SD = 14.81). The oldest was an 80-year-old woman, while the youngest was a neonate. Ninety percent (119/131) of the patients were male. Diabetes mellitus was a comorbidity in 47% of the study population (Table 2).

Eleven percent of the patients had previous urogenital or colorectal manipulation, including debridement done in a different hospital, cystoscopy, colonoscopy, minor fistula surgery, and catheter insertions. Eighteen percent had a previous cancer diagnosis, including colorectal cancer, multiple myeloma and leukemia, and pulmonary malignancies. The median time for the first antibiotic infusion was 6 hours, while the median time to surgery was 13 hours.

Almost half of the records (87/131 patients) did not include the time of first antibiotic dosage and time of surgery.

The overall mortality rate was 15% (20/131). Age did not differ statistically between survivors and non-survivors. The proportion of women in the non-survivors was significantly higher than in the survivor group (25% vs 6%, p = 0.02). In other terms, women had 4.9 times higher odds of dying from FG.

Similarly, more patients had to undergo bowel diversion in the non-survivor group (60% vs 32%, p = 0.02) with bowel diversion having a relative risk of dying from FG at 1.62.

Non-survivors had lower mean serum hemoglobin and a higher mean serum creatinine on admission. A larger percentage of non-survivors had abnormal WBC counts (93% vs 70%). These differences, however, did not reach clinical significance.

**Table 1.** Frequency distribution of Fournier's gangrene cases per year

| Year | Number of Cases |
|---|---|
| 2009 | 9 |
| 2010 | 9 |
| 2011 | 8 |
| 2012 | 3 |
| 2013 | 9 |
| 2014 | 13 |
| 2015 | 11 |
| 2016 | 20 |
| 2017 | 30 |
| 2018 | 19 |

**Table 2.** Demographic and clinical profile of patients with Fournier's gangrene, according to survival

| Parameter | Survivors | Non-Survivors | Total Population | P-value |
|---|---|---|---|---|
| Age (Years) | 47.59 + 14.81 | 49.6 + 13.95 | 47.59 + 14.81 | 0.573 |
| Men | 104/111 (93.69%) | 15/20 (75%) | 119/131 (90.84%) | 0.020 |
| With previous urogenital or colorectal manipulation | 13/107 (12.15%) | 1/20 (5%) | 14/127 (11.02%) | 0.696 |
| With a cancer diagnosis | 16/105 (15.24%) | 7/20 (35%) | 23/125 (18.4%) | 0.550 |
| With diabetes mellitus | 49/103 (47.57%) | 7/16 (43.75%) | 56/119 (47.06%) | 0.796 |
| With HIV infection | 5/15 (33.33%) | 1/2 (50%) | 6/17 (35.29%) | 1.000 |
| Mean serum Hgb on admission (g/L) | 114.5 (n=98) | 106.5 (n=14) | 112 (n=112) | 0.423 |
| Mean serum creatinine on admission (umol/L) | 86 (n=96) | 97 (n=15) | 88 (n=111) | 0.626 |
| Abnormal WBC (Abnormal <4 or > 11 $10^9$cells/L) | 69/99 (69.70%) | 13/14 (92.86%) | 82/113 (72.57%) | 0.327 |
| Number of surgeries (Median) | 1 (n=110) | 1 (n=20) | 1 (n=130) | 0.659 |
| Bowel diversion done (Yes) | 35/110 (31.81%) | 12/20 (60%) | 47/130 (36.15%) | 0.022 |
| Median door-to-knife time (Hours) | 13.32 (n=73) | 13.87 (n=14) | 13.53 (n=87) | 0.543 |
| Median door-to-needle time (Hours) | 6.58 (n=73) | 5.82 (n=14) | 6.58 (n=87) | 0.522 |

The median door-to-knife time was greater in non-survivors by 33 minutes, while the median door-to-needle time was greater by 45 minutes in survivors. These differences did not reach clinical significance: time elapsed less than 13.8 hours before surgery conferred 0.99 odds of mortality (95% CI 0.96, 1.02), while a door-to-needle time of fewer than 6.6 hours conferred a 0.98 risk of mortality (95% CI 0.80, 1.08).

## DISCUSSION

The mortality rate in the study was 15%. This is similar to the biggest review of literature by Eke in 2010 with 1700 cases, which pegged the mortality rate at 16%. In another contemporary series, the mortality rate of FG was also high at 20-50%.[4]

In local studies, mortality rates were higher. A smaller number of patients were included and these were earlier studies. In 1987, Suncuaco-De Vera cited a mortality rate of 27% (3/11 patients) with aggressive surgical debridement for all cases. Moreover, not all patients were given broad-spectrum parenteral antibiotics.

There were two significant factors highlighted in the study: female sex and bowel diversion. Female sex conferred five times increased risk of dying from FG. The rarity, yet seemingly increased severity, of FG in women, is established. In a review article by Volkze in 2018, a database of 25 million state patients identified only 39 cases, bringing the incidence to 2%. The lower incidence of FG in females is owing to better drainage of secretions in the female pelvis.[8] However, this contributes to a faster rate of ascending infection, allowing for the inflammatory process to spread more rapidly.

The higher mortality of patients with bowel diversions can be explained by several hypotheses. Firstly, it may be a surrogate marker of the severity of the disease process such as the increased extent of necrotic tissue (involvement of sphincters). Secondly, an abdominal assault as in opening the peritoneum may cause additional contamination or seeding of infection. In this study, a diverting colostomy was done in 37% of the patient population. This is higher than most percentages reported in the literature.[3,4,14]

Diabetes mellitus was the most common comorbidity occurring in 47% of patients, presumably because of the known immunologic derangement conferred by the disease. A cancer diagnosis was present in 18%, while urogenital or colorectal manipulation was a significant predisposing event in 11% of patients. All of these concur with published literature.[3,4,6]

Data availability is the main study limitation. Over the 10 years, data collection was incomplete, as the transition to electronic medical records was only partly completed in the latter half of the study period. Of the 131 patients, time for admission, surgery, and antibiotic infusion were available for only 87 patients despite exhaustive chart review. As electronic medical records are slowly becoming the norm, the author hopes that further studies be done to reflect more recent patient data.

The size of the study population is one of the strengths of the study as most single-center retrospective studies had less than 100 cases for the same study period.[5, 15-17]

## CONCLUSION

Among patients with FG, the proportions of females and those undergoing bowel diversion were higher in those who did not survive. In this study, the time-to-infusion of antibiotics or time to surgery did not differ significantly between survivors and non-survivors.

A standardized data collection protocol in major Philippine centers may enable clinicians to draw more conclusions about this disease that is still quite common in low-resource areas.

### Statement of Authorship

Both authors contributed in the conceptualization of work, acquisition and analysis of data, drafting and revising and final approval of the version to be published.

### Author Disclosure

Both authors declared no conflicts of interest.

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