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The impact of nutritional status on treatment outcomes of patients with limb-threatening diabetic foot ulcers

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ABSTRACT

Aim: This study aimed to investigate the nutritional status of patients with limb-threatening diabetic foot ulcers (DFUs) and its impact on treatment outcomes.
Methods: A total of 478 consecutive patients (mean age, 65.4 years) treated for limb-threatening DFUs were enrolled. Nutritional status assessment using the Mini Nutritional Assessment (MNA) and Geriatric Nutritional Risk Index (GNRI) was performed by three qualified dieticians within 48 hours of admission. Limb-preservation outcomes were stratified into major lower extremity amputation (LEA) (above the ankle, n = 33), minor LEA (distal to ankle, n = 117) and no amputation (non-LEA, n = 328).
Results: Most patients were identified as being at risk of malnutrition (70.5%) or malnourished (14.6%) (mean MNA score, 20.6 ± 3.4). MNA scores decreased with increasing severity of LEA (mean, 21.1, 20.0, and 17.9, respectively; *P* for linear trend <0.001), associated inversely with the tendency to require LEA (*P* for linear trend was 0.001), and associated independently with both major and minor LEA outcomes (adjusted odds ratio [aOR] = 0.80, 95% confidence interval [CI], 0.65–0.99, *P* = 0.042 and aOR = 0.89, 95% CI, 0.80–0.99, *P* = 0.032, respectively). The predictive value was sustained in patients younger than age 65 years. Though GNRI results had similar associations with outcomes, its predictive value was limited in minor LEA and younger population.
Conclusions: Patients' nutritional status was shown to have significant influence on limb-preservation outcomes for limb-threatening DFUs. Nutritional assessment of this patient population using the MNA is recommended.

1. Introduction

Diabetic foot ulcers (DFUs) occur in about 10%–25% of diabetic patients during their lifetimes (Lavery, Armstrong, Wunderlich, Tredwell, & Boulton, 2003; Nather et al., 2008) and are the leading cause of non-traumatic lower-extremity amputations worldwide (Boulton, Vileikyte, Ragnarson-Tennvall, & Apelqvist, 2005; Global Lower Extremity Amputation Study Group, 2000). The failure of lower-limb preservation in diabetic patients with DFU is usually the result of delayed wound healing because of tissue hypoxia, chronic inflammation (Huang et al., 2012; Lin et al., 2010; Moulik, Mtonga, & Gill, 2003; Sun et al., 2012; Tsai et al., 2013), metabolic derangement, and immune deterioration (Brem & Tomic-Canic, 2007; Cunningham-Rundles, McNeeley, & Moon, 2005).

Nutrition has been reported to play a role in tissue regeneration (Arnold & Barbul, 2006; MacKay & Miller, 2003; Thomas, 2001) and in immune modulation (Stechmiller, 2010; Wild, Rahbarnia, Kellner, Sobotka, & Eberlein, 2010). Nutrients such as arginine, glutamine, and β-hydroxy-β-methylbutyrate have been reported to be clinically valuable in the healing of foot ulcers (Armstrong et al., 2014; Mechanick, 2004; Zhang et al., 2013). Nevertheless, the role of nutrition in patients with DFU is less clear cut. This study aimed to investigate the nutritional status of patients with limb-threatening DFU and its impact on treatment outcomes.

The Mini Nutritional Assessment (MNA) is a highly sensitive, objective screening tool (Cereda, 2012) and its use in diabetic patients has been recommended in the International Diabetes Federation Global Guideline for Type 2 Diabetes (Dunning, Sinclair, & Colagiuri,

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2014). Therefore, in this study, the MNA was used to evaluate the nutritional status of hospitalized patients with DFU. The Geriatric Nutritional Risk Index (GNRI) (Bouillanne et al., 2005) was also used for the purpose of comparing nutritional status results.

2. Patients and methods

2.1. Patients

From year 2011 to 2012, consecutive type 2 diabetic patients hospitalized and treated for limb-threatening DFU at the Diabetic Foot Center of Chang Gung Memorial Hospital were enrolled. Those patients who were younger than age 20 years or pregnant were excluded. Sixteen patients who died during treatment were excluded from the analysis to avoid the confounding effects of mortality and small sample size. Finally, data of a total of 478 patients were analyzed. The Institutional Review Board of Chang Gung Memorial Hospital approved the study protocol (no. 103-0857B), and the study was conducted according to the principles set forth in the Helsinki Declaration of 1975, as revised in 1983. Signed informed consent was obtained from each subject.

2.2. Methods

All patients received care from a multidisciplinary team and individual treatment planning was done. Revascularization and lower-extremity amputation (LEA) were performed according to established guidelines and team consensus (American Diabetes Association, 2003; Lin et al., 2010; Sun et al., 2012; Tsai et al., 2013). The treatment outcomes were stratified by limb-preservation into minor LEA (i.e., amputation performed distal to the ankle joint), major LEA (i.e., amputation performed through or proximal to the ankle joint) (Sun et al., 2012), and non-LEA (i.e., no amputation performed).

Nutritional assessments were performed by three senior dietitians within 48 hours of admission. Each dietitian was qualified to assess inter-rater reliability. Nutrition status was evaluated by the MNA in the Nestlé Nutrition Institute format (Guigoz, 2006). The MNA (maximum score, 30 points) has 18 items organized into 4 domains, including anthropometric measurements (body mass index [BMI], and mid-arm and calf circumference), general assessments (recent weight loss, mobility, and psychological problems), diet history (number of meals, appetite, and feeding mode), and subjective assessments (self-perception of health and nutrition status). Based on the MNA definitions, nutritional status was characterized as: "well nourished" (score, 24–30), "at risk of malnutrition" (score, 17–23.5), or "malnourished" (score, <17) (Bouillanne et al., 2005).

The nutrition-related risk was estimated using the GNRI, and was calculated from serum albumin level, current body weight, and ideal body weight according to the Lorentz formula (Bouillanne et al., 2005) as follows:

$$\text{GNRI} = (1.489 \times \text{albumin, g/L}) + (41.7 \times \text{current weight/ideal weight})$$

The nutrition-related risk of each individual was either absent, low, or moderate-to-major (GNRI >98, 92–98, and <92, respectively) (DeLegge & Drake, 2007).

Patients' medical history was taken to elicit information such as age, sex, BMI, duration of diabetes, concurrent cardiovascular disease, and a physical examination was performed to determine Wagner grade of the foot lesion (Karthikesalingam et al., 2010). Initial laboratory data included hemoglobin, leukocytes, C-reactive protein (CRP), serum albumin, serum creatinine, estimated glomerular filtration rate by MDRD (eGFR), glycated hemoglobin (HbA1c), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), total cholesterol, and triglycerides.

2.3. Statistical analysis

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS for Windows, Version 19.0) software (SPSS Inc., Chicago, IL). One-way ANOVA with linear trend test was used to analyze the differences in normally distributed continuous variables, and the chi-square for linear trend test was used to analyze the trends of categorical variables. Multivariate logistic regression analyses, adjusted for age, sex, presence of dialysis, Wagner classification, WBC counts, ankle-brachial pressure index, eGFR, and hemoglobin, CRP, HbA1c, and LDL-C levels, were used to identify the independence of the MNA and GNRI scores as predictors of treatment outcomes both for study population and subjects younger than 65 years. To calculate the adjusted odds ratios (aOR) for major and minor LEA, "non LEA" was used as a baseline for comparison. The Wagner classification was divided into two categories (grade <3 vs. grade ≥3) for comparison. The WBC count was divided by 1000 to fit the clinical intervention when ORs were calculated and interpreted. Statistical significance was set at $P < 0.05$ for all tests.

3. Results

3.1. Patients' demographic and clinical characteristics demonstrated a high prevalence of poor nutritional status

The mean age of study patients was 65.4 ± 13.1 years, and the majority of patients were men (56.9%; Table 1). The mean BMI was 25.6 ± 4.6, which is considered overweight according to the Taiwanese definition (normal, 18.5–24; overweight, 24–26.9 kg/m^2) (Chu, 2005). The prevalence of end-stage renal disease (ESRD), stroke history, and previous cardiovascular disease was 16.1%, 16.5%, and 18.2%, respectively, indicating the fragility of our patients. Wagner wound grade in most of the ulcers (68.8%) was ≥3.

The mean (± standard deviation) MNA and GNRI scores were 20.6 ± 3.4 and 97.0 ± 13.1, respectively, which corresponded to "at risk of malnutrition" for the MNA or the "low nutrition-related risk" for the GNRI (Table 1). The MNA scores gradually decreased as foot outcomes ranged from non- to major LEA (mean, 21.1, 20.0, and 17.9, respectively; P for linear trend <0.001). Similarly, the GNRI also decreased as the foot outcomes worsened (mean, 99.3, 94.1, and 86.5, respectively; P for linear trend <0.001).

3.2. The associations between amputation levels and MNA or GNRI scores

The associations between nutritional status and various foot outcomes are depicted in Fig. 1. Based on the MNA classification, nutritional status was normal in 15.2% of our patients, at risk in 70.0%, and poor in 14.8%. Deteriorating nutritional status was positively associated with worse foot outcomes (linear trend, $P < 0.001$) (Fig. 1a). Similarly, as the risk of malnutrition (GNRI scores) increased, foot outcomes deteriorated (Linear trend, $P < 0.001$; Fig. 1b).

The amputation rates based on nutritional status (MNA or GNRI scores) are depicted in Fig. 2. Nutritional status, as defined by the MNA, was inversely associated with LEA rate (Fig. 2a). The major LEA rate was almost eleven times higher in the malnourished (MNA <17) group than in the well-nourished (MNA 24–30) group (15.5% vs. 1.4%). As shown in Fig. 2b, the major LEA rate was nearly six times higher in the malnourished (GNRI <92) group (11.3% vs. 1.8%).

3.3. Patients' nutritional status is an independent predictor of outcomes

In the multivariate logistic regression analyses, the MNA scores and GNRI scores were analyzed separately to prevent the confounding effects of interrelatedness between the nutritional assessments (Table 2). In addition to traditional risk factors (such as Wagner classification, WBC count, hemoglobin level, and CRP level), the MNA