

Malnutrition Universal Screening Tool (MUST) predicts disease activity in patients with Crohn's disease.

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Abstract

Background:

Malnutrition in patients with inflammatory bowel disease (IBD) is common and under-recognized in patients with Crohn's disease (CD) and ulcerative colitis (UC).

Aims:

We examined the relationship between nutritional risk and disease activity in outpatient inflammatory bowel disease patients, using the Malnutrition Universal Screening Tool (MUST).

Methods:

The study was conducted in outpatient IBD clinics in London, Ontario over two months. We examined the association between the MUST scores and the Harvey Bradshaw Index (HBI) and the PMI (Partial Mayo Score), for CD and UC, respectively. Logistic regression was used to examine associations between demographic data, disease characteristics and laboratory values with nutritional risk score.

Results:

There were a 154 patients were studied over a 2 month period. A high MUST score was strongly associated elevated Harvey Bradshaw Index scores ($p=0.005$) for patients with Crohn's disease, but not with the Partial Mayo Index scores ($p=0.597$) for patients with ulcerative colitis. Nutritional risk scoring did not correlate with lower levels of disease activity. We noted significant associations in the odds of elevated nutritional risk and decreased albumin (OR 1.96, $p<0.001$), decreased Vitamin D (OR 1.51 $p=0.032$), and decreased creatinine (OR 1.47, $p=0.050$).

Conclusions:

The MUST predicts disease activity in patients with Crohn's disease but there is a floor effect. Further studies are required to determine if targeted treatment and monitoring of the nutritional state affects clinical outcomes in patients with CD/IBD.

Introduction

Malnutrition in patients with inflammatory bowel disease (IBD) is common, under-recognized, and negatively influences clinical outcomes[1]. In the broadest sense, malnutrition is defined by deficiencies in macronutrients (protein, fat, carbohydrates) and/or micronutrients (vitamins, minerals) that adversely effect function at the tissue level, predisposing to negative outcomes. There is an intuitive relationship between reduced absorption of nutrients and the edematous and ulcerated small or large bowel mucosa. However malnutrition in IBD patients is multi-factorial and can often be insidious.[2] The causes of nutritional deficiencies include anorexia secondary to fear of inducing abdominal symptoms, cachexia related to inflammatory cytokines, increased energy requirements due to inflammation, dietary restrictions, and medication side effects.[3, 4]

CLINICAL RELEVANCY STATEMENT

- ***We report that malnutrition risk screening in patients with Crohn's disease predicts clinical outcomes at one year.***
- ***We need studies examining targeted nutritional therapy and the effects of clinical outcomes in patients with inflammatory bowel disease.***

There are specific micronutrient deficiencies occur in patients with IBD depending upon their general nutritional status as well as the activity and location of their disease.[5] These micronutrient deficiencies may occur even in patients who otherwise appear well nourished.[6]

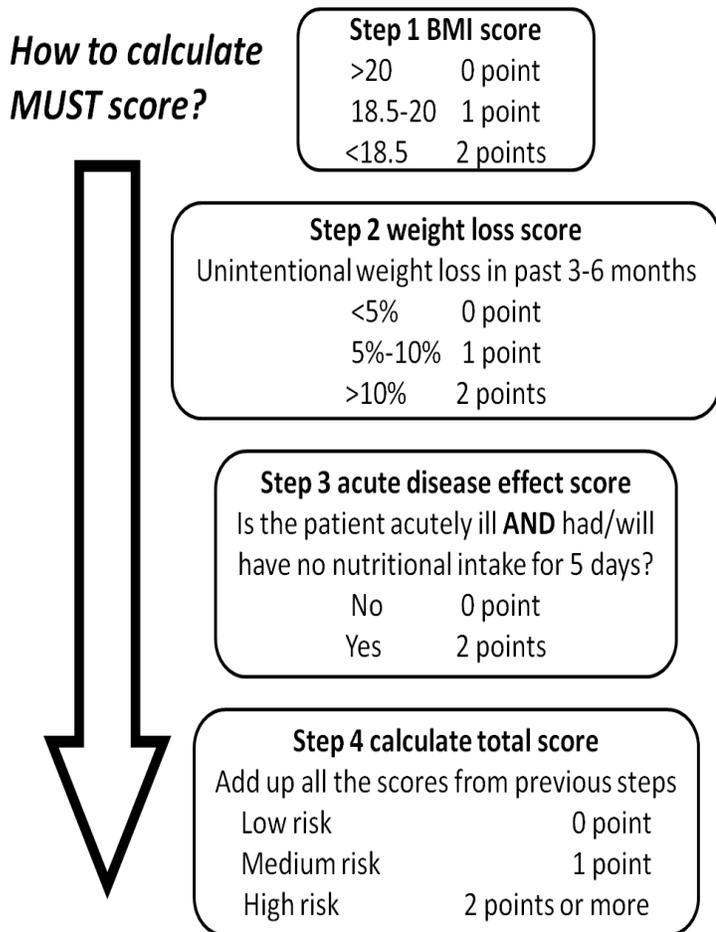
Prevalence of malnutrition in IBD

The reported rates of malnutrition in outpatient IBD clinics vary on how malnutrition is defined and measured [7]. The current literature focuses on protein-energy malnutrition and specific micronutrient deficiencies, such as Vitamin D deficiency.[6, 8] When utilizing validated assessment methods of assessing protein-energy malnutrition such as the Subjective Global Assessment (SGA) [9], rates of malnutrition have been reported to be as high as 24% in patients with IBD in clinical remission[10] and 64% of patients with active IBD.[7] Many reported prevalence rates of malnutrition are based on specific anthropometric and laboratory measures, such as body mass index (BMI), skinfold thickness, mid-arm circumference and serum protein levels.[7, 10, 11] However, these measures do not take into account decreased oral intake and disease-related effects on the nutritional state. Furthermore, some of these measures are not practical in a setting of a busy outpatient clinic and relying exclusively on serum protein levels, such as serum albumin, can be misleading.[5]

AUTHOR CONFLICT OF INTEREST STATEMENT AND INFORMATION

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Figure 1: MUST Score



Challenges in screening nutritional status

The physician community in Canada has focused on the Subjective Global Assessment (SGA). The SGA was developed by Canadian researchers[9], but is more of an assessment tool rather than a screening tool, and requires expertise in nutritional assessment, limiting its ease of use. Although the SGA is a commonly recommended method in evaluating malnutrition in Canada, it often does not occur, due to the detailed nature of assessments, the need for clinical expertise, and high inter-rater variability[12]. In the setting of an academic center with a focus on drug trials, and multiple assessments performed by attending physicians, medical learners, nurses, research assistants, and other allied health professionals, the pressure to perform these tasks in a short time period can limit nutritional screening.[13] Additionally, the absence of objective values makes teaching the methodology of SGA difficult and resource intensive. The malnutrition universal screening tool (MUST) is a simple, three-step screening tool validated for use by health care providers in varied populations, which includes medical, surgical and oncological patients[14]. The MUST was developed to detect both under-nutrition and obesity in adults, and was designed for use in multiple settings including hospitals. The questionnaire focuses on body mass index (BMI), weight loss and the presence of serious disease. The final score is then derived to determine whether the nutrition intervention is required (See Figure 1). The tool has consistently been highly rated by healthcare workers for ease of use [12, 15, 16].

Given the favorable characteristics of the MUST screening system, we felt it was an ideal nutritional risk screening tool for outpatient IBD patients. However, for the MUST tool to gain more traction in clinical

practice, we felt that demonstrating that MUST screening was predictive of disease severity, was a critical step moving forward. Our purpose is to determine if the MUST tool will predict disease activity in patients with inflammatory bowel disease. We also examined the relationship between malnutrition risk and traditional markers of nutritional status.

Methods

Subjects

This is a sub-study of a larger study conducted in outpatient, academic multi-professional IBD clinics at St. Joseph’s Healthcare Centre and at Victoria Hospital in London, Ontario. In the larger study, we examined the ability of patients to self-screen nutritional risk, with methods published elsewhere [12]. For this sub-study, patients were above the age of 18, diagnosed with IBD, and were consecutively recruited. Patients were excluded from enrollment if they were pregnant, experiencing a mental or physical impairment that prevented measurement, or because of English language difficulties. Patients were brought in to the clinic room and were recruited by a member of the health care provider (HCP) team (medical learners, clinic nurse, research assistant or attending physician). The health care provider administered the MUST tool, including height measurements using a stadiometer, and assessed disease activity using the Harvey Bradshaw Index (HBI) [17] for CD and the Partial Mayo Index score[18] for UC. Low, medium and high nutritional risk was defined as a MUST=0, 1, or ≥ 2 respectively. Researchers were not permitted to increase length of clinical encounters and there was no time allocated for screening. The health care provider also assessed disease activity using the Partial Mayo Index (PMI) for UC [18] and the Harvey Bradshaw Index (HBI) for CD [17]. The PMI is a simpler version of the complete Mayo score and is scored from 0-9. Each is composed of four categories (bleeding, stool frequency, physician assessment and endoscopic appearance) rated from 0-3 that are summed to give a total score that ranges from 0-12 [18]. Several trials have utilized just the non-endoscopic components of this index to assess disease activity and response to therapy in the outpatient clinic settings. The Harvey Bradshaw Index is simpler version of the Crohn’s Disease Activity Index (CDAI). It consists only of clinical parameters including general well-being, abdominal pain, number of liquid stools per day, abdominal mass, and complications [19]. It is purported, on the basis of a 0.93 correlation coefficient, to give essentially the same information as CDAI, and scores range from 0 to greater than 16 [19]. Patients were then asked to perform blood-work, including complete blood count (CBC), erythrocyte sedimentation rate (ESR), C reactive protein (CRP), protein markers (albumin and pre-albumin) and various other micronutrient markers.

Statistical analysis

For patients with CD and UC, we examined the association between the MUST scores and the HBI[17] and the PMI[18], respectively, using analysis of variance. Logistic regression was used to examine associations between patient demographic data, disease characteristics and laboratory values with MUST score categorized as either low or moderate and above. Backwards elimination was used to find a subset of patient demographic and disease characteristics or laboratory values that were independently associated with the malnutrition scores. A p value of <0.05 was considered significant.

Results

Demographic Data

There were 154 patients studied. There were 64% (n=98) with Crohn’s disease. The average age was 42.8 +/- 16 years, and the population was predominantly female (n=101). For clinical data, there were no missing data points. There were 16 patients for where there was missing or

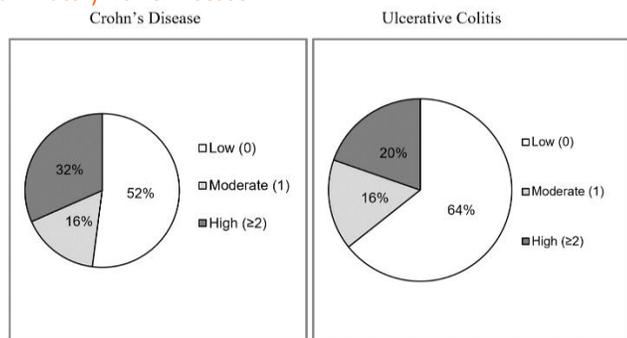
partially missing laboratory data. See Table 1.

In patients with Crohn’s disease, 52% were at low risk for malnutrition (MUST=0), 16% were at moderate risk (MUST=1), and 32% were at high risk (MUST score≥2). In patients with UC, 64% (n=36) were at low risk for malnutrition (MUST score=0), 16% (n=9) were at moderate risk (MUST score=1), and 20% (n=11) were at high risk (MUST score≥2). See Figure 2. Overall, 45.5% of patients studied were at moderate or high risk for malnutrition. See Figure 2. We report average laboratory results for patients with CD and UC on Table 1.

Table 1. Demographic Data

	Ulcerative Colitis	Crohn’s Disease
Percentage of patients with UC or CD (%) (n=154)	36.4% (n=56)	63.6% (n=98)
Mean age (years)	44.1	43.3
Percentage of male sex(%) (n=53)	37.7% (n=20)	62.3 % (n=33)
Sex (female) (n=101)	35.6% (n=36)	64.4% (n=65)
Laboratory markers-mean value (SD)		
Pre-albumin mg/L	0.28 (0.07)	0.25 (0.09)
Albumin g/L	43.6 (4.1)	41.6 (4.4)
Vitamin D nmol/L	81.3 (33.3)	69.5 (32.4)
Vitamin B12 pmol/L	396.0 (266.9)	351.2 (250.8)
Vitamin B6 nmol/L	72.0 (93.1)	61.4 (81.1)
Creatinine umol/L	71.3 (20.2)	66.6 (22.9)
Erythrocyte Sedimentation Rate – ESR mm/hr	15.8 (14.3)	23.6 (18.3)
C-reactive protein-CRP mg/L	7.5 (19.1)	13.2 (19.7)
White Blood Count-WBC 10 ⁹ /L	7.2 (2.5)	8.1 (3.8)
Hemoglobin-Hb g/L	132.1 (19.8)	123.0 (18.8)
Platelets 10 ⁹ /L	272.0 (81.2)	303.9 (141.7)

Figure 2: Distribution of MUST scores among patients with Inflammatory Bowel Disease



MUST=Malnutrition Universal Screening Tool

Disease Activity

For CD patients the average Harvey Bradshaw Index score for low, medium and high nutritional risk was 5.7, 4.4 and 9.3. A moderate or high MUST score (MUST score≥2) was strongly associated with the elevated HBI scores (p=0.005) for patients with CD. We did not observe an increasing mean HBI score between low and medium malnutrition risk. See table 2.

Table 2: Correlation between Disease Activity and Nutritional Risk Score using MUST

Disease Activity Index	MUST Score			P Value
	Low (0)	Moderate (1)	High (≥2)	
HBI Score (CD only)	5.7 (4.7), n=49	4.4 (3.6), n=16	9.3 (7.3), n=31	.005
PMI Score (UC only)	3.0 (4.5), n=36	2.8 (2.8), n=8	4.5 (4.4), n=10	.597

Each entry represents mean (standard deviation), number of observations

HBI = Harvey Bradshaw Index

PMI = Partial Mayo Score

CD = Crohn’s disease

UC = Ulcerative colitis

MUST = Malnutrition Universal Screening Tool

For UC patients the average partial Mayo score for low, medium and high nutritional risk was 3.0, 2.8 and 4.5 respectively. While the mean HBI was higher in nutritionally high risk patients, the association was not statistically significant (p=0.597). We did not observe an increasing mean HBI score between low and medium malnutrition risk. See Table 2.

On multivariable analysis we noted significant associations between increased nutritional risk and decreased albumin (OR 1.96, p<0.001), decreased Vitamin D (OR 1.51 p=0.032), and decreased creatinine (OR 1.47, p=0.050) (see Table 3).

Table 3. Association between laboratory markers and nutritional risk

	Odds Ratio (95% CI)	P Value
Albumin (g/L)	1.96 (1.79, 2.10) (for every QR decrease)	<0.001
Vitamin D (nmol/L)	1.51 (1.30, 1.82) (for every QR decrease)	0.032
Creatinine (umol/L)	1.47 (1.25, 1.79) (for every QR decrease)	0.050

C=0.71, Hosmer & Lemeshow $\chi^2=14.621$, p=0.067 (Non-significant -> No evidence of a lack of fit)

Legend:

()=standard deviation value

UC=Ulcerative colitis

ESR=erythrocyte sedimentation rate

CRP=C reactive protein

WBC=white blood cell count

Discussion

There were a high percentage of patients who were at moderate or high malnutrition risk using the MUST screening tool at 45.5%. Disease activity was assessed using well-validated scoring systems with the HBI and PMI for CD and UC, respectively. We describe a significant association between elevated MUST scores and elevated HBI scores (p=0.005), in patients with Crohn’s disease. In patients UC, the mean

disease activity score was higher in patients at elevated nutritional risk but the association was not significant. This may largely be related to lower sample size for UC group, as over two-thirds of the study sample had CD. However, one would expect that CD is more likely to result in malnutrition. Unlike ulcerative colitis, Crohn's disease is generally more severe, typically resulting in transmural inflammation, and most often affects the small bowel, predisposing to reduced absorption of macro and micronutrients.

We note that the expected trend of increasing means between disease activity scores and mild and moderate MUST scores was not observed. This is likely related to the small sample size of patients at moderate risk. However, it may also represent a floor effect of the MUST screening tool. That is, nutritional risk profiling with MUST does not distinguish lower levels of disease activity.

We measured laboratory markers which are often used by IBD practitioners to guide assessment of nutritional status [11]. Of the biochemical markers measured, serum albumin, vitamin D and creatinine were found to be significantly associated with MUST score on multivariable analysis. The association of elevation MUST with lower albumin levels is important. Albumin is often viewed as a surrogate marker for protein turnover and a marker of malnutrition. However, the lower albumin may not be reflective of a malnourished state directly, but rather a reflection of disease activity. Albumin is an negative acute phase protein, which declines in response to inflammation.[11, 20]. With that said, C-reactive protein and ESR, traditional measure of systemic inflammation, were not significantly associated with MUST score. We also noted that a low serum creatinine correlated with a moderate/high MUST score ($p=0.050$). This may be because creatinine is crude marker of muscle mass and protein-energy deficiency [21].

Micronutrient deficiency can have significant negative health effects on IBD patients, and monitoring of micronutrient levels and appropriate replacement is recommended by several societies, especially for vitamin D [22]. Multivariable analysis revealed a significant association between elevated MUST score and a lower 25-hydroxy vitamin D level ($p=0.032$). The relationship between IBD and vitamin D has recently become a controversial topic of intense research, summarized well in several recent reviews [23-26]. In general, epidemiologic studies have demonstrated a high prevalence of vitamin D deficiency/insufficiency among patients with IBD (regardless threshold level used) and conversely, a higher vitamin D level is associated with a lower risk of CD [22]. This pattern has been interpreted in two ways. The first is that reduced vitamin D levels are a causative factor in IBD. Alternatively, reduced vitamin D levels are an epiphenomenon related to the nutritional effects of IBD, in addition to demography which includes predominantly affects Caucasians living in northern climates. Several studies are ongoing to delineate if Vitamin D is a causative factor in the development of IBD. The association between increased nutritional risk and low creatinine is likely because creatinine is a crude marker for body mass [14].

There are several limitations in our study. We are limited in external generalizability given our study was in one centre and involved tertiary academic practices. The lower number of patients at medium nutritional risk and with ulcerative colitis were also significant limitations. We also did not study the effect of interventions with being identified at high risk, but are currently performing studies examining this question. We did not examine outcomes over nutritional risk over time, but these issues are being examined currently.

Conclusion

In this study, we demonstrate that MUST screening correlates to disease activity in patients with CD. No additional time was allocated for nutritional screening with the MUST tool. We are advocating for

further screening studies in larger populations using the MUST screening tool to determine if MUST score is predictive of UC severity, and to compare MUST screening results to more detailed nutritional assessments.

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