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Fournier's Gangrene: Epidemiology and Outcomes in the General US Population

Key Words

Fournier's gangrene · Mortality · Necrotizing infection ·
 Epidemiology · Outcomes · Management

Abstract

Purpose: Case series reported 20–40% mortality rates for patients with Fournier's gangrene with some series as high as 88%. This literature comes almost exclusively from referral centers. **Materials and Methods:** We identified and analyzed inpatients with Fournier's gangrene who had a surgical debridement or died in the US State Inpatient Databases. **Results:** One thousand six hundred and forty one males and 39 females with Fournier's gangrene represented <0.02% of hospital admissions. Overall, the incidence was 1.6 cases per 100,000 males and case fatality was 7.5%. Sixty six percent of hospitals cared for no cases per year, 17% cared for 1 case per year, 10% cared for 2 cases per year, 4% cared for 3 cases per year, 1% cared for 4 cases per year, and only 1% cared for ≥5 cases per year. Teaching hospitals had higher mortality (adjusted OR 1.9) due primarily to more acutely ill patients. Hospitals treating more than 1 Fournier's gangrene case per year had an adjusted 42–84% lower mortality ($p < 0.0001$). **Conclusions:** Most hospitals rarely care for Fournier's gangrene patients. The population-based mortality rate (7.5%) was substantially lower than the case series from tertiary care centers. Hospitals that treated more number of Fournier's gangrene patients had lower mortality rates, thereby supporting the rationale that regionalized care worked well for patients with this rare disease.

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Introduction

In 1883 Jean Alfred Fournier described idiopathic gangrene in previously healthy young men with acute onset and rapid progression [1]. Over the years, this definition has changed substantially. Today, an etiology can almost always be identified, and the disease is not limited to young males [2, 3]. Fournier's gangrene is a urologic emergency characterized by progressive necrotizing infection of the external genitalia or perineum [1]. Standard teaching is that management depends on early recognition, broad-spectrum antibiotics, resuscitation and aggressive debridement [1–5].

Literature reports 20–40% mortality rates, with some studies reporting mortality as high as 88% (table 1) [6]. These reports tend to be from tertiary referral centers with most studies dealing with less than 100 patients [7]. It is difficult to generalize these findings to other practice settings. Previous reports also reflect differences in referral patterns, surgical management, clinical volumes, and institutional differences. For example, authors diverge widely in their recommendations for urinary and fecal diversion, use of hyperbaric oxygen, and early skin grafting [7–11]. Because previous reports do not include data from community hospitals, there are no population-based data on incidence, regional trends, or case fatality rates. There have been efforts to predict mortality such as the Fournier's Gangrene Severity Index that uses vital signs and laboratory tests to calculate a score [12, 13]. This index was based on data gathered from only 30 pa-

Table 1. Contemporary listing of Fournier's gangrene case series

Primary author	Year	Journal	Mortality rate, %	Number of Fournier's cases
Chalya	2015	BMC Res Notes	29	84
Erdogan	2015	Eur J Trauma Emerg Surg	12	84
McCormack	2015	Can Urol Assoc J	20	26
Ngugi	2014	Afr Health Sci	21	146
Li	2015	Urol Int	21	28
Garcia	2015	Cir Esp	26	59
Yilmazlar	2014	Ulus Travma Acil Cerrahi Derg	21	120
Eskitascioglu	2014	Ulus Travma Acil Cerrahi Derg	4	80
Lin	2014	Int J Urol	19	85
Tuncel	2014	Scand J Urol	14	50
Vyas	2013	Ind J Urol	20	30
Czymek	2013	Colorectal Dis	16	86
Aliyu	2013	ISRN Urol	16	38
Benjelloun	2013	World J Emerg Surg	24	50
Bjurlin	2013	Urology	5	41
Katib	2013	Cent European J Urol	0	20
Verma	2012	J Cutan Aesthet Surg	27	95
Aridogan	2012	Urol Int	30	71
Ersoz	2012	Signapore Med J	23	52
Sugihara	2012	BJU Int	17	379
Altarac	2012	Urol Int	37	41
Goktas	2012	Ulus Travma Acil Cerrahi Derg	11	36
Vargas	2012	Arch Esp Urol	17	42
Koukouras	2011	Urol Int	16	45
Mehl	2010	Rev Col Bras Cir	20	40
Malik	2010	J Pak Med Assoc	18	73
Lujan Marco	2010	BJU Int	16	51
Morua	2009	Arch Esp Urol	12	50
Czymek	2009	Infection	18	33
Sorensen	2009	J Urol	7.5	1,641
Medina	2008	Actas Urol Esp	34	90
Corcoran	2008	J Urol	10	68
Basoglu	2007	Surg Today	8.8	45
Carvalho	2007	Int Braz J Urol	16	80
Dje	2006	African J Urology	18	78
Ayan	2005	Anz J Surg	22	41
Edino	2005	African J Urology	13	24
Yeniyol	2004	Urology	24	25
Daali	2002	African J Urology	17	60
Norton	2002	Am Surg	9	33
Eke	2000	Br J Surg	16	1,726*
Eke	2000	Int Surg	10	21
Yaghan	2000	Dis Colon Rectum	20	10
Corman	1999	BJU Int	4	23
Brissiaud	1998	Chirurgie	34	44
Kouadio	1998	Med Trop	27	30
Benckekroun	1997	J Urol	9	55
Pizzorno	1997	J Urol	0	11
Laor	1995	J Urol	43	30
Palmer	1995	Br J Urol	43	30
Picramenos	1995	Prog Urol	30	10
Attah	1992	Br J Urol	0	13
Baskin	1990	J Urol	21	29
Clayton	1990	Surg Gynecol Obstet	18	57
Wolach	1989	Br J Urol	20	10
Fahal	1988	Br J Urol	25	9
Enriquez	1987	Dis Colon Rectum	25	28
Spirnak	1984	J Urol	45	20
Stone and Martin	1972	Ann Surg	88	33

* Review article

tients presenting to a referral center over a 15-year period. Other investigators reported variable accuracy using the Fournier's Gangrene Severity Index to predict mortality [13–18].

We used a large population-based database to better understand the epidemiology and outcomes of Fournier's gangrene. Our initial goals were to determine the incidence, patient characteristics, and hospital experience with Fournier's gangrene. We hypothesized that case series from tertiary referral centers do not accurately reflect the clinical spectrum and outcomes in the general population. The database was then used to examine differences in case severity and management between teaching and non-teaching hospitals, and to determine predictors of mortality in Fournier's gangrene.

Materials and Methods

Study Population

The US State Inpatient Databases (SID) was established by the Healthcare Cost and Utilization Project (HCUP). The SID includes data from 100% of admissions and discharges from all US civilian hospitals in participating states [19]. The SID is the largest US hospital care dataset.

We analyzed data from 13 states for 2001 and from 21 states for 2004. In 2001, data were purchased from Colorado, Florida, Iowa, Massachusetts, Maryland, Maine, North Carolina, New Jersey, New York, Oregon, Utah, Washington, and West Virginia. In 2004, we also purchased data from Arizona, Kentucky, Michigan, Nebraska, Nevada, Rhode Island, South Carolina, Vermont, and Wisconsin; but data from Maine were unavailable.

Case Definition and Data Abstraction Strategy

The International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9) code for Fournier's gangrene (608.83) is listed under 'Diseases of the Male Genital Organs'. There is no Fournier's gangrene code for females. To identify female cases, we searched for patients with diagnosis codes for gangrene (785.4) and either vulvovaginal gland abscess (616.3) or vulvar abscess (616.4).

Of the 10.7 million males in the SID for the years and states analyzed, the ICD-9 Fournier's gangrene code (608.83) identified 2,238 cases [20, 21]. Because early debridement is essential [2–5], cases were required to have had a genital or perineal debridement, unless they died in the hospital. Debridements in the anatomic areas of interest were defined by ICD-9 procedure codes (48.8–48.82, 48.9, 49.0, 49.01, 49.02, 49.04, 49.39, 49.93, 54.0, 54.3, 61.0–61.99, 62.0–62.19, 62.2–62.42, 63.3, 63.4, 64.0, 64.2, 64.3, 64.92, 64.98, 71.0, 71.09, 71.22, 71.24, 71.29, 71.3, 71.5, 71.6–71.62, 71.8, 71.9, 83.0–83.09, 83.19, 83.21, 83.3–83.39, 83.4, 83.42, 83.44–83.49, 86.0, 86.04, 86.09, 86.22, 86.28, 86.3, 86.4, 86.9, 86.99). Overall, 597 cases were excluded because they were discharged alive without undergoing a surgical debridement. Of the remaining 1,641 cases, 995 (61%) came from states that reported the number of distinct oper-

ating room visits. Using the ICD-9 procedure codes, the average number of genital/perineal debridements per admission was determined. To investigate surgical management, we determined the frequency of suprapubic tube placement, penectomy, orchiectomy, colostomy, and surgical wound closure with or without skin grafting. Of the 15.1 million females in the dataset, only 42 were identified with a diagnosis of gangrene (785.4) and either vulvovaginal gland abscess (616.3) or vulvar abscess (616.4). Overall, 3 cases were excluded, as they were discharged alive without a surgical debridement, leaving 39 total females with Fournier's gangrene. Due to the differential identification and the low yield, analyses of female Fournier's gangrene cases were restricted by demographic and descriptive factors.

To evaluate the potential role of comorbidities on outcome, the Charlson comorbidity index was calculated for each patient. This represents the most extensively studied index for risk adjustment and mortality prediction [22–25]. To more specifically examine the effect of specific comorbidities individual covariates were analyzed including preexisting obesity, diabetes, congestive heart failure, peripheral vascular disease, chronic pulmonary disease, hypertension, renal failure, liver disease, AIDS, coagulopathy, peptic ulcer disease, and anemia.

Data Analyses

Population-based incidence rates were calculated using US Census Bureau [26] data. Incidence and mortality rates were determined for the four US Census Bureau-defined regions (Northeast, South, Midwest, and West) [27]. Trends were compared to the 2005 Behavioral Risk Factor Surveillance System prevalence rates for diabetes and obesity using linear regression analyses [28].

Although most patient and hospital demographic variables were obtained from the SID, some variables were obtained by linking hospital identification numbers with the National Inpatient Sample, a separate database also operated by the HCUP. Because age was not linearly associated with mortality, age was categorized as <40, 40–49, 50–59, 60–69, and ≥70. Fournier's gangrene cases treated at an institution was categorized as 0, 1, 2–4, 5–9, or ≥10 cases per year due to a non-normal case distribution. The chi-square test was used to evaluate binary variables, Student's *t* test allowing for unequal variance was used to evaluate continuous variables, and the Wilcoxon rank-sum was used to compare medians. Multivariate logistic regression analyses with robust SEs were used to determine patient and hospital factors that predicted mortality adjusted for confounding variables.

Results

Patient and Hospital Demographics

We identified 1,641 males with Fournier's gangrene. The overall case fatality rate was 7.5% (124 deaths/1,641 cases). Male cases had a mean age of 50.9 ± 18.6 , were most commonly white, and many had comorbidities (table 2). Fournier's gangrene patients were more likely to have diabetes (OR 3.3, 95% CI 2.9–3.7) and obesity (OR 3.7, 95% CI 3.1–4.3) than other males in the SID after adjustment

Table 2. Patient and hospital characteristics of male patients with Fournier's gangrene

Patient demographics	Male Fournier's cases (n = 1,641)	All other males in SID (n = 11.2 million)	p value
Age, years, n (%)			<0.0001
<40	379 (23)	3,606,816 (32)	
40–49	341 (21)	1,286,656 (12)	
50–59	407 (25)	1,481,863 (13)	
60–69	250 (15)	1,584,606 (14)	
≥70	264 (16)	3,224,827 (29)	
Age, years, mean ± SD	50.9±18.6	48.5±28.3	
Race/ethnicity, n (%)*			<0.0001
White	836 (51)	6,042,041 (54)	
Black	307 (19)	1,316,227 (12)	
Hispanic	109 (7)	801,713 (7)	
Other	49 (3)	477,827 (4)	
Charlson comorbidity index, mean ± SD	1.2±1.4		
Comorbidities, %			
Diabetes	37	14	<0.0001
Obesity	11	4	<0.0001
Hypertension	31	31	0.64
Alcohol abuse	5	3	<0.0001
Tobacco smoker	15	15	0.69
Illicit drug abuse	1.5	2.3	0.0007
Admission source			<0.0001
Transferred from outside hospital, n (%)	110 (7)	451,481 (4)	
Case fatality rate, n (%)	124 (7.5)	298,313 (2.7)	<0.0001

* Numbers may not add to 100% due to missing values.

for age (table 2). Males with Fournier's gangrene had similar rates of hypertension (OR 0.9, 95% CI 0.8–1.0), tobacco and alcohol use (OR 1.0, 95% CI 0.8–1.2) and were less likely to use illicit drugs (OR 0.5, 95% CI 0.3–0.8).

Only 39 women were identified who met our case definition for Fournier's gangrene. Females with Fournier's gangrene were similar to male cases in age, ethnicity, comorbidities, number of surgical debridements, and discharge needs. Female cases were more acutely ill at presentation, as they had double the requirement for mechanical ventilation and dialysis, longer mean and median length of stay, greater total hospital charges and higher case fatality (12.8%, 5/39 cases) than the male cases, although none of these factors met statistical significance.

Admissions for Fournier's gangrene were rare, representing less than 0.02% of all SID hospital admissions. The 1,764 hospitals analyzed cared for an average of 0.6 ± 1.2 Fournier's gangrene cases per year (median 0, range 0–23), while 66% cared for no Fournier's gangrene cases during the 2 study years (fig. 1). Results were similar when 2001 and 2004 data were analyzed individually.

Fig. 1. Distribution of annual cases per hospital.

Epidemiology and Regional Trends

The overall incidence was 1.6 Fournier's gangrene cases per 100,000 males annually (table 3). The incidence peaked and remained steady after age 50 at 3.3 cases per 100,000 males.

Table 3. Age-stratified incidence rates of male Fournier's gangrene cases

	Incidence rates		
	Fournier's cases	total male population in SID	incidence rate per 100,000 males
Age			
0–9	36	14,050,384	0.3
10–19	83	14,864,893	0.6
20–29	85	14,187,958	0.6
30–39	175	15,238,114	1.1
40–49	341	15,905,127	2.1
50–59	407	12,363,771	3.3
60–69	250	7,685,933	3.3
≥70	264	8,093,712	3.2
Total	1,641	102,389,892	1.6 per 100,000 males

Table 4. Incidence rates of Fournier's gangrene by region and comparison to 2005 Behavioral Risk Factor Surveillance System prevalence rates of diabetes and obesity diagnoses

US region	Male cases (n = 1,641)	Total male population in SID (n = 102,389,892)	Male incidence per 100,000	Mortality rate, %	Estimated diabetes prevalence*, %	Estimated obesity prevalence*, %
Northeast	651	39,850,544	1.6	8.8	7.1	22.3
Midwest	150	11,451,728	1.3	6.7	7.4	26.5
South	567	30,532,528	1.9	6.2	9.1	27.1
West	273	20,555,092	1.3	8.1	6.3	22.9

* 2005 Behavioral Risk Factors Surveillance System prevalence rates by region.

The incidence of Fournier's gangrene was highest in the South and the lowest in the West and Midwest US (table 4). Fournier's gangrene incidence increased 0.2 per 100,000 males for each 1% increase in the regional prevalence of diabetes ($p = 0.02$). The incidence was not related to the regional prevalence of obesity ($p = 0.95$). The regional mortality rate was not related to the regional prevalence of diabetes ($p = 1.00$) or obesity ($p = 0.35$). Similar findings were observed when individual states were analyzed, rather than US regions.

Transferred patients were similar in age, ethnicity, surgical procedures, length of stay, total hospital charges, and discharge needs to patients who were not transferred. There was a higher case fatality rate among transferred cases (12.7%) than cases that were not transferred (7.1%, $p = 0.09$).

The 633 patients with a diagnosis of Fournier's gangrene that did not undergo debridement prior to discharge had lower mortality (5%), were less likely to require ICU care, mechanical ventilation, or dialysis, had an average length of stay almost half as long (7 vs. 13 days), and many patients were observed overnight and dis-

charged the following day. These observations led us to conclude that the survivors from this group were unlikely to truly have a necrotizing soft tissue infection and, thus, were appropriately excluded.

Hospital Demographics

The 1,641 male Fournier's gangrene cases were treated at 593 hospitals. Patients were more likely to be treated at large, urban hospitals (table 5). Only 18% of the 1,720 hospitals in the SID were designated as teaching hospitals but they treated more than half of the Fournier's gangrene cases. Overall, 71% of the teaching hospitals treated at least one Fournier's gangrene case compared to only 30% of the non-teaching hospitals.

Clinical Management

Patients required multiple surgeries (average of 2.2 ± 1.6 , range 0–11), and multiple debridements (average of 1.5 ± 1.0 , range 0–8) per admission. Many patients required additional procedures (e.g. suprapubic tube, colostomy, orchiectomy, penectomy, etc.), while 10% re-

Table 5. Characteristics of hospitals treating patients with Fournier's gangrene

Hospital demographics	Number of cases (%)
Hospital location	
Urban	1,404 (86)
Rural	126 (8)
Hospital bed size	
Small	128 (8)
Medium	364 (22)
Large	1,038 (63)
Hospital ownership	
Non-profit	532 (32)
Private	163 (10)
Public	117 (7)
Government	718 (44)
Teaching hospital	820 (50)

Numbers may not add to 100% due to missing values.

quired mechanical ventilation, and 1.4% underwent dialysis. Overall, 7% of patients underwent reconstruction of their wound (with or without skin grafting) during their hospitalizations. The median hospital stay was 8 days. Hospital charges were more than 50% higher for those who died than for those who survived (median \$40,871 vs. \$26,574, $p = 0.0001$). After discharge, 30% of Fournier's gangrene cases required home health care or a skilled nursing facility stay.

Teaching Hospitals vs. Non-Teaching Hospitals

Most Fournier's gangrene cases were treated at teaching hospitals and these patients were younger, more likely to be nonwhites, and more often admitted via transfer (table 6). Patients treated at teaching hospitals had a more severe form of the disease. They underwent more surgeries (especially genital/perineal debridements), mechanical ventilation, had longer lengths of stay, and higher total hospital charges. The case fatality rate at teaching hospitals was 8.9% compared to 6.4% at non-teaching hospitals ($p = 0.06$, unadjusted).

Mortality Predictors

In univariate analyses, increasing age (OR 4.0–18.8) was associated with increased mortality (table 7). Mortality increased 50% for each one-point increase in Charlson comorbidity ($p < 0.001$). Four specific comorbidities were associated with increased mortality: hypertension (OR 1.5), congestive heart failure (OR 3.7), renal failure (OR 5.3), and coagulopathy (OR 4.4). On univariate

analyses, hospital ownership and admission via transfer were associated with mortality. Mortality was higher with increased length of stay (OR 1.6% per day). There was a suggestion that patients presenting to urban institutions and teaching hospitals had increased mortality (both $p = 0.06$). The number of Fournier's gangrene cases treated per year did not predict mortality in unadjusted analyses.

Each operation that a patient required also increased the unadjusted odds of death by 27%, likely reflecting more severe Fournier's gangrene. Certain procedures had an increased mortality: colostomy (OR 1.9), penectomy (OR 3.2), mechanical ventilation (OR 8.2), and dialysis (OR 10.1) during admission, suggesting more severe infection at admission.

On multivariate analyses, patient factors that independently predicted mortality included: increasing age category (adjusted OR, aOR 4.0–15.0), Charlson comorbidity index (aOR 1.20 per point), and admission via transfer (aOR 1.9), after adjusting for hospital location, size, ownership, US region, teaching center status and number of Fournier's gangrene cases treated annually (table 8). When comorbidities were analyzed separately, specific risks associated with increased mortality included: heart failure (aOR 2.1), renal failure (aOR 3.2), and coagulopathy (aOR 3.4). Race and number of surgeries did not predict mortality.

In a separate model evaluating hospital-associated predictors, mortality was 42–84% lower at hospitals treating more than 1 Fournier's gangrene case per year ($p < 0.0001$), after adjustments for patient age, race, Charlson comorbidity index, and admission via transfer. Patients at teaching hospitals had higher mortality (aOR 1.9) than those at non-teaching hospitals. However, when the model was adjusted for the number of surgeries, teaching hospital status was not an independent predictor of mortality.

Discussion

These population-based epidemiological studies provide a broader perspective than previous studies of Fournier's gangrene. The major advantage of our population-based approach was the ability to identify a large number of Fournier's gangrene cases managed at multiple centers, including tertiary care referral hospitals and non-referral hospitals, limiting case-selection and publication biases.

Table 6. Demographic characteristics of hospitals treating Fournier's gangrene cases

	Teaching hospitals (n = 215)	Non-teaching hospitals (n = 362)	p value
Fournier's gangrene cases, n (%) [†]	820 (50)	710 (43)	
<i>Case demographic characteristics</i>			
Age, years, mean ± SD	49.7±18.8	52.1±18.7	0.05
Race/ethnicity, %			<0.001
White	59	72	
Black	28	17	
Hispanic	8	9	
Other	5	2	
Admission source, %			<0.001
Transferred from another hospital	11	2	
<i>Hospital demographic characteristics, %</i>			
Hospital location			<0.001
Urban	98	85	
Rural	2	15	
Hospital bed size			0.03
Small	7.7	9.2	
Medium	21.5	26.5	
Large	70.9	64.4	
Hospital ownership			<0.001
Non-profit	26	45	
Private	0.4	23	
Public	7	9	
Government/other	67	24	
Number of annual Fournier's gangrene cases			<0.001
1	9	26	
2–4	53	71	
5–9	26	4	
≥10	12	0	
Mean ± SD	2.4±2.1	1.5±0.8	
<i>Management factors during each admission</i>			
Total surgeries, mean ± SD*	2.3±1.7	1.9±1.3	<0.001
Genital/perineal debridements, mean ± SD*	1.6±1.0	1.4±0.9	0.001
Additional surgical procedures, %			
Suprapubic tube placement	7	8	0.49
Colostomy	10	8	0.09
Orchiectomy	24	30	<0.01
Penectomy	1	1	0.98
Surgical wound closure	11	4	<0.001
Supportive care, %			
Mechanical ventilation	13	8	<0.01
Dialysis	0.7	1.8	0.06
Median length of stay, days	10	7	<0.0001
Median total hospital charges	\$31,900	\$22,862	<0.0001
Case fatality rate, %	8.9	6.4	0.06

[†] No information on teaching hospital status was available for 16 hospitals (3%) treating 111 (7%) of the Fournier's gangrene cases.

* Mean ± SD number of surgeries and debridements were calculated based on the 61% cases where the dates of surgical intervention were reported.

Table 7. Unadjusted in-hospital mortality risk for 1,641 Fournier's gangrene cases

	OR (95% CI)	p value		OR (95% CI)	p value
<i>Patient-associated factors</i>			Teaching hospital	1.4 (0.98–2.12)	0.06
Age, years		<0.001	Admission source		
<40	Ref.		Transferred from		
40–49	4.0 (1.3–12.3)		another hospital	1.9 (1.1–3.4)	0.04
50–59	7.5 (2.6–21.4)		Cases Fournier's		
60–69	13.8 (4.8–39.4)		gangrene (per year)		0.55
≥70	18.8 (6.7–53.1)		1	Ref.	
Race/ethnicity		0.60	2–4	0.8 (0.5–1.3)	
White	Ref.		5–9	1.1 (0.6–1.9)	
Black	0.70 (0.41–1.20)		≥10	0.6 (0.2–1.8)	
Hispanic	1.01 (0.49–2.10)		Length of stay (each day)	1.6 (0.7–2.5)	0.001
Other	0.73 (0.22–2.43)		<i>Management variables</i>		
Charlson comorbidity			Each surgical debridement		
index (per 1 point			(per debridement)	1.27 (1.1–1.5)	0.001
increased index)	1.5 (1.3–1.6)	<0.001	Surgical procedures		
Specific comorbidities*			Suprapubic tube		
Diabetes	0.94 (0.64–1.37)	0.74	placement	1.3 (0.8–2.3)	0.29
Obesity	0.64 (0.32–1.30)	0.22	Colostomy	1.9 (1.2–3.2)	0.01
Hypertension	1.5 (1.0–2.1)	0.05	Orchiectomy	0.31 (0.16–0.58)	<0.001
Congestive heart failure	3.7 (2.3–5.8)	<0.001	Penectomy	3.2 (1.1–9.9)	0.04
Renal failure	5.3 (3.2–8.7)	<0.001	Wound closure	0.63 (0.27–1.47)	0.29
Coagulopathy	4.4 (2.4–8.1)	<0.001	Supportive care		
<i>Hospital-associated factors</i>			Mechanical ventilation	8.2 (5.5–12.1)	<0.001
Bedsize		0.88	Dialysis	10.1 (4.3–23.6)	<0.001
Small	Ref.		* Additional comorbid conditions were evaluated and were not significant including: preexisting peripheral vascular disease, chronic pulmonary disease, liver disease, AIDS, peptic ulcer-disease, and anemia.		
Medium	1.19 (0.55–2.58)				
Large	1.09 (0.53–2.23)				
Urban hospital	2.68 (0.97–7.38)	0.06			
Hospital ownership		0.02			
Private, non-profit	Ref.				
Private for profit	1.7 (0.8–3.4)				
Public	1.4 (0.6–3.2)				
Government/other	2.1 (1.3–3.4)				

Table 8. Multivariate predictors of Fournier's gangrene mortality

	aOR (95% CI)	p value		aOR (95% CI)	p value
<i>Patient-related[^]</i>			Fournier's cases per year		<0.0001
Age, years		<0.0001	1	Ref.	
<40	Ref.		2–4	0.53 (0.30–0.95)	
40–49	4.0 (1.1–14.1)		5–9	0.58 (0.27–1.24)	
50–59	7.3 (2.2–24.7)		≥10	0.16 (0.04–0.66)	
60–69	11.0 (3.1–38.9)		Teaching center status	1.9 (1.1–3.1)	0.01
≥70	15.0 (4.5–49.7)		[^] Patient-related predictors were adjusted for hospital location, US region, hospital bed size, hospital ownership, teaching center status, and cases of Fournier's gangrene per year. Patient race and number of surgeries did not predict mortality risk.		
Charlson comorbidity index			[†] Hospital-related predictors were adjusted for patient age, race, Charlson comorbidity index, and patient admission via transfer. Hospital location, bed size, ownership and US region did not predict mortality risk.		
(per point)	1.20 (1.0–1.4)	0.04			
Comorbidities					
Congestive heart failure	2.1 (1.1–3.8)	0.02			
Renal failure	3.2 (1.6–6.4)	0.001			
Coagulopathy	3.4 (1.6–7.4)	0.002			
Admission via transfer	1.9 (1.0–3.7)	0.048			
Hospital-related [†]					

We confirmed that Fournier's gangrene is indeed rare, representing less than 0.02% of hospital admissions in the United States with an overall incidence of 1.6 cases per 100,000 males per year. Most hospitals (66% overall) cared for no patients with Fournier's gangrene during a given year, and only 1% of hospitals cared for ≥ 5 cases per year. Thus, even high-volume centers cared for a patient with Fournier's gangrene every few months. As practitioners at a high-volume, teaching-center in the United States, our perspective on the management, mortality, morbidity and risk factors might differ from what is seen in the general US community.

Overall mortality was 7.5% in our population-based study. This was substantially lower than rates reported in the literature (table 1). The highest mortality was reported in 1972 by Stone and Martin (88% mortality among 33 patients). More contemporary series report fatality rates in the 20–40% range. In our studies, mortality was highest for transferred patients (12.7%) possibly representing the most acutely ill cases. What is projected in our study is a lower rate than that revealed by most prior studies and is less than the Centers for Disease Control and Prevention population-based mortality rate for Group A streptococcal necrotizing soft tissues infections (24%), suggesting that Fournier's gangrene is less lethal than other necrotizing soft tissue infections [29].

Increased patient age (aOR 4.0–15.0, $p < 0.0001$) proved the strongest independent predictor of mortality. Patients in hospitals that treated more Fournier's gangrene cases had 42–84% lower mortality ($p < 0.0001$) than hospitals treating only 1 case per year. This may reflect more aggressive diagnosis, management, and treatment at more experienced hospitals. Patients admitted via transfer also had a higher independent risk of mortality (aOR 1.9). This may reflect a more severe form of the illness among transferred patients, lack of critical care facilities at the transferring hospitals, or delays in management and/or treatment. These findings support the need to increase regionalization of care for patients with Fournier's gangrene. Because management often requires care from urologic surgeons, general surgeons, intensivists and plastic surgeons, a multidisciplinary approach at facilities with greater experience might improve patient outcomes.

Teaching hospitals cared for a majority of Fournier's gangrene cases while 30% of non-teaching hospitals treated patients with Fournier's gangrene ($p < 0.0001$). Patients at teaching hospitals were more acutely ill, required more surgical procedures (especially genital/peri-

neal debridements), more mechanical ventilation and other supportive care. These factors likely account for longer lengths of stay, higher hospital charges, and higher case fatality at teaching hospitals. Patients in teaching hospitals had nearly double the unadjusted mortality rate. We hypothesized that this might reflect differences in the severity, management or supportive care, or that diagnostic criteria for Fournier's gangrene at teaching hospitals might differ from those followed at non-teaching hospitals. After adjusting for the number of surgeries a patient required during admission, which is a marker of disease severity, the teaching center status was not an independent predictor of mortality. These observations suggest that higher mortality at teaching hospitals likely reflects a more severely ill population. Patient race and other hospital-related factors assessed (location, size, ownership and US region) did not independently predict mortality.

Deaths tended to occur late during hospitalization. Patients who died had longer lengths of stay and greater hospital charges. These findings may reflect a more indolent course of Fournier's gangrene following initial therapy. Deaths might reflect in-hospital complications, but we have no data to substantiate these events.

Morbidity from Fournier's gangrene was high. Similar to other reports, cases in this series often required many operations, especially genital/perineal debridements, orchiectomy, cystostomy and/or colostomy [30–33]. Overall, 30% of survivors required ongoing care after hospital discharge. Given the rarity (7%) of surgical reconstruction of wounds during the initial hospitalizations, we suspect this ongoing care was necessary to facilitate closure of many patients' open wounds.

This study has certain crucial limitations. Our approach was retrospective using administrative data and subject to the inherent biases of retrospective designs. The database provided no clinical or microbiologic variables to support the diagnosis, determine the degree/severity of infection or percent surface area of skin involvement, or calculate a Fournier's Gangrene Severity Index [12–14]. We were unable to examine urethral stricture as comorbidity because this information was not in the dataset. We could not determine if differential coding of comorbidities occurred, with comorbidities more likely to be captured in the more severely ill patients and in those who died. We may have excluded patients managed with antibiotics only because our case definition required a surgical debridement. However, our subgroup analysis revealed that patients who did not receive a debridement did not merit a diagnosis of

Fournier's gangrene. It is also possible that case fatality was inflated slightly because we included all subjects who died with a Fournier's gangrene diagnosis code, but required survivors to have both a Fournier's gangrene diagnosis code and a genital/perineal debridement. The number of distinct visits to the operating room could be determined for 61% of cases, potentially limiting this variable as a marker of disease severity. Also, we have limited information on women in this regard.

Conclusions

This is the largest study of Fournier's gangrene and the first population-based study allowing accurate estimation of incidence and case fatality. Our study provides the required data on the management of this complex condition in the United States. We are aware of no other comparable data from other areas. We provide new insights into the rarity and hospital experience with Fournier's gangrene, regional trends and comorbidities. Our findings agree with those of prior literature on the age of onset and comorbid risk factors. However, we found substantially lower mortality than case-series from referral centers. We provide the first comparison of outcomes for patients treated at different hospital types and the first population-based study evaluating

predictors of mortality. Our findings support earlier observations from tertiary care referral centers documenting the frequent need for surgical procedures and supportive care.

The large number of cases identified provided a unique opportunity to identify patient-associated and hospital-associated factors predictors of mortality. Fournier's gangrene patients treated at teaching hospitals required more surgical procedures, more supportive care, longer lengths of stay, greater hospital charges and higher mortality rates, reflecting a more severely ill patient population. Hospitals that treated more number of Fournier's gangrene patients had lower mortality rates supporting the need to regionalize care for patients with this rare disease.

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