Study Protocol

TJ-IRB202411010

Retrospectively Analyze the Correlation Between Body Composition Based on CT Measurement and Pathological Grading and Prognosis in Patients with Gastroenteropancreatic Neuroendocrine Neoplasms

Version date: 2024.11.4

I.Research Background

Neuroendocrine Neoplasms (NENs) are a heterogeneous group of tumors. Although relatively rare, their incidence has increased rapidly over the past decade (1). NENs can occur in any organ or tissue, with 62-70% occurring in the gastrointestinal-pancreatic system (GEP-NENs)(2).

According to the WHO classification criteria, NENs are divided into well-differentiated gastroenteropancreatic neuroendocrine tumors (GEP-NETs), poorly differentiated gastroenteropancreatic neuroendocrine carcinomas (GEP-NECs), and mixed neuroendocrine/neuroepithelial tumors (MiNENs). Based on the Ki-67 proliferation index and/or mitotic count, GEP NET is classified into grades G1, G2, and G3. GEP NET G3, GEP NEC, and MiNENs are considered high-grade GEP NENs, while NET G1 and NET G2 are considered low-grade GEP NENs(3,4). Treatment for high-grade and low-grade neuroendocrine tumors differ(5). Patients with high-grade neuroendocrine tumors tend to have shorter median overall survival and poorer prognosis(6). Therefore, pathological grading is of great significance for clinical diagnosis, treatment, and prognosis of patients. However, most information can only be obtained after surgical and histological evaluation(7). Thus, exploring markers associated with GEP-NENs grading and prognosis is of great importance for patient diagnosis and treatment.

Excess body fat is one of the causes of various cancers. Studies have shown that BMI is a risk factor for neuroendocrine tumors(9). Although BMI is used to assess obesity, it does not specifically reflect the distribution of body fat or distinguish between muscle and fat tissue (10). Computed tomography (CT) can economically and effectively obtain body composition parameters such as muscle and fat(11). Recently, CT images at the third lumbar level have been considered a widely available method and have been used to study body composition in several diseases(12-14). However, two-dimensional parameters have their limitations: cannot explain differences in fat and muscle distribution among individuals. Prognostic analysis using three-dimensional body composition parameters is relatively rare.

In this study, we attempted to explore the relationship between 3D body

composition parameters and grading and prognosis of NENs through a larger sample size.

II. Research Objectives

This study aims to analyze the association between body composition measured by CT and the pathological grading and prognosis of patients with GEP-NENs confirmed by surgical pathology through a retrospective review of CT imaging data..

III. Research Design

This study is a retrospective study.

IV. Selection of subjects

1. Inclusion criteria

(1) a confirmed diagnosis of GEP-NENs via histopathology with a WHO grading.

(2) available enhanced CT scans that included full abdominal imaging before surgery or biopsy.

2. Exclusion criteria

(1) therapeutic interventions before surgery or biopsy

(2) poor image quality or incomplete CT images of the whole abdomen.

V. Sample size

Retrospective analysis of GEP-NENs patients from 3 Hospitals from April 2014 to April 2024. The number of included cases was 633 patients.

VI. Research process

1. Clinical Data Collection: Through the Radiology Information System (RIS) , we queried the list of patients with GEP-NENs from April 2014 to April 2024. Based on postoperative pathology and imaging examination types, combined with the exclusion criteria of this study, clinical cases were screened.

2. Collection of imaging data: Use PACS system to sort out the patient's imaging data information through inclusion and exclusion criteria, screen the cases that can be enrolled.

3. Image data processing: Through PACS system, DICOM format image data is downloaded by workstation, and the image is post-processed and analyzed on the computer with image post-processing software.

VII. Statistical analysis

Data are presented as medians (range) or number (proportion). The Shapiro-Wilk test for normality is employed. Depending on their distribution, Mann-Whitney U or student t tests are performed. We conduct univariate logistic regression analysis to evaluate the relationship between certain variables and a high grade of GEP-NENs. Variables with $p<0.05$ are chosen for multivariate analysis, for which odds ratios (ORs) with 95% confidence intervals (CIs) are computed. The optimal cut-off of continuous variables are obtained by using X-tile. A univariate and multivariable Cox proportional hazard model is constructed to determine predictive factors for prognosis. PFS and OS are estimated using the Kaplan-Meier method and compared by the log-rank test. Statistical analyses are conducted using SPSS (version 26.0, IBM) and GraphPad Prism (version 8.3.0, GraphPad Software Inc., USA), with a significance threshold of $p<0.05$

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