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RESEARCH ARTICLE

Fournier's Gangrene in Turkish Population: Analysis of Two Decades

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ABSTRACT

Aim: The nature and rarity of Fournier's gangrene (FG) limit conducting clinical studies with large patient population.We aimed to determine risk factors,predictors of mortality of FG among the Turkish population using published data.

Method: A literature review was conducted via PubMed Central using keywords "FG"and"Turkey" revealing 95 articles between January 2000 and December 2020. Studies including less than 20 patients,consecutive studies of the same author were excluded.In total,41 studies were included.The correlation between mortality and the other variables were analyzed.

Results: There were 1919 patients reported in 41 studies.Majority of the patients were male(83.11%) with a median age of 55.Median mortality was 17.39%. Sixteen studies were published between 2000 and 2010(first decade). Mortality rate was lower in the studies published between 2010 and 2020(14.72%± 7.1vs.22.46%±11.62,p= 0.011).Cutaneous origin was negatively correlated with mortality (r= -0.615,p=0.033) while chronic renal failure(r= 0.705,p=0.005) and fecal diversion (r=0.371,p= 0.037) were positively correlated.The rate of females in high mortality group was higher than low mortality group (27.25%vs.4.35% p=0.034)

Conclusion: Features of the FG patients in Turkish population are comparable to the literature data. Avoiding unnecessary fecal diversion, proper assessment of comorbidities,female gender and origin of the disease may have impact on the mortality.

Keywords: Fecal diversion, Fournier's gangrene, mortality, renal failure, Turkey

Introduction

Fournier's Gangrene (FG) is a rare, life-threatening, rapidly progressive, polymicrobial, and synergistic form of infective necrotizing fasciitis of the perineal, genital, or perianal regions. FG leads thrombosis of the small subcutaneous vessels and necrosis of the overlying skin. It was initially described by Baurienne in 1764. However, it was named by Jean Alfred Fournier, a Parisian dermatologist and venerologist, who reported it in 1883 [1]. The treatment of FG basically consists of hemodynamic resuscitation, aggressive surgical debridement, and broad-spectrum antibiotics [2,3].

Reported overall mortality rates for FG vary between 0 and 88% [4,5]. However, studies published during the last three decades report mortality rate ranging from 20 to 40%. In 2000, Eke reviwed 1726 cases of FG from the literature written in English and reported a mortality rate of 16% [6]. The study of Furr et al, including the largest patient number in the literature, reported 4.7% inpatient mortality [7].

Since FG is rare disease, designing a prospective clinical study may not be feasible. For overcoming this limitation, which is associated with the nature of FG, we aimed to conduct a retrospective study including large patient number. Thus, we retrospectively reviewed the published literature reporting mortality and risk factors regarding FG from the Turkish population during the last two decades.

Materials and Methods

A database search was conducted from the PubMed Central (PMC) by using the keywords "Fournier's gangrene" and "Turkey" between the dates January 2000 and December

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2020. The search revealed 95 articles. Articles including less than 20 patients and published from a country other than Turkey were excluded. In case of consecutive publications from the same first author and institution, only the article with largest patient number was included. Finally, there were 41 studies included. A flow chart showing the included papers was showed in Figure 1 and a full list of manuscripts were presented in Appendix- 1. Institutional review board approval was obtained for this study.

Data regarding patient demographics, etiological origin of FG, comorbidities, treatment methods, and mortality rate were collected from the reviewed articles. Overall data, and the subgroups including two decades (2000- 2010 and 2010- 2020) were analyzed for the factors affecting mortality. We aimed to evaluate whether there were differences between the patient characteristics and especially outcomes (mortality) between the two decades. Because we believed that the outcomes would be improved with the better understanding of the disease and advances in the treatment modalities.

Statistical Analysis

Statistical analyses were performed by using SPSS Statistics for Windows version 23.0 (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp). Normality check for the data was performed by using Shapiro-Wilk test. Variables distributed normally were reported in mean± standard deviation, and two independent groups were compared by using t-test. Variables not distributed normally, were reported in median (minimum- maximum) and two independent groups were compared by using Mann-Whitney U test. The correlation between the variables were analyzed by using Spearman correlation coefficient. The value of $\alpha \leq 0.05$ was accepted statistically significant.

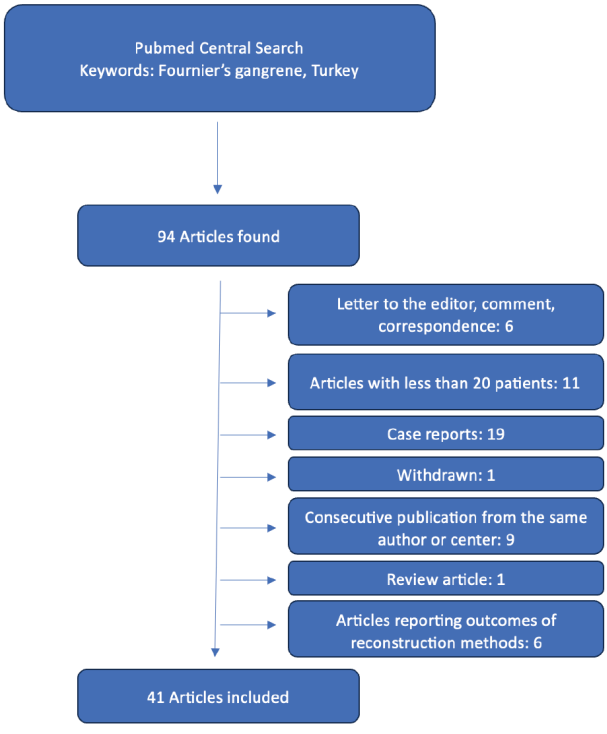

Figure 1. Flow chart of included manuscripts

Results

Median patient number was 38 (20- 120). Distribution of the patient numbers based on the publication date were presented in Figure 2. Reported median mortality was 6 (1- 129) patients. Mortality rates were calculated for every single study, and the median mortality rate was 17.39% (2.89- 40.54). The distribution of mortality rates by the years were shown in Figure 3. Diabetic (diabetes mellitus- DM) patient numbers were reported in all studies, except two. The DM patient rate was 50.02± 16.59% among the overall population.

Sixteen (39%) studies were published in the first decade (2000- 2010) while 25 (61%) were published in the second decade (2010- 2020). Mortality rate was 22.46± 11.62% for the studies published in the first decade while it was 14.72± 7.10% for the second decade. Mortality rate was significantly high for the first decade (p= 0.011). Furthermore, DM patient rate was higher in the second decade (p= 0.022).

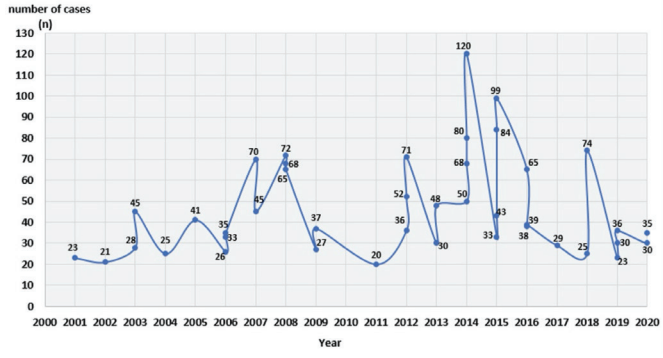

Figure 2. Distribution of the patient volume of the included studies based on publication date

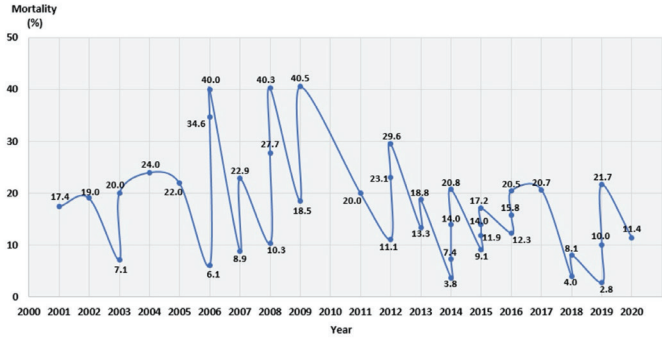

Figure 3. Distribution of the mortality rates by years

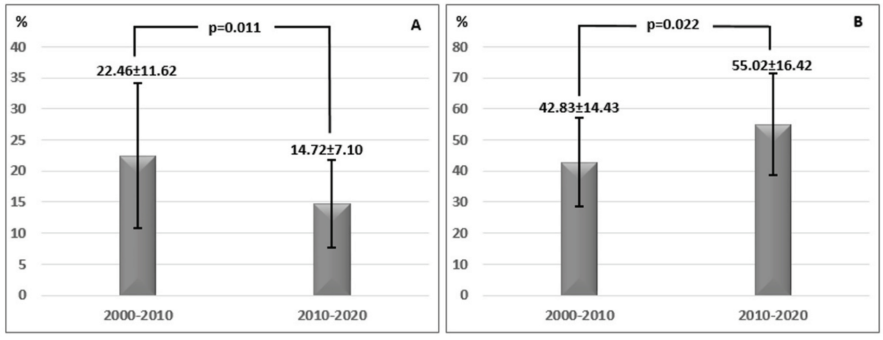

Figure 4. Comparison of mortality (A) and diabetic (B) patient rates between the two decades (2000- 2010 and 2010- 2020)

Figure 4 presents the comparison of mortality rates and DM patients between the two decades. Table 1 summarizes the comparison of data obtained from reviewed articles and shows differences between the two decades.

The association between the mortality rate and other variables were analyzed. Mortality rate was negatively correlated with cutaneous origin, and positively correlated with chronic renal failure (CRF) and fecal diversion (Table 2).

Studies were classified into two groups based on the median mortality rate (≤17.39 "low mortality" vs. >17.39 "high mortality"). Female patient, chronic renal failure and anorectal origin rates were common in high mortality group while cutaneous origin rate was common in low mortality group (Table 3).

Discussion

FG is a devastating disease that may rapidly progress to sepsis, septic shock with multi-organ failure, and death [8]. In the present study, data collected from the previously published articles by the Turkish institutions between 2000 and 2020 were analyzed to determine risk factors and mortality in Turkish population. It was shown that FG is still associated with significant mortality rate (17.39%),

Table 1. Comparison of the data reported in the articles between two decades

Variables	2000-2010		2010-2020		p-value
	n	Descriptive statistics	n	Descriptive statistics	
Patient number*	16	36(21- 72)	25	39(20-120)	0.259
Age#	16	54.58±3.91	25	57.04±4.29	0.072
Debridement count*	5	3(2.00- 7.33)	9	2.36(1.55-6.21)	0.298
Symptom time*	5	6.40 (3.50- 8.09)	11	5.48 (3.74-7.50)	0.510
Male (%)*	16	91.55 (59.46- 100)	25	82.61 (44.00-100)	0.500
Anorectal/Colorectal (%)*	14	47.30 (9.09- 63.08)	14	46.25 (6.06- 78.26)	0.982
Urogenital (%)*	13	15.38 (4.44- 69.70)	15	35.00 (4.35- 68.00)	0.294
Cutaneous (%)*	7	21.21 (4.88- 33.33)	5	15.38(7.50- 24.32)	0.343
Idiopathic (%)*	10	22.25 (4.44- 71.43)	9	33.33 (19.23- 73.53)	0.095
Hypertension (%)*	4	13.25 (5.56- 28.00)	7	20.00 (10.26- 51.92)	0.164
Cardiac comorbidity (%)*	4	13.18 (7.32- 31.43)	8	10.39 (4.35- 22.00)	0.368
Chronic renal failure (%)*	7	3.57 (2.22- 20.00)	7	4.65 (1.25- 17.31)	0.710
Malignancy (%)*	6	7.29 (2.22- 24.62)	13	6.67 (1.47- 19.72)	0.966
Alcoholism (%)*	7	8.33 (4.41- 30.30)	4	6.97 (3.33- 26.67)	0.648
Fecal diversion (%)*	12	33.57 (4.76- 75.61)	20	18.37 (4.00- 66.67)	0.076
Urinary diversion (%)*	8	11.77 (1.54- 100.00)	8	6.55 (1.01- 73.33)	0.279

Variables reported in *median (minimum-maximum) or #mean± standard deviation, n: Number of studies reporting the variable

female gender, anorectal origin, chronic renal failure, fecal diversion may be associated with poor outcomes.

Studies published in the last three decades report mortality rates between 0- 43% [5,9]. However, studies with large patient numbers published during the last two decades reported mortality rates as low as 4.7- 16% [6,7,10]. The median mortality rate was 17.39% in our study. This rate is comparable with the Eke's study (16%), but higher than the studies published from North America. On the other hand, we determined a higher mortality rate for the first decade (2000- 2010) than the second decade (2010- 2020). Emerging technologies and advances in medical knowledge seem to improve outcomes of FG by providing better surgical and medical care.

Previously published two studies with largest patient populations reported different gender rates for FG. Eke reported 10:1 rate dominancy of males, while Sorensen et al. reported 2.32% of 1680 patients were females [6,10]. In this study, majority of the 1919 patients consisted of males while female patient rate was 16.88%. The impact of gender on the prognosis of FG is controversial. There are several studies reporting female gender either as a risk factor or does not affect the prognosis [11-13]. In the present study, rate of female patients was higher in high mortality group. The association between the gender and mortality in FG may be explained by anatomical features of the female pelvis, allowing widespread necrotizing fasciitis [12].

Table 2. The correlation between mortality rate and other variables

	r	p- value
Male (%)	-0.257	0.104
Anorectal/Colorectal (%)	0.253	0.194
Urogenital (%)	-0.099	0.617
Cutaneous (%)	-0.615	**0.033**
Idiopathic (%)	-0.330	0.168
Diabetes mellitus (%)	0.148	0.368
Hypertension (%)	-0.342	0.304
Cardiac comorbidity (%)	0.161	0.618
Chronic renal failure (%)	0.705	**0.005**
Malignancy (%)	0.360	0.130
Alcoholism (%)	-0.118	0.729
Fecal diversion (%)	0.371	**0.037**
Urinary diversion (%)	-0.129	0.633

Table 3. Comparison of low and high mortality groups

Variables	Low mortality group		High mortality group		p-value
	n	Descriptive statistics	n	Descriptive statistics	
Patient number*	21	38(23- 99)	20	38(20- 120)	0.411
Age*	21	55.20 (51.98- 66.30)	20	54.60(46.22- 65.91)	0.489
Debridement count*	6	2.20(1.55- 3.00)	9	2.68(1.79- 7.33)	0.282
Symptom time*	10	5.34 (3.74- 6.40)	6	7.00 (3.50- 8.09)	0.263
Females (%)*	21	4.35(0.00- 56.00)	20	27.25(0.00- 46.67)	**0.034**
Anorectal origin (%)*	13	31.25(6.06- 60.29)	15	49.17(14.29- 78.26)	**0.041**
Urogenital origin (%)*	14	37.25 (4.41- 69.70)	14	16.35 (4.35- 56.67)	0.306
Cutaneous origin (%)*	5	24.32 (15.38- 33.33)	7	11.27 (4.88- 24.44)	**0.048**
Idiopathic (%)*	11	32.00 (13.33- 73.53)	8	21.16 (4.44- 71.43)	0.206
Diabetes mellitus (%)#	20	46.71± 15.25	19	53.50± 17.61	0.206
Hypertension (%)*	5	20.00 (16.25- 33.33)	6	13.25 (5.56- 51.92)	0.247
Cardiac comorbidity (%)*	6	10.65 (8.75- 22.00)	6	10.90 (4.35- 31.43)	0.937
Chronic renal failure (%)*	8	3.26 (1.25- 9.09)	6	7.99 (3.08- 2.00)	**0.043**
Malignancy (%)*	10	4.85 (1.47- 17.57)	9	12.20 (2.22- 24.62)	0.182
Alcoholism (%)*	7	7.14 (3.33- 30.30)	4	8.93 (5.71- 12.20)	0.648
Fecal diversion (%)#	15	22.32± 13.63	17	33.80± 19.90	0.070
Urinary diversion (%)*	10	7.20 (1.01- 73.33)	6	9.56 (1.54- 100.00)	0.562

Variables reported in *median (min-max) or #mean ± standard deviation. n: number of studies reporting the variable

However, there is need for further studies to establish a precise explanation.

Major sources of the infection are the local skin, colon, anus and rectum, and the lower urinary tract [6]. Infection is in polymicrobial and synergistic pattern including gram-positive, gram-negative aerobe and anaerobic bacteria [14]. Colonic, anal, and rectal sources are associated with worst prognosis [2,6]. Perianal infection is the most common cause (19- 50%) either as primary infection or secondary to perianal surgical interventions [2]. In this study, cutaneous origin was negatively correlated with mortality, while anorectal origin rate was higher in high mortality group that were parallel to the previously published data.

Comorbidities such as DM, obesity, alcoholism, smoking, CRF, liver failure, malignancy, and HIV infection play important role in the prognosis of FG. All these conditions may impair microcirculation and/ or immunity [15]. Particularly, DM is a well-defined risk factor that may influence the frequency and the prognosis of the disease [16]. In the present study, the rate of DM patients was significantly higher in the last decade (2010- 2020) compared to the first decade (2000- 2010), but we failed to show a correlation between DM and mortality rate like the previously published studies from our department [13,17]. On the other hand, CRF was found to be positively correlated with mortality rate.

The gold standard treatment of FG includes aggressive and repeated debridement of necrotic tissue, in conjunction with broad spectrum antibiotic and hemodynamic supportive measures in the intensive care unit [13]. Recurrent surgical debridement may cause wide perianal tissue defect and impair anal sphincter functions due to direct trauma. As a result of those entities, fecal contamination of the wound may be unavoidable. Fecal diversion is an option for those patients for facilitating the wound care. However, fecal diversion does not improve outcomes, and increase morbidity and cost [18]. Additionally, mortality rate was reported to be higher in patients with a diverting stoma [19]. Similarly, we found a positive correlation between fecal diversion and mortality rate in this study. However, need for a stoma is common in patients with extensive disease and that should be kept in mind extensive disease may be another factor impairing outcomes.

Study Limitations

The major limitation of this study is its retrospective nature. Since every single article has its original study design, reviewing variables from previously published articles may be associated with missing data that may affect the results of this study. Another important issue, manuscripts were published by different specialties from different centers and management of the disease may show differences between the centers and specialties that may affect the outcomes. However, the large patient number gives this study its clinical value. Additionally, this is the first study reflecting data about the FG patients in Turkish population.

Conclusion

As a conclusion, FG is still a fatal disease. Mortality rate and correlated risk factors of FG in Turkish population seem comparable to the literature data. Cutaneous origin may be associated with better outcomes while female gender, CRF and need for fecal diversion may be associated with poor prognosis.

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