Prognostic impact of nutritional risk assessment in patients with chronic schizophrenia

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ARTICLE INFO

ABSTRACT

Protein–energy wasting is associated with poor outcome in various clinical settings. However, the prevalence of malnutrition and the prognostic impact of nutritional status are poorly understood in institutionalized patients with chronic schizophrenia. This study aimed to assess the predictive ability of the Geriatric Nutritional Risk Index and Onodera's Prognostic Nutritional Index for long-term outcomes in patients with chronic schizophrenia. All measurements, including nutritional scores, were performed at baseline after the enrollment of 542 (64.6% men, mean age 53.8 ± 9.7 years) patients with chronic schizophrenia. The median follow-up period was 408 days. The endpoints were falls and infection-related hospitalizations. At study completion, 34 patients suffered falls and 40 patients were admitted to hospitals due to infection. Both indices showed significant association with infectious complications, whereas only the Onodera's Prognostic Nutritional Index was significantly associated with falls. The adjusted hazard ratios (95% confidence intervals) of low Onodera's Prognostic Nutritional Index were 2.38 (1.16–4.86) for falls and 1.99 (1.05–3.76) for infectious complications. The Onodera's Prognostic Nutritional Index is more appropriate than the Geriatric Nutritional Risk Index in identifying patients with chronic schizophrenia who are at risk for malnutrition and nutrition-related morbidity. Further studies are needed to explore whether early detection of patients with schizophrenia who are at risk for malnutrition could lead to the reduction of morbidity and mortality with the aid of appropriate interventions.

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1. Introduction

Schizophrenia is a debilitating illness, with a higher mortality rate compared with that of the general population. More than two-thirds of deaths among patients with schizophrenia are attributed to physical illnesses, predominantly cardiovascular disease (Walker et al., 2015). The reasons for the increased risk of death include the effects of antipsychotics and unhealthy lifestyles and the high prevalence of cardiovascular risk factors, such as type 2 diabetes mellitus and metabolic syndrome (Vancampfort et al., 2015, 2016). Despite progress in medical treatment during the past decades, the years of potential life lost due to schizophrenia have not been significantly influenced over time (Hjorthoj et al., 2017). Therefore, development of promising adjunctive therapies, for example, nutritional interventions, to extend the lifespan of these patients is needed.

The pattern of malnutrition can be divided into undernutrition, overnutrition, and micronutrient deficiencies (White et al., 2012).

Recently, many researchers have used the term protein–energy wasting (PEW) to describe the condition of protein and energy depletion because loss of protein and energy stores is caused not only by reduced nutrient intake but also by oxidative stress, superimposed hypercatabolic states, and nonspecific inflammation (Fouque et al., 2008). Patients with schizophrenia usually have a higher intake of saturated fats and a lower consumption of plant-based foods than the general population (Dipasquale et al., 2013). Such eating habits are likely to contribute to the development of obesity-related metabolic disorders. Well-balanced vegetarian diets could prevent diet-related chronic illnesses, whereas a restrictive vegetarian diet may lead to specific micronutrient deficiencies and thereby result in symptoms similar to those of schizophrenia (Kuo et al., 2009; McGrath et al., 2011; Sabate, 2003). However, few studies have examined the prevalence and impact of undernutrition among patients with chronic schizophrenia. A study in Japan found a higher prevalence of underweightness in a cohort of 23,116 adult patients with schizophrenia than in the general population (13.8% vs 7.9%) (Sugai et al., 2015). The prevalence of undernutrition among inpatients with schizophrenia was higher than that among outpatients and the general population, especially among people aged ≥60 years. People who are suffering from malnutrition are more likely

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to have a poor quality of life, reduced physical performance, and an increased risk of mortality (Jeejeebhoy, 2012). Thus, assessing the nutritional status of these patients is essential to improve their well-being.

Some fully objective nutritional assessment indices, such as the Nutritional Risk Index (NRI), Geriatric Nutritional Risk Index (GNRI), and Onodera's Prognostic Nutritional Index (OPNI), have been developed and widely used in patients with a wide range of clinical conditions (Bouillanne et al., 2005; Buzby et al., 1988; Onodera et al., 1984). The NRI, which is based on serum albumin concentration and percent **of** usual body weight, has been shown to identify nutritional risk in hospitalized patients (Buzby et al., 1988). Because it is difficult to determine the usual weight of elderly patients, Bouillanne et al. replaced usual body weight with ideal body weight in the NRI formula to predict the risks of morbidity and mortality in hospitalized elderly patients (Bouillanne et al., 2005). GNRI has been further validated to be a useful tool for nutritional screening in various disorders (Kinugasa et al., 2013; Lee et al., 2013). Onodera et al. first proposed using serum albumin concentrations and lymphocyte counts to assess the nutritional status of surgical patients. This is an efficient method to detect patients at risk of postoperative complications. OPNI has been widely applied to predict the prognosis in patients with a history of chronic renal failure, acute myocardial infarction, and various solid tumors (Basta et al., 2016; Kang et al., 2012; Mori et al., 2015).

To date, the prognostic impact of nutritional status in institutionalized patients with chronic schizophrenia has been poorly understood. Both overnutrition and undernutrition affect innate and adaptive immunities, leading to increased susceptibility to infectious diseases (Schaible and Kaufmann, 2007). Nutritional status is also associated with fall-related injuries, with a U-shaped relationship between body mass index (BMI) and falls (Himes and Reynolds, 2012). One study found that obesity was correlated with an increased incidence of falling in the elderly and a higher risk of disability following a fall (Himes and Reynolds, 2012). Other investigators have found that underweightness and lower bone mass density are predictors of poor prognosis after falls (Greenspan et al., 1994). People with schizophrenia engage in sedentary behavior, have decreased muscle strength, and take psychotropic medications, which are potential risk factors for falls and consequently increase the risk of fracture (Stubbs et al., 2015). Moreover, these patients have high rates of adverse events, such as nosocomial infections, postoperative respiratory failure, and sepsis during hospitalization, compared with the general population (Daumit et al., 2006). These morbidities may contribute to premature mortality. Therefore, the purpose of this study was to assess the validity of two objective nutritional indices, GNRI and OPNI, to identify patients with chronic schizophrenia at risk of these complications. We also analyzed the association of various traditional nutritional parameters with falls and infections in this population.

2. Experimental/materials and methods

2.1. Setting and participants

A total of 572 clinically stable inpatients aged ≥ 20 years who were diagnosed with schizophrenia or schizoaffective disorder according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, at Yuli Hospital were recruited initially between January 1 and January 31, 2013. Patients were excluded from this study if they met any of the following criteria: an acute psychotic attack that required treatment in an acute psychiatric ward, a medical or surgical problem that required an acute referral, or refusal to participate in this study. Finally, 542 patients were enrolled and followed up until June 30, 2014. The study protocol was approved by the institutional review board of Yuli Hospital, Ministry of Health and Welfare, Hualien, and was conducted in compliance with the Declaration of Helsinki. Written informed consent was obtained from all participants before the study began. The patients also gave consent for publication of their clinical details.

2.2. Study design

History taking, physical examination, and laboratory tests were performed after the patients were recruited in the study. The comorbidity of each patient was quantified according to the Charlson comorbidity index (CCI), a summary score based on 17 medical conditions with different assigned weights (Quan et al., 2011). High scores represent a greater comorbidity burden and are associated with poorer prognosis. Medication data were collected, and no major modifications were made in psychotropic drugs during the follow-up period. Dose equivalents of antipsychotics, anticholinergics, benzodiazepines, and mood stabilizers were calculated as defined daily doses (DDDs) according to the WHO Collaborating Centre for Drug Statistics Methodology (Whocc.no., 2017).

2.3. Measures and variables

2.3.1. Primary outcomes

The primary endpoint was the occurrence of falls or infectious complications from the time of inclusion. A fall was defined as an event which results in a person coming to rest unintentionally on the floor, ground or other lower level (World Health Organization, 2017). The criteria used to define infections were (1) body temperature of >38 °C requiring antibiotic therapy and (2) clinical signs and symptoms associated with (a) the isolation of a pathogenic organism or (b) an identifiable site of infection by clinical examination or imaging tests, respectively. Infectious complications were classified as pneumonia, wound infection, urinary tract infection, intra-abdominal abscess, and sepsis.

2.3.2. Nutritional assessment

Fasting blood samples were taken for determination of complete blood count with differential, glucose, creatinine, albumin, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, and triglycerides. The data from these analyses were then applied to the GNRI and OPNI.

The GNRI was calculated as follows: $(1.489 \times \text{serum albumin, g/L}) + (41.7 \times \text{present weight/ideal body weight})$, with ideal body weight derived from the Lorentz formula (Bouillanne et al., 2005). Present body weight/ideal body weight was set at 1 when the patient's body weight exceeded the ideal body weight. From these GNRI values, the patient was classified as being at one of four grades of nutrition-related risk, based on previous studies: no risk (GNRI >98), low risk (GNRI 92–98), moderate risk (GNRI 82–92), and major risk (GNRI < 82).

The OPNI was calculated using the following equation: serum albumin concentration (g/L) $\times$ 1 + total lymphocyte count (per μL) $\times$ 0.005 (Onodera et al., 1984). OPNI values of ≥50 are conventionally defined as normal, those of 45–50 as mild malnutrition, those of 40–45 as moderate malnutrition, and those of <40 as severe malnutrition (Kanda et al., 2011).

Traditional variables were also used to determine the degree of malnutrition, such as underweightness (defined as BMI <18.5), obesity (defined as BMI ≥25), hypocholesterolemia (defined as serum cholesterol concentration < 3.89 mmol/L), hypoalbuminemia (defined as serum albumin concentration < 35 g/L), and lymphocytopenia (defined as total lymphocyte count <1.5 $\times$ 10^9/L) (WHO expert consultation, 2004; Yamada et al., 2008).

2.4. Statistical analysis

Continuous data are presented as means ± standard deviation unless stated otherwise, and categorical variables are expressed as percentages. To assess the risk of first hospitalization due to infections or falls based on GNRI or OPNI, we obtained hazard ratios (HRs) with 95% confidence intervals (CIs) using Cox proportional hazard models controlled for age, sex, and CCI. In several studies, a significant