Risk Factors Associated with Limb Amputation in Necrotizing Fasciitis at dr. Cipto Mangunkusumo General Hospital Jakarta

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Abstract

Introduction. Early diagnosis and management of necrotizing fasciitis of the extremities has an impact on mortality and morbidity. Studies have shown a correlation of risk factors (e.g., gender, gangrene, and comorbid) with increased risk of amputations in necrotizing fasciitis.

Method. A cross-sectional study conducted on subjects diagnosed as necrotizing fasciitis managed at dr. Cipto Mangunkusumo General Hospital during January 2012 to December 2015. The subject characteristics i.e. gender, age, comorbid, wound presentation, pulse, respiratory rate, temperature, serum creatinine level, hemoglobin content, sodium, and leukocytes level were the variables subjected to statistical analysis.

Results. There were 70 subjects enrolled; fifty percent were males, and 60% were less than 60 years old. The most comorbid found were hypertension (34.3%), diabetes mellitus (28.6%), and kidney disease (22.9%). Amputation occurred in 24.28% subjects. Female was shown to have a greater risk of amputation than male (p = 0.012). Diabetes mellitus, skin necrosis, gangrene and serum creatinine level ≥1.6 mg/dL were significantly associated as an amputation risk factor (p < 0.005). Based on modified LRINEC scoring, 45 subjects were of high risk and 25 were of medium risk. Multivariate analysis showed three strong predictors for amputation were diabetes mellitus (risk ratio 7.685; 95% CI 1.898–31.122; p = 0.004), gangrene (risk ratio 6.151; 95% CI 1.539–24.584; p = 0.010), and serum creatinine level >1.6 mg/dL (risk ratio 4.098; 95% CI; 0.937–17.255; p = 0.054).

Conclusion. Diabetes mellitus, gangrene, and serum creatinine level >1.6 mg/dL referred as risk factors associated with limb amputation in necrotizing fasciitis.

Keywords: necrotizing fasciitis, limb loss, diabetes mellitus, gangrene, serum creatinine level

Introduction

Necrotizing fasciitis is a severe infection that originates from the fascia which is rapid and extensively extends to adjacent tissues. Necrotizing fasciitis spreads along the fascia,1,2 may occurred in neck, abdominal, scrotum and perianal with the highest prevalence found in the limbs (73%).1 The treatment is surgical infection control namely debridement and necrotomy as well as adequate antibiotics. Delay in management results in extensive tissue loss, limb loss, and increased mortality. Prevalence of mortality and limbs loss due to necrotizing fasciitis is 15–29% and 20.3–26%.2–7

In the early stages, necrotizing fasciitis is often misdiagnosed as cellulitis or abscess due to none-specific clinical sign. With delayed diagnosis, the infection process continues let the mortality and morbidity high. Therefore, it is important to identify and diagnose early, followed by appropriate management, which will reduce the risk of amputation and mortality as well.4 Studies have shown a correlation of risk factors with limb amputation in necrotizing fasciitis. Through a study involving 80 subjects with necrotizing fasciitis, Dworkin et al found free predictors of limb loss were female, diabetes mellitus, documented gangrene on first hospital presentation and comorbid. Anaya et al reported 166 subjects with necrotizing fasciitis showed that shock on presentation and clostridial infections were the free predictors of limb loss.5,7

This study aimed to find out factors responsible for major amputations in patients with necrotizing fasciitis of the upper and lower extremities.

Method

The cross-sectional study conducted to find out risk factors for amputation of the extremity in patients diagnosed as necrotizing fasciitis managed at dr. Cipto Mangunkusumo General Hospital during January 2012 to December 2015. These subjects included all diagnosed with necrotizing fasciitis of upper and lower extremities. Data collected from medical records. Those with incomplete data or died before surgery were excluded. Subject characteristics i.e. gender, age, comorbid, wound presentation, pulse, respiratory rate, temperature, creatinine level, hemoglobin content, sodium, and leukocytes level referred to the variables of laboratory risk indicator for necrotizing fasciitis (LRINEC) scores used. The scores categorize the risk as low or no suspicion with score <5 points (probably <50%), moderate risk with 6–7 points (probably 50–70%), and ≥8 high risk or strong suspicion (probably >75%).4 Multivariate comparisons using Chi–square tests and multivariate logistic regression to explore the risk ratio (RR) with 95% of confidence intervals were carried out. The analysis proceeded using SPSS for windows version 20 with p <0.25 considered as significant.
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Results

A total of 70 subjects enrolled on the study, consist of 35 females (50%) and 35 males (50%). Out of total subjects, 60% were those less than 60 years old. The most documented comorbid were hypertension (24 subjects, 34.3%), diabetes mellitus (20 subjects, 28.6%), and kidney disease (16 subjects, 22.9%). Characteristics’ demography carried out using bivariate analysis on those amputated. The occurrence of amputation was 24.28% (17 subjects). Females were shown to have a greater risk of amputation than males (p = 0.012). Diabetes mellitus, skin necrosis, gangrene and creatinine level ≥1.6 mg / dL were the factors significantly showed amputation risk (p <0.005), while as the other factors were not. Subject characteristics, clinical manifestations and analysis were shown in Table 1.

Table 1. Subject characteristics

| Variables                | Amputation | p value* | OR (95% CI) |
|--------------------------|------------|----------|-------------|
|                           | Yes (n = 17) | No (n = 53) |              |
| Gender                   |            |          |             |
| – Female                 | 13         | 22       | 0.012       |
| – Male                   | 4          | 31       | 4.58 (1.32 – 15.9) |
| Age                      |            |          |             |
| – >60 years              | 7          | 21       | 0.909       |
| – ≤60 years              | 10         | 32       | 1.07 (0.35–3.24) |
| Comorbid                 |            |          |             |
| – Diabetes mellitus      | 11         | 9        | <0.001*     |
| – Hypertension           | 4          | 20       | 0.283       |
| – Kidney disease         | 5          | 11       | 0.513       |
| Wound presentation       |            |          |             |
| – Skin necrosis          | 16         | 26       | 0.001*      |
| – Gangrene               | 12         | 12       | <0.001*     |
| – Erythema               | 11         | 22       | 0.095       |
| – Blisters               | 10         | 23       | 0.268       |
| Heart rate (bpm)         |            |          |             |
| – 60–100                 | 6          | 16       | 0.693       |
| – >100                   | 11         | 37       | 1.26 (0.38–4.00) |
| Respiratory rate (bpm)   |            |          |             |
| – 14–20                  | 7          | 20       | 0.800       |
| – ≥20                    | 10         | 33       | 1.16 (0.38–3.52) |
| Temperature (°C)         |            |          |             |
| – 36.5–37.5              | 12         | 43       | 0.273       |
| – >37.5                  | 5          | 10       | 0.56 (0.16–1.95) |
| Serum creatinine         |            |          |             |
| – ≥1.6                   | 12         | 19       | 0.012       |
| – <1.6                   | 5          | 34       | 4.3 (1.31–14.04) |
| Hemoglobin content (g/dL)|            |          |             |
| – <11                    | 6          | 18       | 0.276       |
| – ≥11                    | 13         | 33       | 1.82 (0.60–5.46) |
| Sodium (mEq/L)           |            |          |             |
| – <135                   | 9          | 37       | 0.092       |
| – ≥135                   | 4          | 20       | 2.28 (0.78–7.98) |
| Leukocytes (cells/mm³)   |            |          |             |
| – ≤15,000                | 9          | 37       | 0.202       |
| – >15,000                | 8          | 16       | 0.49 (0.16–1.49) |

Table 2. Modified LRINEC scoring system

| Variables                  | Score | Total subjects | Amputations |
|----------------------------|-------|----------------|-------------|
|                            |       |                | Yes | No |
| Leukocytes (mg/dL)         |       |                |     |    |
| – 15000–25000              | point | 20             | 5   | 15 |
| – >25000                   | point | 4              | 3   | 1  |
| – <15000                   | point | 46             | 9   | 37 |
| Hemoglobin content (g/dL)  |       |                |     |    |
| – 11–13.5                  | point | 46             | 13  | 33 |
| – <11                      | point | 24             | 6   | 18 |
| Sodium <135 mEq/L          | point | 46             | 9   | 37 |
| Serum creatinine ≥1.6 mg/dL| point | 31             | 12  | 19 |
| Blood glucose ≥180 mg/dL   | point | 20             | 11  | 9  |

Table 3. Independent predictors of amputation on necrotizing fasciitis

| Risk factors | p value | RR (95% CI) |
|--------------|---------|-------------|
| Diabetes mellitus | 0.004  | 7.685 (1.808–31.122) |
| Gangrene        | 0.010  | 6.151 (1.539–24.584) |
| Serum creatinine ≥1.6 mg/dL | 0.054  | 4.098 (0.973–17.255) |
A modification of LRINEC scores were applied as CRP was not a routine during hospital presentation. Thus, the total score subsided by 4 (points of CRP). With such a modification, a total of 45 subjects found as high risk (score ≥4) and 25 of moderate risk (score 2–3) as shown in table 2. The multivariate analysis (binary logistic regression test) on clinical factors carried out to find out the strong predictor(s) of amputation. Three variables were noted as the predictors were diabetes mellitus (p = 0.004, RR 7.685.), gangrene (p = 0.010, RR 6.151), and creatinine level >1.6 mg/dL. (p = 0.054, RR 4.098) as shown in table 3.

Discussion

Necrotizing fasciitis is a life-threatening progressive disease.8–10 Early detection of clinical characteristics is essential for early diagnosis and surgical intervention to reduce morbidity. The most important thing in the management of this entity is surgical intervention. Despite adequate management, mortality remains high, which is found in vary (6–36%).8,9,12,13 In the study, amputation rate of 70 subjects enrolled remains high, which is 24.28% (17 subjects), compared to other studies (Ohio 13.8% and Thailand 15.4%).12,13

The use of laboratory risk indicator for necrotizing fasciitis (LRINEC) consist of C-reactive protein (CRP), leukocytes count, hemoglobin content, sodium, serum creatinine and blood glucose were very helpful to establish a diagnosis and distinguish necrotizing fasciitis to other soft-tissue infections. In this study a modification of LRINEC scoring applied as CRP were not a routine examination during hospital presentation nota bene in emergency setting. With the absence of CRP, then the total points were subsided by 4, accordingly. Thus, the scoring turned to low risk with score ≤1 (probably <50%), 2–3 moderate risk points (50–70%) consist of 25 subjects, and ≥4 high risk (>75%) consist of 45 subjects.

We found that the risk factors for amputation on necrotizing fasciitis were age of >60 years, diabetes mellitus, skin necrosis, gangrene and serum creatinine ≥1.6 mg / dL. These factors are like in previous studies.12,14–17 A multivariate analysis shown that diabetes mellitus was the strongest predictive factor for amputation events, in lined with previous studies.18–20 Fasciitis in diabetes mellitus is associated with poor outcomes due to underlying vascular pathology in diabetes lead to inadequate tissue perfusion leading to gangrene. Necrotizing fasciitis with skin necrosis and gangrene were significantly associated with amputation (p = 0.001 and p <0.001, respectively), while as gangrene plays a role as an independent predictor (p <0.05); this was found like study of Khammanu (2015).18 Dworkin (2009) also reported that gangrene is significantly associated with amputations (p = 0.005).3 Skin necrosis, in addition to tissue edema and muscular necrosis as the impact of infection that spreads through lymphatic as well as vascular systems frequently followed by thrombosis of microvasculature and associated neuronal dysfunction.19 Gangrene occurs due to lack of perfusion as the impact of thrombosis. Thus, gangrenous tissue should be removed, necrotoy or amputation is required, accordingly.13,20

In the study showed that serum creatinine levels of ≥1.6 mg/dL were associated with risk of amputation, as the study of Khammanu (2015).18 High serum creatinine levels associated with renal dysfunction are a common finding with associated septic shock in necrotizing fasciitis. Other study of Santos (2006) found no correlation between serum creatinine levels with major amputation.21,22,23 Acute kidney injury found as a complication of traumatized rhabdomyolysis, tissue necrosis and ischemic reperfusion injury. Rhabdomyolysis lead to a rapid increase of serum creatinine. Intravenous fluids should be given as soon as possible, and oral intake should be controlled. In addition, nephrologist should be involved for management.23

This finding may be of a benefit in clinical practice, however the study limitation was the sample enrolled to a study. This is reasonable as the medical records is not designed for a study.

Conclusion

In conclusion, diabetes mellitus, gangrene, and serum creatinine level >1.6 mg/dL referred as risk factors associated with limb amputation in necrotizing fasciitis.

Conflict of interest

Author disclose there was no conflict of interest.

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