Evaluation of Body Mass Index and Survival of Nasopharyngeal Carcinoma by Propensity-Matched Analysis

An Observational Case-Control Study

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Abstract: The effect of pretreatment body mass index on survival of nasopharyngeal carcinoma remains contradictory.

All patients (N = 1778) underwent intensity-modulated radiotherapy with or without chemotherapy. Body mass index was categorized as underweight (<18.5 kg/m²), normal weight (18.5–22.9 kg/m²), overweight (22.9–27.5 kg/m²), and obesity (>27.5 kg/m²). Propensity score matching method was used to identify patients with balanced characteristics and treatment regimen. Disease-specific survival (DSS), overall survival (OS), distant metastasis-free survival (DMFS), and locoregional relapse-free survival were estimated by Kaplan–Meier method and Cox regression.

Following propensity matching, 115 (underweight vs normal), 399 (overweight vs normal), and 93 (obese vs normal) pairs of patients were selected, respectively. In univariate analysis, underweight patients had inferior DSS/OS (P = 0.042) and DMFS (P = 0.025) while both overweight and obese patients showed similar survival across all the endpoints (P ≥ 0.098) to those with normal weight. In multivariable analysis, underweight remained predictive of poor DSS/OS (P = 0.044) and DMFS (P = 0.040), whereas overweight (P = 0.124) or obesity (P ≥ 0.179) was not associated with any type of survival.

Underweight increased the risk of death and distant metastasis, whereas overweight or obese did not affect the survival of nasopharyngeal carcinoma. This provides support for early nutritional intervention during the long waiting time before treatment.

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a distinct type of head and neck cancer, with particular etiology, epidemiology, symptoms, and therapeutic strategies. Despite the application of magnetic resonance imaging (MRI) and intensity-modulated radiotherapy (IMRT) and the assistance of chemotherapy regimens, the survival of patients with locoregionally advanced NPC remains unsatisfactory.

It was reported that NPC patients with diverse body mass index (BMI) had different survival rates. But the results were quite contradictory. Two studies reported similar survival rates between patients with BMI <18.5 kg/m² and 18.5–22.9 kg/m², while another study observed adverse survival in case of BMI <18.5 kg/m². Shen and colleagues found significant survival advantage of BMI ≥ 27.5 kg/m² over 18.5–22.9 kg/m², whereas this was the very reverse of the finding in the study by Huang and colleagues. These inconsistent findings were possibly related to the following issues.

METHODS

Patients

This study was approved by the institutional review board at Sun Yat-sen University Cancer Center. Formal consent is not required for this retrospective study, and individual informed consent was obtained in the initial treatment.
consent was waived given the anonymous analysis of routine data. We included 1778 histologically proven and nonmetastatic NPC patients who underwent definitive IMRT with or without chemotherapy. Details of IMRT had been described previously.3 Most of patients with advanced stage received induction, concurrent, and adjuvant chemotherapy or combined treatment. Induction chemotherapy mainly consisted of cisplatin plus 5-fluorouracil, cisplatin plus taxane, or triplet of cisplatin plus 5-fluorouracil and taxane every 3 weeks for 2 to 3 cycles. Cisplatin-based concurrent chemotherapy was given weekly or every 3 weeks. Adjuvant chemotherapy was mainly delivered with 2 cycles of cisplatin plus 5-fluorouracil every 3 weeks. All patients were restaged according to the 2010 International Union against Cancer/ American Joint Committee on Cancer (UICC/AJCC) staging system for NPC.

Every 3 to 6 months during the first 3 years and every 6 to 12 months thereafter, patients were conventionally assessed by clinical symptoms, physical examinations, immunoglobulin A against viral capsid antigen (VCA-IgA) and early antigen (EA-IgA) of Epstein–Barr virus test, Epstein–Barr virus deoxyribonucleic acid copy number test (from 2009), and imaging methods, including MRI scan of the nasopharynx and neck, chest radiography, and/or computed tomography (CT), technetium-99m-methylene diphosphonate whole-body bone scan or CT/ MRI scan of specific bones, and abdominal sonography and/or CT. Positron emission tomography-CT, biopsy, and/or fine-needle aspiration may be adopted as appropriate in doubtful cases of locoregional relapses or distant metastases. Patients with relapse, distant metastasis, or in persistent disease underwent salvage treatment including reirradiation, chemotherapy, and surgery.

**Statistical Analysis**

WHO cut points for Asian people were used to categorize patients by BMI as underweight (<18.5 kg/m²), normal weight (18.5–22.9 kg/m²), overweight (22.9–27.5 kg/m²), and obese (>27.5 kg/m²). In the lack of a randomized controlled trial, we used propensity score matching method to well balance characteristics across BMI and consequently reduce possible biases to a minimum in a retrospective analysis.14 Propensity scores were computed by logistic regression for each patient in both case (underweight, overweight, or obese) and control (normal weight) sets. We considered sex, age, smoking, drinking, histology, titers of VCA-IgA and EA-IgA, T-stage, N-stage, clinical stage, and chemotherapy regimens in this analysis. Patients in case and control sets were then matched without replacement at the equal ratio. Covariates balance between case and control sets was examined by t test (continuous variable), χ² test, or Fisher exact test (categorical variable) as appropriate.

Disease-specific survival (DSS, the time from treatment to the death resulting from NPC or treatment complications), overall survival (OS, the time from treatment to the death from any cause), distant metastasis–free survival (DMFS, the time from treatment to the first distant metastasis), and locoregional relapse–free survival (LRFS, the time from treatment to the first locoregional relapse) were estimated using Kaplan–Meier methods and log-rank test. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated with the Cox proportional hazards model.15 Multivariate analyses were performed using Cox proportional hazards model with enter method for BMI, T-stage and N-stage, and forward likelihood ratio method for other covariates.

All statistical analyses were performed using IBM SPSS Statistics version 22.0. Two-sided P values < 0.05 were considered to be significant.

**RESULTS**

**Patients**

Overall, 1778 patients were included in the study. Table 1 displayed the baseline characteristics. Respectively, 708 (39.8%), 123 (6.9%), 792 (44.5%), and 155 (8.7%) patients had normal weight, underweight, overweight, and obesity at the time of diagnosis. The average age at diagnosis, sex, smoking, drinking, and histological type were quite balanced among these patients. Compared with normal weight patients, underweight patients were more likely to be diagnosed with early T-stage, N-stage, and clinical stage and to avoid chemotherapy, whereas precisely the opposite happened to patients with overweight or obesity (all P ≤ 0.002). Additionally, overweight patients showed significantly higher titer of VCA-IgA (P = 0.015) and EA-IgA (P = 0.003) than those with normal weight.

Following propensity score matching, 115 pairs (underweight vs normal), 399 pairs (overweight vs normal), and 93 pairs (obese vs normal) of patients were totally matched in the aspect of average age at diagnosis, sex, smoking, drinking, histological type, T-stage, N-stage, clinical stage, and chemotherapy regimens (Table 2). All subsequent analyses were based on the propensity-matched cohorts.

**BMI and Survival**

Interestingly, all the death events resulted from cancer or treatment complications. Thus, DSS was equal to OS in this study.

In the underweight versus normal weight cohort, the median follow-up was 47.9 months (10.2–106.7 months). Overall, the 4-year DSS/OS, DMFS, and LRFS rates were 81.5% versus 90.1% (P = 0.042), 78.5% versus 88.9% (P = 0.025), and 84.5% versus 89.4% (P = 0.232) for patients with underweight versus normal weight, respectively (Figure 1A–C). Compared with normal weight patients, underweight patients had 2.1-fold higher probability of death (P = 0.044) and distant metastasis (P = 0.040) but similar risk of locoregional relapse (P = 0.219) by multivariate analysis (Table 3).

In the overweight versus normal weight cohort, the median follow-up was 48.2 months (3.3–105.7 months). Univariate analysis showed no significant differences in risk of death (4-year DSS/OS 91.2% vs 88.6%, P = 0.240), distant metastasis (87.8% vs 85.1%, P = 0.240), or locoregional relapse (93.9% vs 91.3%, P = 0.098) between overweight and normal weight patients (Figure 1D–F). In multivariate analyses, overweight was not significantly associated with any type of survival (all P ≥ 0.124) (Table 3).

In the obese versus normal weight cohort, the median follow-up was 42.0 months (8.0–105.7 months). Obese patients were found to be similar to those with normal weight in risk of death (3-year DSS/OS 93.0% vs 92.0%, P = 0.833), distant metastasis (91.8% vs 93.0%, P = 0.378), and locoregional relapse (91.0% vs 90.1%, P = 0.217) by univariate analysis (Figure 1G–I) and multivariate analysis (all P ≥ 0.179) (Table 3).

**DISCUSSION**

As accumulating evidence demonstrated stronger association between obesity and mortality in never than ever smokers,9–11 it means that smoking can absolutely reduce the increase in relative mortality resulted from excess BMI. What is more, smoking is known to promote the development of NPC in population16 and increase the risk of treatment failure and
| TABLE 1. Baseline Characteristics of the Included 1778 Patients Before Propensity Score Matching |
|----------------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                       | Normal 18.5–22.9 | <18.5 (N = 123) | Overweight 22.9–27.5 | Obese ≥27.5 (N = 155) |
|                                       | (N = 708) | P | (N = 792) | P | (N = 155) | P |
| Age                                   | 0.472 | 0.176 | 0.009 |
| Mean                                  | 45.82 | 46.62 | 45.06 | 43.30 |
| SD                                    | 11.11 | 12.34 | 10.65 | 9.97 |
| Median                                | 45.00 | 45.00 | 44.00 | 43.00 |
| Sex                                   | 0.786 | 0.365 | 0.696 |
| Male                                  | 533 (75.3) | 94 (76.4) | 580 (73.2) | 119 (76.8) |
| Female                                | 175 (24.7) | 29 (23.6) | 212 (26.8) | 36 (23.2) |
| Smoking                               | 0.213 | 0.356 | 0.791 |
| Ever                                  | 266 (37.6) | 39 (31.7) | 316 (39.9) | 60 (38.7) |
| Never                                 | 442 (62.4) | 84 (68.3) | 476 (60.1) | 95 (61.3) |
| Drinking                              | 0.316 | 0.422 | 0.592 |
| Ever                                  | 79 (11.2) | 10 (8.1) | 99 (12.5) | 15 (9.7) |
| Never                                 | 629 (88.8) | 113 (91.9) | 693 (87.5) | 140 (90.3) |
| Histology                             | 0.277 | 0.876 | 0.856 |
| I + II                                | 47 (6.6) | 5 (4.1) | 51 (6.4) | 11 (7.1) |
| III                                   | 661 (93.4) | 118 (95.9) | 741 (93.6) | 144 (92.9) |
| VCA-IgA y                             | 0.306 | 0.015 | 0.512 |
| <80                                   | 220 (31.1) | 44 (35.8) | 193 (24.4) | 41 (26.5) |
| 80–320                                | 339 (47.9) | 60 (48.8) | 413 (52.1) | 78 (50.3) |
| ≥320                                  | 149 (21.0) | 19 (15.4) | 186 (23.5) | 36 (23.2) |
| EA-IgA y                              | 0.168 | 0.003 | 0.109 |
| <10                                   | 353 (49.9) | 72 (58.5) | 325 (41.0) | 64 (41.3) |
| 10–40                                 | 219 (30.9) | 34 (27.6) | 284 (35.9) | 52 (33.5) |
| ≥40                                   | 136 (19.2) | 17 (13.8) | 183 (23.1) | 39 (25.2) |
| T-stage                               | <0.001 | <0.001 | 0.002 |
| T1                                    | 130 (18.4) | 41 (33.3) | 86 (10.9) | 18 (11.6) |
| T2                                    | 156 (22.0) | 36 (29.3) | 142 (17.9) | 24 (15.5) |
| T3                                    | 260 (36.7) | 28 (22.8) | 342 (43.2) | 57 (36.8) |
| T4                                    | 162 (22.9) | 18 (14.6) | 222 (28.0) | 56 (36.1) |
| N-stage                               | 0.001 | <0.001 | 0.002 |
| N0                                    | 191 (27.0) | 54 (43.9) | 121 (15.3) | 23 (14.8) |
| N1                                    | 393 (55.5) | 55 (44.7) | 483 (61.0) | 90 (58.1) |
| N2                                    | 90 (12.7) | 12 (9.8) | 155 (19.6) | 28 (18.1) |
| N3                                    | 34 (4.8) | 2 (1.6) | 33 (4.2) | 14 (9.0) |
| Clinical stage                        | <0.001 | <0.001 | <0.001 |
| I                                     | 71 (10.0) | 31 (25.2) | 12 (1.5) | 1 (0.6) |
| II                                    | 165 (23.3) | 39 (31.7) | 157 (19.8) | 30 (19.4) |
| III                                   | 281 (39.7) | 34 (27.6) | 381 (48.1) | 58 (37.4) |
| IV                                    | 191 (27.0) | 19 (15.4) | 242 (30.6) | 66 (42.6) |
| CT                                    | <0.001 | <0.001 | <0.001 |
| No                                    | 178 (25.1) | 92 (74.8) | 16 (2.0) | 0 |
| IC                                    | 100 (14.1) | 6 (4.9) | 27 (3.4) | 0 |
| CC                                    | 320 (45.2) | 7 (5.7) | 331 (41.8) | 20 (12.9) |
| IC + CC                               | 61 (8.6) | 6 (4.9) | 381 (48.1) | 125 (80.6) |
| CC + AC                               | 44 (6.2) | 11 (8.9) | 28 (3.5) | 4 (2.6) |
| IC + CC + AC                          | 5 (0.7) | 1 (0.8) | 9 (1.1) | 6 (3.9) |

All P values were calculated with taking normal weight as reference. 
AC = adjuvant chemotherapy, CC = concurrent chemotherapy, CT = chemotherapy, EA = early antigen, IC = induction chemotherapy, IgA = immunoglobulin A, SD = standard deviation, VCA = viral capsid antigen. 
† Based on the criteria of WHO histological type (1991): I—Squamous-cell carcinomas, II—Differentiated nonkeratinizing carcinoma, III—Undifferentiated nonkeratinizing carcinoma. 
‡ In accordance with the criteria adopted in the previous studies. 
¶ Fisher exact test.
TABLE 2. Baseline Characteristics in 3 Cohorts of Matched Pairs After Propensity Score Matching

|                          | Normal (N = 115) | Underweight (N = 115) | P      | Normal (N = 399) | Overweight (N = 399) | P      | Normal (N = 93) | Obese (N = 93) | P      |
|--------------------------|------------------|-----------------------|--------|------------------|----------------------|--------|-----------------|----------------|--------|
| Age                      | 48.39            | 47.13                 | 0.438  | 45.45            | 45.07                | 0.611  | 43.30           | 44.57          | 0.404  |
| Median                   | 47.00            | 46.00                 |        | 45.00            | 44.00                |        | 42.00           | 45.00          |        |
| Sex                      |                  |                       |        |                  |                      |        |                 |                |        |
| Male                     | 85 (73.9)        | 88 (76.5)             | 0.647  | 296 (74.2)       | 300 (75.2)           | 0.745  | 74 (79.6)       | 73 (78.5)     | 0.857  |
| Female                   | 30 (26.1)        | 27 (23.5)             |        | 103 (25.8)       | 99 (24.8)            |        | 19 (20.4)       | 20 (21.5)     |        |
| Smoking                  | 0.887            |                       |        | 244 (61.2)       | 244 (61.2)           |        | 60 (64.5)       | 61 (65.6)     |        |
| Ever                     | 36 (31.3)        | 37 (32.2)             | 1.000  | 155 (38.8)       | 155 (38.8)           | 1.000  | 33 (35.5)       | 32 (34.4)     | 0.878  |
| Never                    | 79 (68.7)        | 78 (67.8)             | 0.757  | 349 (87.5)       | 355 (89.0)           | 0.389  | 80 (86.0)       | 82 (88.2)     |        |
| Drinking                 |                  |                       |        |                  |                      |        |                 |                |        |
| Ever                     | 9 (7.8)          | 9 (7.8)               | 0.510  | 50 (12.5)        | 44 (11.0)            |        | 13 (14.0)       | 11 (11.8)     | 0.662  |
| Never                    | 106 (92.2)       | 106 (92.2)            |        | 290 (70.5)       | 291 (71.2)           |        | 87 (91.1)       | 89 (91.2)     |        |
| Histology *              |                  |                       |        |                  |                      |        |                 |                |        |
| T1                       | 6 (5.2)          | 5 (4.3)               |        | 29 (7.3)         | 23 (5.8)             | 0.389  | 7 (7.5)         | 7 (7.5)        |        |
| T2                       | 109 (94.8)       | 110 (94.7)            |        | 370 (92.7)       | 376 (94.2)           |        | 86 (92.5)       | 86 (92.5)     |        |
| VCA-IgA †                |                  |                       |        |                  |                      |        |                 |                |        |
| <80                      | 38 (33.0)        | 42 (36.5)             | 0.731  | 119 (29.8)       | 108 (27.1)           | 0.672  | 27 (29.0)       | 25 (26.9)     | 0.365  |
| ≥320                     | 27 (23.7)        | 28 (24.3)             |        | 101 (25.8)       | 99 (24.8)            |        | 20 (21.5)       | 21 (22.4)     |        |
| EA-IgA †                 |                  |                       |        |                  |                      |        |                 |                |        |
| <10                      | 72 (62.6)        | 66 (57.4)             | 0.705  | 180 (45.1)       | 169 (42.4)           | 0.735  | 42 (45.2)       | 41 (44.1)     | 0.780  |
| ≥40                      | 14 (12.2)        | 17 (14.8)             |        | 83 (20.8)        | 87 (21.8)            |        | 27 (29.0)       | 24 (25.8)     | 0.809  |
| N-stage                  |                  |                       |        |                  |                      |        |                 |                |        |
| N0                       | 26 (22.6)        | 28 (24.3)             | 0.952  | 68 (17.0)        | 77 (19.3)            | 0.331  | 10 (10.8)       | 12 (12.9)     | 0.809  |
| N1                       | 67 (58.3)        | 57 (49.6)             |        | 252 (63.2)       | 243 (60.9)           |        | 59 (63.4)       | 49 (52.7)     |        |
| N2                       | 17 (14.8)        | 26 (22.6)             |        | 58 (14.5)        | 66 (16.5)            |        | 13 (14.0)       | 17 (18.3)     |        |
| N3                       | 5 (4.3)          | 4 (3.5)               |        | 21 (5.3)         | 13 (3.3)             |        | 9 (9.7)         | 8 (8.6)       |        |
| Clinical stage           |                  |                       | 0.429  | 0.373            |                      |        |                 |                |        |
| T1                       | 5 (4.3)          | 9 (7.8)               | 0.544  | 11 (2.8)         | 10 (2.5)             | 0.544  | 3 (3.2)         | 1 (1.1)       | 0.581  |
| T2                       | 20 (17.4)        | 15 (13.0)             |        | 76 (19.0)        | 97 (24.3)            |        | 14 (15.1)       | 18 (19.4)     |        |
| T3                       | 49 (42.6)        | 46 (40.0)             |        | 183 (45.9)       | 189 (47.4)           |        | 33 (35.5)       | 36 (38.7)     |        |
| T4                       | 41 (35.7)        | 45 (39.1)             |        | 129 (32.3)       | 103 (25.8)           |        | 43 (46.2)       | 38 (40.9)     |        |
| CT                       |                  |                       | 0.296  | 1.000            |                      |        |                 |                | 0.876  |
| No                       | 75 (65.2)        | 86 (74.8)             |        | 15 (3.8)         | 15 (3.8)             |        | –              | –             |        |
| IC                       | 12 (10.4)        | 6 (5.2)               |        | 27 (6.8)         | 26 (6.5)             |        | –              | –             |        |
| CC                       | 13 (11.3)        | 6 (5.2)               |        | 269 (67.4)       | 270 (67.7)           |        | 22 (23.7)       | 20 (21.5)     |        |
| CC + AC                  | 5 (4.3)          | 5 (4.3)               |        | 59 (14.8)        | 59 (14.8)            |        | 61 (65.6)       | 64 (68.8)     |        |
| IC + CC + AC             | 2 (1.7)          | 1 (0.9)               |        | 5 (1.3)          | 5 (1.3)              |        | 4 (4.3)         | 5 (5.4)       |        |

AC = adjuvant chemotherapy, CC = concurrent chemotherapy, CT = chemotherapy, EA = early antigen, IC = induction chemotherapy, IgA = immunoglobulin A, SD = standard deviation, VCA = viral capsid antigen.  
* Based on the criteria of WHO histological type (1991): I—Squamous-cell carcinomas, II—Differentiated nonkeratinizing carcinoma, III—Undifferentiated nonkeratinizing carcinoma.  
† In accordance with the criteria adopted in the previous studies.  
‡ Fisher exact test.
So it is of particular importance to account for the confounding influence of smoking. Secondly, adiposity was found to accelerate the tumor growth and progression via insulin resistance, hyperinsulinemia, hyperglycemia, and chronic low-grade inflammation. Thus, the consequent on the interaction between excess BMI and tumor stage would cover the true survival differences across BMI if balancing tumor stage is failed. And similar interaction between BMI and chemotherapy may further increase the interference. Accordingly, the true prognostic impact of BMI on NPC survival cannot be exactly evaluated before completely balancing these factors.

In contrast to prior studies, our study included all patients receiving IMRT, fully balanced characteristics, and chemotherapy regimen using propensity matching method and further adjusted for these confounders with multivariate analysis. We found that underweight patients had 2-fold higher risk of death and distant metastasis than those with normal weight, whereas both overweight and obese patients were similar to those with normal weight across all the endpoints (DSS, OS, DMFS, and LRFS).

The mechanism by which underweight before treatment may lower NPC survival is not well understood. It is usually assumed that underweight is possibly associated with an advanced stage and an aggressive type of tumor. But this cannot completely explain the adverse survival for underweight NPC. This disease hardly hinders oral intake and causes severe weight loss on the whole, despite that certain patients possibly suffer weight loss owing to preclinical diseases. What is more important, we actually observed that underweight patients were more likely to be those with early stage NPC before propensity matching (Table 1). Further, the inferior survival for underweight patients was observed by comparison of underweight and normal weight patients with similar tumor stage and chemotherapy regimen after propensity score matching. So the intrinsic trait of underweight maybe works in a much more profound way. Underweight patients are often malnourished or even cachectic. Among these patients, the decrease of protein anabolism and caloric intake, coupled with the increase of protein catabolism, lipolysis, and resting energy expenditure, eventually causes impaired immunity and reduced survival. Additionally, the established influence of protein-energy malnutrition on immunity more likely results in the increased infectious toxicity and inflammation reaction in underweight patients. The induced and persisted high level of systemic inflammatory factors, such as tumor necrosis factor-α, and interleukin-6, can facilitate tumor cell proliferation and progression and enhance malignant properties. Finally, the malnutrition status of underweight patients may reduce chemotherapy response and increase chemotherapy toxicity.

Overweight or even obese patients were reported to have higher survival rate than those with normal weight in prior
relapse–free survival, NS

and inhibit apoptosis in NPC.25 And insulin-resistant adipocytes insulin-like growth factor 1, which promote cell proliferation has been linked to increased circulating levels of insulin and survival. Inversely, adiposity in overweight and obese patients weight or obesity itself showed no protective effect on NPC during subsequent chemoradiotherapy. Moreover, this survival overweight or obesity showed survival advantage over normal for the management of pretreatment weight if we found that unknown at the time of diagnosis. It would be actually helpless multivariate analysis, because midtreatment weight loss is balanced after propensity matching, adiposity can still likely to be diagnosed with advanced-stage disease (Table 1).

|                      | DMFS  |                     | LRFS  |                     |
|----------------------|-------|---------------------|-------|---------------------|
|                      | HR (95% CI) | P | HR (95% CI) | P | HR (95% CI) | P |
| Underweight vs normal | 2.11 (1.02–4.37) | 0.044 | 2.09 (1.04–4.21) | 0.040 | 1.02 (0.99–1.05) | 0.219 |
| T-stage              | 2.39 (1.47–3.90) | <0.001 | 1.79 (1.20–2.66) | 0.004 | 1.74 (1.08–2.81) | 0.024 |
| N-stage              | 2.25 (1.43–3.55) | <0.001 | 2.14 (1.40–3.28) | 0.001 | 1.51 (0.89–2.57) | 0.129 |
| Age (continuous)     | 1.05 (1.03–1.07) | <0.001 | NS           | NS            | NS           |
| Smoking              | 1.74 (1.15–2.62) | 0.009 | NS           | NS            | NS           |
| Obese vs normal      | 1.00 (0.97–1.02) | 0.750 | 0.98 (0.95–1.02) | 0.391 | 0.98 (0.95–1.01) | 0.179 |
| T-stage              | 1.12 (0.71–1.76) | 0.621 | 1.07 (0.65–1.74) | 0.800 | 1.33 (0.81–2.17) | 0.259 |
| N-stage              | 1.64 (1.00–2.67) | 0.049 | 2.22 (1.32–3.72) | 0.003 | 0.79 (0.43–1.47) | 0.465 |
| Age (continuous)     | 1.04 (1.00–1.08) | 0.046 | NS           | NS            | NS           |

CI = confidence interval, DMFS = distant metastasis–free survival, DSS = disease-specific survival, HR = hazard ratio, LRFS = locoregional relapse–free survival, NS = not significant, OS = overall survival.

Table 3. Summary of Important Prognostic Factors in Multivariate Analysis *

In conclusion, underweight patients showed inferior survival while both overweight and obese patients had similar survival to those with normal weight. Importantly, this large-scale propensity-matched study identifies underweight to be a manageable risk factor and provides support for early nutritional intervention during the long waiting time before the initial treatment.

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