Abstract

Objective. To assess the value of several diagnostic methods of nutritional status during the initial management of a head and neck cancer.


Setting. Tertiary referral center.

Subjects and Methods. Ninety patients with head and neck cancer participated in the study. Assessment of their nutritional status was made with anthropometric, biological, body, and muscle measurements (the last by computed tomography: L3 muscle mass index [L3MMI]). Assessment of muscle performance (functional reflection of nutritional status) was made via the Short Physical Performance Battery test. The malnutrition thresholds were set according to the literature.

Results. Mean body mass index (BMI) was 24.6 ± 5.4 kg/m². Mean weight loss and albumin levels were –4.5 ± 10.5 kg and 37.1 ± 5.2 g/L, respectively. Fourteen percent of patients were diagnosed as malnourished on the basis of BMI, 54% according to the Nutritional Risk Index (NRI), and 58% by L3MMI. There was 64% agreement between NRI and L3MMI (P < .001). All patients identified as malnourished by BMI were considered as such by the other assessment methods; however, many malnourished patients had normal or high BMI. The Short Physical Performance Battery score was low particularly among patients considered to be the most undernourished by the other methods.

Conclusion. NRI and L3MMI are the best methods to identify patients as being malnourished. Functional muscle assessment can determine the severity of malnutrition.

Keywords
malnutrition assessment, functional muscle assessment, head and neck cancer, tomodensitometry

Malnutrition can be defined as a subacute or chronic state in which the combination of nutritional imbalance and inflammatory activity modifies body composition (decrease in body muscle and fat) and impairs organ function (immune, muscle, and cognitive deficiencies). Several studies showed the importance of muscle mass in nutritional status, specifically suggesting that variations in muscle tissue (ie, sarcopenia) are correlated with complications deriving from malnutrition. In addition, sarcopenia is found among patients with normal or elevated body mass index (BMI). In head and neck cancer (HNC), malnutrition is an aggravating factor because it increases complications and decreases the efficacy and tolerance of the treatment. Hence, assessment of nutritional status is a complementary indicator of prognosis irrespective of the treatment undertaken.

Studies on nutritional assessment established malnutrition thresholds (MTs) adapted to different diagnostic methods, of which the most widely used is the variation in weight over the previous 6 months. This assessment is improved when it is factored into the calculation of the Nutritional Risk Index (NRI), a composite score combining loss of weight and serum albumin levels. The NRI is considered the benchmark for assessing nutritional risk.

Biological, physical, and functional parameters are alternative means of assessing nutritional status. The anthropometric parameters are weight, height, tricipital skinfold thickness, and upper arm circumference (UAC). These values are used to calculate BMI and, by extrapolation, to estimate body composition. Other techniques for measuring body composition, such as bioelectrical impedance analysis,

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have been developed.\textsuperscript{9,10} They allow one to obtain an estimate of fat body mass, lean body mass (ie, muscle mass + visceral mass + body fluids), and muscle mass.\textsuperscript{10}

Recent computed tomography (CT) methods can estimate muscle mass from measurement of the muscle surface on an axial section through the third lumbar vertebra. This recent method is a “revolution” in nutritional assessment because it describes muscle wasting as both a prominent feature of a patient with cancer (despite normal or heavy body weight) and a strong prognostic factor.\textsuperscript{11}

Nutritional status can also be assessed in a functional way by measuring muscle strength or performance. Assessment of muscle mass by walking speed is now an acknowledged marker of mortality in the elderly.\textsuperscript{12} The Short Physical Performance Battery (SPPB) is a muscle performance test, easy and quick to perform, and it can detect sarcopenia.\textsuperscript{2} This test is also a functional nutritional assessment.

Published reports stressed the need to rapidly diagnose and initiate management of malnutrition.\textsuperscript{13} However, there are few studies of the particular case of HNC, and the different markers have never been tested simultaneously to assess malnutrition—in particular, the physical and functional measurements of muscle mass. The aim of this work was therefore to study the different methods to assess the nutritional status in HNC.

Materials and Methods

We performed a prospective exploratory study. Ninety patients, 13 women (14%) and 77 men (86%), were recruited between January 1, 2014, and September 1, 2014. All adult patients currently diagnosed with a first HNC were included. Patients with recurrence or a second cancer were excluded. The study population was described by frequencies and percentages for qualitative and categorical data and by mean \( \pm \) SD for quantitative data. Comparison of 2 qualitative data was performed by the chi-square test (or Fisher’s exact test when appropriate). Quantitative data were compared between groups by Student’s \( t \) test (or Kruskal-Wallis test when normality was rejected by Shapiro-Wilk test). Agreement among the different markers was determined by kappa coefficient. All tests were 2-sided, and a \( P \) value \(<5\%\) was considered significant. All statistics were computed with Stata 12 (StataCorp, College Station, Texas).

Muscle function was assessed by the SPPB. The test comprises 3 tasks (balance, 4-m walk, and 5 chair stands) with a maximum score of 12. Impaired muscle function was defined as a score \(<8\).\textsuperscript{2,12}

Albumin (g/L) and prealbumin (g/L) levels were collected. The MTs were 35 g/L and 0.11 g/L, respectively. With these data, the following scores were calculated:

- NRI = $1.519 \times$ albumin + (current weight / usual weight) \( \times \) 100. MT was set \( \leq \) 97.5.\textsuperscript{2}
- Percentage weight loss over the previous 6 months = [(comfortable weight – current weight) / current weight] \( \times \) 100. MT was set at \( \geq 5\%\).\textsuperscript{13}
- BMI = current weight / height\(^2\) (kg/m\(^2\)). MTs were set according to age: \( \leq 18.5 \) for patients \( \leq 70 \) years and \( \leq 21 \) for patients \( > 70 \) years.
- Upper arm muscle circumference\textsuperscript{8} (mm) = UAC in cm – (\( \pi \times \) tricipital skinfold thickness in mm). MTs were set according to sex and age: \( \leq 240 \) for men \((\leq 220 \) after the age of 65 years) and \( \leq 190 \) for women.
- Lean muscle mass measured by the formula of Kyle.\textsuperscript{9}
- Muscle mass measured by the formula of Janssen.\textsuperscript{10}
- Lean mass index (kg/m\(^2\); per Kyle). Ratio of lean muscle mass:height\(^2\). MTs were set at 17 for men and 15 for women.\textsuperscript{9,10}
- Muscle mass index (kg/m\(^2\); per Janssen). Ratio of muscle mass:height\(^2\). MTs were set at 10.76 for men and 6.76 for women.\textsuperscript{9,10}

The patients then underwent a CT nutritional assessment at a lumbar vertebral landmark (L3). This landmark was validated for patients with cancer. The method is described elsewhere.\textsuperscript{11} It allows determining the L3 muscle mass index (L3MMI; cm\(^2\)/m\(^2\)). MTs were set at 52.4 for men and 38.5 for women.

All the MTs were defined according to the literature.\textsuperscript{2,6-13}

Statistical Analyses

The study population was described by frequencies and associated percentages for qualitative and categorical data and by mean \( \pm \) SD for quantitative data. Comparison of 2 qualitative data was performed by the chi-square test (or Fisher’s exact test when appropriate). Quantitative data were compared between groups by Student’s \( t \) test (or Kruskal-Wallis test when normality was rejected by Shapiro-Wilk test). Agreement among the different markers was determined by kappa coefficient. All tests were 2-sided, and a \( P \) value \(<5\%\) was considered significant. All statistics were computed with Stata 12 (StataCorp, College Station, Texas).
Results

Ninety consecutive patients underwent nutritional assessment: 78% of whom had a history of alcohol consumption; 77%, tobacco consumption; and 63%, both. Mean age at diagnosis was 61 ± 11 years (range, 33-94 years). Mean weight was 71 ± 17 kg (range, 45-126 kg). Mean BMI was 24.6 ± 5.4 kg/m² (range, 16.1-43.6 kg/m²). Mean weight loss over the previous 6 months was -4.49 ± 10.5 kg.

Nutritional assessment according to sex showed a mean weight of 63 ± 13 kg for the women and 72 ± 17 kg for the men. Mean BMIs were comparable: 25 ± 6 (men) versus 24 ± 5 (P = .72). The proportion of patients identified as being malnourished varied depending on the nutritional assessment included laboratory findings. The mean albumin level was 37.1 ± 5.2 g/L; prealbumin level, 0.21 ± 0.07 g/L; and NRI, 96.2 ± 10.1 (98 ± 10 for the women and 96 ± 10 for the men; P = .54).

Change in body weight over the previous 6 months was -4.49 ± 10.5 kg (range, 10.5 kg to 24.6 kg). Analysis of the correlation among BMI, Janssen’s muscle mass index and NRI was performed in Table 4. The appetite of patients differed between those who were malnourished (VAS score, 7) and the group not suffering from malnutrition (VAS score, 8), so we can say that malnourished patients have less appetite. Although the difference is only slight, it is statistically significant (P = .04), which therefore makes it an aggravating factor for the nutritional status of these patients.

Likewise, evolution of the disease was accompanied by changes in dietary intake: 88% of patients with stage 1 disease and 100% of patients with stage 2 ate a solid diet, as opposed to 50% of patients with stage 3 and 57% of patients with stage 4. Most patients (57 of 89), whether malnourished or not, made no change in their eating habits and continued to have a solid diet. However, once changes in their eating habits were made, the proportion of malnourished patients markedly increased. Of 57 patients with a solid diet, 25 were malnourished (44%); of 27 with a dual diet, 19 were malnourished (70%); and of the 5 who had a liquid diet only, 1 was not malnourished (80%). Thus, patients with a liquid or dual diet were predominantly malnourished (P < .001).

Analysis of nutritional status on the basis of NRI and according to tumor location evidenced no statistical difference. However, a greater proportion of patients with tumors in the oropharynx and hypopharynx were malnourished (55% and 59%, respectively).

The appetite of patients differed between those who were malnourished (VAS score, 7) and the group not suffering from malnutrition (VAS score, 8), so we can say that malnourished patients have less appetite. Although the difference is only slight, it is statistically significant (P = .04), which therefore makes it an aggravating factor for the nutritional status of these patients.

Multivariate analysis based on the NRI was performed in an attempt to identify predictive factors of malnutrition. The factors taken into account were age, sex, tumor stage and location, tobacco and alcohol abuse, and pain. None, however, was statistically predictive of malnutrition.

Functional nutritional assessment brought out the interesting complementary finding that physical performance is clinically impaired in later stages of malnutrition. Patients not suffering from malnutrition according to NRI all had an SPPB score >8, thus within normal limits. When the SPPB score is very low, NRI is always abnormal. In contrast, only patients with a very low NRI score had a correspondingly low SPPB score (P < .001). SPPB had 100% specificity and positive predictive value (PPV; Table 2).

Analysis of the correlation among BMI, Janssen’s muscle mass index, L3MMI, and NRI is given in Table 3. BMI had excellent specificity and PPV but poor sensitivity and negative predictive value. No statistically significant correlation was found between Janssen’s muscle mass index and NRI. There was, however, a significant correlation between L3MMI and NRI (P < .001). Finally, a weak correlation occurred between Janssen’s muscle mass index and L3MMI (P < .001; Table 4).

Discussion

The aim of this study was to assess the value of several diagnostic methods of nutritional status among patients with HNC. At the beginning of management, NRI identified 54% of patients as being malnourished, a proportion that corresponds to that in reports of other types of cancer.14,15 This study shows the weakness of certain markers routinely used. BMI is widely used, but it was able to diagnose malnutrition in only 14% of patients. In contrast, it had a specificity of 98% and a PPV of 92%; hence, the information that it provided was reliable. While it is still of value for nutritional screening, it gives too many false negatives to be used alone.

The most widely used marker in reports is weight loss in the previous 6 months. With an MT of 10% weight loss,
Table 1. Numeric Values of the Different Evaluation Methods and Nutritional Status per the Evaluation Method for the Total Patient Population.

<table>
<thead>
<tr>
<th>Nutritional Status Evaluation Method</th>
<th>Abbreviation</th>
<th>Formula</th>
<th>Patients Who Had the Test, n</th>
<th>Percent Malnutrition Threshold</th>
<th>Mean Value in the Population</th>
<th>Malnourished Patients per Evaluation Method, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutritional risk index</td>
<td>NRI</td>
<td>N/A 1.519 × albumin + (current weight / usual weight) × 100</td>
<td>N/A 89</td>
<td>(\leq 97.5)</td>
<td>96.2 ± 10.1</td>
<td>54</td>
</tr>
<tr>
<td>Weight loss in last 6 mo</td>
<td>N/A</td>
<td>N/A [(comfortable weight – current weight) / current weight] × 100</td>
<td>% 90</td>
<td>(\geq 5% ; \geq 10%</td>
<td>-4.5 ± 10.5 ; -4.5 ± 10.5</td>
<td>38 ; 28</td>
</tr>
<tr>
<td>Body mass index</td>
<td>BMI</td>
<td>Current weight / height² kg/m² 90</td>
<td>(\leq 18.5) if (\leq 70) y; (\leq 21) if (&gt;70) y</td>
<td>24.6 ± 5.4</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Prealbumin levels</td>
<td>N/A</td>
<td>N/A g/L 89</td>
<td>0.11</td>
<td>0.2 ± 0.1</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Albumin levels</td>
<td>N/A</td>
<td>N/A g/L 89</td>
<td>(\leq 35)</td>
<td>37.1 ± 5.2</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Short physical performance battery</td>
<td>SPPB</td>
<td>3 tasks (balance, 4-m walk, and 5 chair stands) with a maximum score of 12</td>
<td>N/A 87</td>
<td>(\leq 8)</td>
<td>10.4 ± 2.9</td>
<td>18</td>
</tr>
<tr>
<td>Upper arm circumference</td>
<td>UAC</td>
<td>N/A mm 87</td>
<td>(\leq 240) for male; (\leq 220) for male ((&gt;65) y); (\leq 190) for female</td>
<td>253.9 ± 37.3</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Lean muscle mass index</td>
<td>Kyle’s LMI</td>
<td>See reference 9 kg /m² 87</td>
<td>(\leq 17) for male; (\leq 15) for female</td>
<td>20.1 ± 3.3</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Muscle mass index</td>
<td>Janssen’s MMI</td>
<td>See reference 10 kg/m² 87</td>
<td>(\leq 10.76) for male; (\leq 6.76) for female</td>
<td>10.6 ± 1.9</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>L3 muscle mass index on tomodensitometry</td>
<td>L3MMI</td>
<td>See reference 11 cm²/m² 78</td>
<td>(\leq 52.4) for male; (\leq 38.5) for female</td>
<td>49.3 ± 10.9</td>
<td>58</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: N/A, not applicable.
only 28% of the patients were considered malnourished. However, with a 5% threshold, the proportion was 38%. It is therefore clear that, as a marker, it is more effective than BMI and should be used in preference, particularly when combined with a composite score such as that of the NRI.

The biological markers are significantly less sensitive than NRI, particularly prealbumin, which diagnosed 8% of patients as having malnutrition, against 31% by albumin. They are subject to large variations depending on the patient’s inflammatory status and therefore cannot be considered as reliable diagnostic indicators. Incorporating them into a score such as the Prognostic Inflammatory and Nutritional Index would correlate the inflammatory score with the nutritional score but would require a biological supplement. In contrast, using them in combination with other markers, such as variation in weight and NRI, could refine diagnosis. Some authors recommended assaying prealbumin during refeeding because its short half-life makes it a good indicator of the efficacy of reinstitution of nutrition.16 Finally, evidence suggests that if used individually these markers are not reliable for the diagnosis of malnutrition.

Anthropometric measurements (UAC) and assessment of muscle function (SPPB) were also weakly sensitive in diagnosis of malnutrition: 28% and 18%, respectively. Assessment of UAC is time-consuming and of comparatively little diagnostic value. Some authors therefore did not recommend it as a first-intention diagnostic.17

It also emerged from our study that physical performance is clinically impaired in later stages of malnutrition. In our series, SPPB, as compared with NRI, had a 100% specificity and PPV. A patient with functional impairment was always assessed as malnourished by NRI, whereas SPPB had only 35% sensitivity. NRI was statistically weaker for patients with a low SPPB score (P < .001). This means that moderate malnutrition diagnosed early by NRI does not sufficiently disrupt muscle function to be detected by SPPB. In contrast, a patient can be considered at greater risk once physical performance is impaired (SPPB ≤8). As such, assessment of muscle function could be a prognostic factor of disease severity.18 Systematic assessment of muscle function among patients with a low NRI score could thus be of value for a more rapid diagnosis of severe malnutrition.

The results of impedance analysis vary according to the tissue compartment studied. When lean body mass is assessed (Kyle’s formula), the proportion of malnourished patients is only 17%. This figure is low and underestimates nutritional status, since assessment of lean body mass is distorted for patients with edema. In contrast, when muscle mass alone is assessed by Janssen’s formula,10 the proportion of malnourished patients is 44%, a rate similar to that obtained with NRI. However, no correlation was found between the formulae, probably because of our limited patient sample size. Impedance analysis is easy to use and potentially of value in the diagnosis of malnutrition in HNC.

The L3MMI test found the highest proportion of malnourished patients (58%). The results of the test were correlated with those of NRI, which shows that it is effective. It

<table>
<thead>
<tr>
<th>Methods</th>
<th>Nonmalnourished</th>
<th>Malnourished</th>
<th>P Value</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (n = 90)</td>
<td></td>
<td></td>
<td>&lt;.01</td>
<td>25</td>
<td>98</td>
<td>92</td>
<td>53</td>
</tr>
<tr>
<td>Nonmalnourished</td>
<td>41</td>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malnourished</td>
<td>1</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMI Janssen (n = 88)</td>
<td></td>
<td></td>
<td>.1</td>
<td>62</td>
<td>52</td>
<td>51</td>
<td>63</td>
</tr>
<tr>
<td>Nonmalnourished</td>
<td>25</td>
<td>24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malnourished</td>
<td>15</td>
<td>24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>L3MMI (n = 78)</td>
<td></td>
<td></td>
<td>&lt;.01</td>
<td>66</td>
<td>67</td>
<td>73</td>
<td>59</td>
</tr>
<tr>
<td>Nonmalnourished</td>
<td>22</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malnourished</td>
<td>15</td>
<td>30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPPB (n = 87)</td>
<td></td>
<td></td>
<td>&lt;.01</td>
<td>35</td>
<td>100</td>
<td>100</td>
<td>57</td>
</tr>
<tr>
<td>No impairment</td>
<td>41</td>
<td>30</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Impairment</td>
<td>0</td>
<td>16</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; L3MMI, L3 muscle mass index; MMI, muscle mass index; NRI, Nutritional Risk Index; SPPB, Short Physical Performance Battery.
is a simple method to use, and interpretation of the results is reliable and reproducible among operators. However, the higher proportion of patients identified as malnourished by CT images does not mean that L3MMI is a better test. While diagnosis of malnutrition and sarcopenia may be more sensitive and made earlier, it is offset by the possibility of false positives. If the diagnostic power of this test was confirmed, it could prove to be a reliable method of screening for malnutrition.

The consistency of the food ingested by patients is a reflection of nutritional status, and a change in eating habits is a sign of dietary distress. In our study, changing from a solid to a dual or liquid diet was accompanied by malnutrition in a majority of cases (72%). The amount and consistency of food ingested should therefore be systematically assessed in HNC.

Regarding these results, it is possible to establish an assessment chart for malnutrition detection at the beginning of the management of patients with HNC (Figure 1). BMI can be a good screening tool to detect malnutrition when BMI is in the low range; then, the patient can be considered malnourished and an appropriate management performed. In case of a normal or higher BMI, there is a further step needed, and we think that the best and easiest method is to estimate the NRI. If the NRI is abnormal, then the patient is considered malnourished; however, if the NRI is normal, then a further analysis of body composition is performed to detect malnutrition. As done in this study, the CT method appears to be the best way to appreciate the nutritional state. So after the CT scan examination, a definite statement on the nutritional status of the patient can be established. Noticeably, this evaluation needs abdominal CT scans, which are not common in HNC. That is why a recent study compared the CT scan at the L3 level (the “new” benchmark of body composition evaluation) with a CT scan at the C3 level, with a good correlation. Another important point is that the correlation between NRI and L3MMI was only 64%. For the moment, we lack evidence about the most valuable methods to detect malnutrition. This is the reason why we think that the classical criteria for detecting malnutrition are useful at the first step when they are positive. However, when these criteria are flawed in specific situations such as obesity, we consider that other methods should be done to better assess the nutritional status of the patients.

**Conclusion**

There exist various methods for the assessment of malnutrition at the beginning of HNC management. However, they do not all share the same sensitivity nor give the same information. Finally, we need to know which methods of nutritional status assessment are the more relevant regarding the prognosis of the disease.

**Author Contributions**

Nicolas Saroul, data analysis, drafting, final approval, accountability for all aspects of the work; Rémy Pastourel, data analysis, drafting, final approval, accountability for all aspects of the work; Aurélien Mulliez, data analysis, drafting, final approval, accountability for all aspects of the work; Nicolas Farigon, data analysis, drafting, final approval, accountability for all aspects of the work; Thierry Mom, data analysis, drafting, final approval, accountability for all aspects of the work; Vincent Dupuch, data analysis, drafting, final approval, accountability for all aspects of the work; Yves Boirie, data analysis, drafting, final approval, accountability for all aspects of the work; Laurent Gilain, data analysis, drafting, final approval, accountability for all aspects of the work.

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**Table 4. Agreement between L3MMI and Janssen’s MMI by Impedancemetric Examination.**

<table>
<thead>
<tr>
<th>L3MMI</th>
<th>Janssen’s MMI, N</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsarcopenic</td>
<td>25</td>
<td>8</td>
</tr>
<tr>
<td>Sarcopenic</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>38</td>
</tr>
</tbody>
</table>

Abbreviations: L3MMI, L3 muscle mass index; MMI, muscle mass index.

**Figure 1. Proposed nutritional assessment chart for treatment of patients with neoplasia of the respiratory and upper digestive tracts. BMI, body mass index; CT, computed tomography; L3MMI, L3 muscle mass index; NRI, Nutritional Risk Index.**
Disclosures

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Sponsorships: None.

Funding source: None.

References