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Patient-reported outcomes and health-related quality of life in male long-term survivors of Fournier's gangrene

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ABSTRACT

Objectives

To describe patient-reported outcomes and health-related quality of life (HRQoL) in male long-term survivors of Fournier's gangrene (FG).

Methods

We retrospectively identified male patients treated for FG via ICD-10 coding in two centres between January 2010 and December 2020. Patients who survived the in-house treatment were invited to participate and to complete the validated questionnaires International Prostate Symptom Score (IPSS), International Index of Erectile Function (IIEF-5), Quality of Life in chronic wounds (WOUND-QoL), Freiburger Life Quality Assessment – wound module (FLQA-w) and the Short Form Health (SF-36).

Results

Finally, 39 patients with a median age of 65.0 years (IQR 53.0–74.0) were identified. Twenty patients had died (51.3%), nine patients were lost to follow up (23.1%) and ten patients participated in the survey (25.6%). The median survival time was 27.0 months (IQR 9.0 – 60.0). The median IPSS was 13.5 (IQR 4.3 – 22.3); five patients (50.0%) had severe erectile dysfunction. Three patients (30.0%) reported problems with the wound, two (20.0%) complained of wound pain and one (10.0%) about the wound-healing situation. The mean global health score on the WOUND-QoL was 1.83 (SD 1.1), which is significantly lower than in the German reference population ($p<0.001$). In the FLQA-w, the mean subscales were for physical aliment 1.8 (SD 1.1), everyday life 1.5 (SD 0.5), social life 1.6 (SD 0.8) and psychological well-being 1.8 (SD 1.2). The mean general health score on the SF-36 was 64.0 (SD 10.5).

Conclusions

In long-term survivors of FG, the wound situation has a deeply negative impact on HRQoL.

INTRODUCTION

Fournier's gangrene (FG) is a very rare, life-threatening, necrotising infection affecting the perineum, perineal region and genitals (1, 2, 3). As the incidence rate is very low, most of the limited knowledge about FG arises from retrospective single-institution studies with very small patient cohorts (4–8). The incidence of FG is 1.6 cases per 100,000 male patients in the United States (9). Unfortunately, the prognosis, survival and outcome of FG has not improved in recent years, despite more intensive critical-care therapy for these patients (3, 10). Kranz et al. showed in ▶

their multi-centre retrospective study of 154 cases that survival time has not improved in recent years (p=0.268), and up to 15.4% of patients die during in-patient treatment (3). Key points for the successful treatment of FG are immediate surgical debridement, accompanied by forced antibiotic therapy and, usually, intensive medical management (11). However, further research to improve the outcome of FG is desperately needed (12). Improving survival is only one aspect of this severe disease. Other areas of concern are the long-term situation of FG patients, including the wound situation, quality of life and general health status. To our knowledge, there are only very sparse data reflecting these issues (13). Suijker et al. performed a retrospective cohort study on quality of life in patients surviving necrotising soft tissue infection and found statistically significant decreased scores on the Short Health Form 36 questionnaire for the domains of physical functioning, role physical functioning and general health, in comparison to the Dutch reference population. They concluded that necrotising soft tissue infections negatively affect the quality of life, especially in the physical domains (13). Naturally, if we can improve the disease's outcome, research on long-term aspects, such as the wound situation or quality of life, are absolutely warranted. With the above in mind, we performed a multi-centre retrospective study of male long-term survivors of FG with the primary aim of describing patient-reported outcomes (PROs) and health-related quality of life (HRQoL), especially concerning the wound. The secondary aim was to describe the general health status of patients who were still receiving follow-up at the hospital that provided their primary care for FG.

METHODS

1. Development of the study and study population

The study was designed according to the guidelines in the synthesis of qualitative research (ENTREQ) found on equatornetwork.org (14). Formally, this is a retrospective cohort study conducted via a postal survey, so for this type of study, formal consent was not required. Regardless, all procedures performed in this study were done in accordance with the ethical standards of the institutional and/or national research committee, and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The two patients undergoing follow-up at the university medical centre gave their written informed consent for photo-documentation.

Consecutively, we retrospectively identified male patients treated for FG via ICD-10 coding in two centres (one university medical centre and one tertiary care centre) between January 2010 and December 2020 (ten years). Patients who survived the in-house treatment were invited to participate in a survey that included the validated questionnaires International Prostate Symptom Score (IPSS), International Index of Erectile Function (IIEF-5), Quality of Life in chronic wounds (WOUND-QoL), Freiburger Life Quality Assessment – wound module (FLQA-w) and the Short Form Health (SF-36). Furthermore, we asked for symptoms of the wound and pain in the wound, including the NRS score, and symptoms of hypogonadism in non-validated questionnaires. On the whole, we sent out three postal reminders and, if there was no response, we contacted the family practitioner for survival data. Patients who were still undergoing follow-up at the university medical centre were also invited to a clinical evaluation and documentation of the wound situation.

2. Definitions

The non-validated questions included an open-question for symptoms of the FG wound and pain in the FG wound with NRS score, as well as commentaries. Additionally, we asked for the symptoms of hypogonadism: loss of libido, erectile dysfunction, fewer and decreased morning erections, overweight or obesity, sarcopenia, low bone mass, depressive mood, fatigue, loss of body hair, hot flushes, sleep disturbances, loss of muscle mass, loss of efficiency and loss of vigour, since there is no validated questionnaire for hypogonadism (15).

The International Prostate Symptom Score (IPSS) is a validated questionnaire for benign prostate hyperplasia and lower urinary tract symptoms (LUTS). A score between 0 and 7 indicates mild symptoms, 8–19 moderate symptoms and 20–35 severe symptoms (16). The International Index of Erectile Function (IIEF-5) is a validated diagnostic tool for evaluating erectile dysfunction (ED). The short five-question version has a sensitivity of 98% and a specificity of 88% in diagnosing ED. A score between 25 and 22 means no ED, 21–17 shows mild ED, 16–12 mild to moderate ED, 11–8 moderate ED and 7–0 severe ED (17). The WOUND-QoL is a validated short questionnaire measuring the quality of life in patients with chronic wounds based on three established disease-specific instruments (18). Furthermore, the Freiburger Life Quality Assessment – wound module (FLQA-w) is a validated instrument for the meas-

urement of quality of life in patients with chronic wounds, especially those with chronic leg ulcers (19). The Short Health Form (SF-36) is a validated quality of life measurement instrument with 36 questions that fit into eight domains or health concepts, such as physical functioning, role physical functioning or bodily pain (20).

Follow-up at the university medical centre included physical and wound examination, blood count, kidney function, signs of infection (CRP) or diabetes (HbA1c) and urine sediment.

3. Statistical analysis

For each numeric variable, the numeric distribution was preliminarily assessed by the Kolmogorov-Smirnov test. Descriptive statistics were performed with mean and standard deviation for normal distribution, or with median and IQR for non-parametric data. For parametric continuous variables, the Student's t-test was used, and for parametric categorical variables, the chi-square test or the Fisher's exact test was used. Quality of life data from the SF-36 questionnaire were converted to domain scores on a 0–100 scale using the appropriate Statistical Package for the Social Sciences syntax and presented as means SD. Using an independent sample t-test, the scores from our population were compared to German reference values. For the WOUND-QoL comparison, the German validation cohort was used. All reported p-values were based on a two-sided hypothesis, and $p<0.05$ was considered to be significant. All statistical calculations were performed using Statistical Package for the Social Sciences 26.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

1. Demographic characterisation of the s tudy population

Thirty-nine male patients with a median age of 65.0 years (IQR 53.0–74.0) at therapy for FG were identified. Twenty patients had already died (51.3%), nine patients were lost to follow-up (23.1%) and ten patients participated in the survey (25.6%), of whom two (5.1%) were examined for follow-up at the university medical centre. The median survival time was 27.0 months (IQR 9.0–60.0). The most frequent cause of death was septic shock (n=5; 12.8%), but often (n=10; 25.6%), the cause of death was unclear. Out of the ten patients who were studied, eight (80.0%) had normal micturition, one (10.0%) had a suprapubic catheter and one (10.0%) practiced self-catheterism.

2. International Prostate Symptom Score, International Index of Erectile Function and symptoms of hypogonadism

The eight patients with normal micturition had a median IPSS of 13.5 (IQR 4.3–22.3). Three (37.5%) had mild symptoms, two (25.0%) had moderate symptoms and three (37.5%) had severe symptoms per the IPSS. Concerning erectile function, the median IIEF-5 score was 6.0 (IQR 2.5–16.5), and seven patients (70.0%) had severe erectile dysfunction. Additionally, we screened for symptoms of hypogonadism. They also reported sleep disturbance (n=3: 30.0%), loss of muscle mass (n=3; 30.0%), loss of libido (n=2; 20.0%), depressive mood (n=2; 20.0%) and loss of efficiency (n=2; 20.0%).

3. Patient-reported outcomes of the wound situation

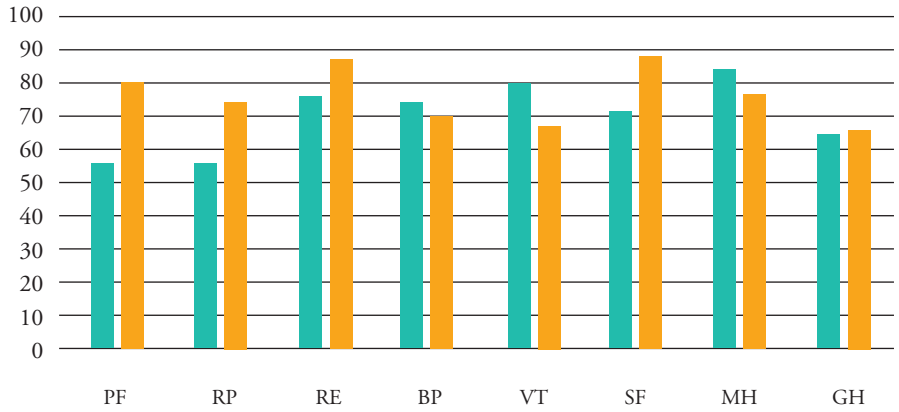
On the whole, three patients (30.0%) reported wound-related problems, two (20.0%) complained of wound pain with a mean NRS score of 0.7 (SD 1.6) and one (10.0%) commented on the wound-healing situation.

The mean global health score on the WOUND-QoL was 1.83 (SD 1.1). Furthermore, the mean subscales of WOUND-QoL were: for body, 1.5 (SD 0.8); psyche, 1.9 (SD 1.4); and everyday life, 2.0 (SD 1.1). All scores on the WOUND-QoL were significantly lower than in the German validation cohort ($p<0.001$).
On the FLQA-w, the mean subscales were for physical aliment 1.8 (SD 1.1), everyday life 1.5 (SD 0.5), social life 1.6 (SD 0.8), psychological well-being 1.8 (SD 1.2) and satisfaction in different areas of life 1.9 (SD 1.0).

4. Health-related quality of life

The mean general health score (GH) on the SF-36 was 64.0 (SD 10.5). The mean subscales of SF-36 were for physical functioning (PF) 55.0 (SD 5.5), role limitations due to physical health (RP) 55.0 (SD 6.9), role limitations due to emotional problems (RE) 76.0 (SD 9.7), energy/fatigue (VT) 80.0 (SD 4.7), emotional well-being (MH) 84.0 (SD 5.2), social functioning (SF) 71.0 (SD 7.7) and pain (BP) 73.5 (SD 17.6). In summary, PF, RP and RE were significantly decreased ($p<0.001$) in FG patients, compared to the German male same-aged reference population. Figure 1 illustrates this issue. Interestingly, an age ▶

Figure 1: Mean SF-36 subscales of Fournier's gangrene patients in comparison to the reference same-aged German male population



PF = physical functioning; RP = role limitations due to physical health;
RE = role limitations due to emotional problems; BP = pain;
VT = energy/fatigue; SF = social functioning; MH = emotional well-being;
GH = general health

over 70 years was not significantly associated with worse reported outcomes in any of the questionnaires' subscales.

5. Detailed characterisation of the two patients undergoing follow-up

The examined patients had a good performance status, including no clinical signs of infection and adequate kidney function, and an acceptable wound situation. Table 1 compares the clinical features of these two patients, while Figure 2 illustrates their wound situation.

DISCUSSION

We conducted a retrospective cohort study about HRQoL and PROs in male long-term survivors of

Table 1: Clinical comparison of the two patients on follow up at the University Medical Centre

Clinical Parameter	Patient 1	Patient 1
Age	77	58
Survival in months	26	15
Micturition	self-catheterism	Via naturalis
Symptoms	No	Pain
Pain NRS Score	0	2
ECOG Performance Status	1	0
Hb in mmol/l	7.0	9.4
Leukocyte count in Gpt/l	6.78	5.24
Platelet count in Gpt/l	228	267
Creatinine in µmol/l	63.0	89.0
Urea in mmol/l	8.52	8.85
HbA1c in %	5.6	8.6
Urine sediment	unremarkable	unremarkable

Figure 2: Comparison of the wound situation of the two patients on follow-up at the University Medical Center

Patient 1, aged 77 years 26 months, after initial debridement

Patient 2, aged 58 years 15 months, after initial debriedement

FG. To our knowledge, this is one of the first studies addressing these issues. Most analyses of FG only study in-house treatment or 90-day mortality and outcome. Additionally, quality of life data are often neglected (21). The only study, at least to our knowledge, about HRQoL in soft tissue infection was published by Suijker et al., based on a Dutch cohort. The authors also used the SF-36 for HRQoL assessment (13). Despite the fact that the outcome of FG needs to be improved, it should be clear that quality of life in these patients is also important and should be considered in daily practice. Furthermore, there was an interesting study by Czymek et al. focused on FG outcome data. The authors concluded that patients with FG experience persistent physical and mental health problems for a long period of time following their primary hospital stay and must receive long-term care from a variety of specialists, otherwise the disease leads to an increase in the duration of morbidity and a decrease in quality of life (22). This emphasises how important quality of life issues are in long-term survivors of FG in clinical practice. Therefore, we must suggest the inclusion of psychological support, andrologists, pain or wound specialists in the patient-centred care plans, if necessary.

On the whole, FG is a severe disease, which is kind of self-explanatory, since more than 50% of our cohort had died prior to the beginning of this study. Interestingly, nearly all patients had some kind of LUTS, erectile dysfunction or signs of hypogonadism, which brings us to the conclusion that life-long urological follow up is necessary for these patients. Furthermore, these symptoms can negatively impact the quality of life and should be treated, when indicated.

The wound situation has a negative impact on HRQoL in WOUND-QoL and FLQA-w, especially in the physical aspects. Concerning the HRQoL in SF-36 physical functioning, role limitations due to physical health and emotional problems are most impaired. This is comparable to the study by Suijker et al. of necrotising soft tissue infections, since the authors concluded that this infection negatively affects HRQoL, especially in the physical domains (13). Consequently, this fact should be addressed during in-patient treatment and follow-up of FG patients, but further investigations are necessary. One initial approach could be the development of a disease-specific validated quality of life questionnaire for FG patients, especially addressing the wound situation and physical impairment. Since the incidence of FG is low, prospective studies and high-quality data are difficult to generate. Therefore, we suggest an antecedent register study for FG (12; 23). A register study would have the great advantage that it could also include follow-up and quality of life data, and even results of validated questionnaires.

Luckily, the two patients we studied who were undergoing follow-up had good clinical health status and wound situations, but due to the fact that they are still pursuing follow-up at the treatment hospital, we must assume that this might be an indicator of selection bias.

Interestingly, we not only decided to take male patients to our cohort, but during our timeframe, there were only male patients treated for FG at both institutions. It is well known that urologists are not often involved in the therapy of female FG patients, although they present nearly in the same clinical way as males do (24). Therefore, a register study or further investigations should involve plastic surgery and gynaecology (12).

Since the wound situation harms the quality of life and this is not age-dependant, at least in our population, it seems logical to improve wound healing during treatment. There are several approaches for doing this, such as vacuum-assisted wound closure or hyperbaric oxygenation, but they all need further investigation. It still has not been defined which patients would benefit from a special wound conditioning (22). A register study would also be reasonable for answering these questions.

One great advantage of our study is that it is one of the first investigations addressing HRQoL in FG patients, and the results can be used for further investigations, such as the development of a disease-specific HRQoL survey and, even more important, for clinical practice, since during follow-up LUTS, erectile dysfunction and hypogonadism should be addressed. We must also assume that our study has some limitations, such as its small sample size with only two study centres, which can lead to selection bias. Additionally, there is no clear definition of 'long-term survival' related to FG, since most studies only investigate up to 90 days of survival.

CONCLUCIONS AND IMPLICATIONS FOR CLINICAL PRACTICE AND FURTHER RESEARCH

In long-term survivors of FG, the wound situation has a deeply negative impact on HRQoL, especially in the physical domains. This impact seems not to be age-dependent. Further research is essential to ensure the quality of care. One initial approach could be the development of a disease-specific validated quality of life questionnaire for FG patients, especially addressing the wound situation and physical impairment.

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Key messages

- This is a cohort study about quality of life and the wound situation of long-term survivors of Fournier's gangrene.
- The wound situation has a deeply negative impact on HRQoL, especially in the physical domains.
- This impact seems not to be age-dependent.
- Further research is essential to ensure the quality of care. One initial approach could be the development of a disease-specific validated quality of life questionnaire for FG patients, addressing in particular the wound situation and physical impairment.

Main points

- The wound situation of long-term survivors of Fournier's gangrene has a deeply negative impact on quality of life.
- This effect is not age-dependent.
- Further research should focus on the development of a disease-specific validated assessment tool to ensure quality of life.

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