



Sarcopenia assessed by total psoas index – is it correlated with post-operative complications in all digestive cancers?

Carmen Haiducu^{1,#}, Catalin Adrian Buzea^{1,2,#}, Caterina Delcea^{1,2,#}, Vladislav Brasoveanu^{3,4}, Cristian Mugur Grasu^{1,5}, Gheorghe-Andrei Dan^{1,2}

1) Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

2) Cardiology Department, Colentina Clinical Hospital, Bucharest, Romania

3) Dan Setlacec General Surgery and Hepatic Transplant Department, Fundeni Clinical Institute, Bucharest, Romania

4) Titu Maiorescu University, Bucharest, Romania

5) Radiology Department, Fundeni Clinical Institute, Bucharest, Romania

#Equal contribution

Abstract

Background and aims. In cancer patients sarcopenia may be a predictor for postoperative complications of curative or palliative surgery. Several indices including the total psoas area index (TPAI) are proposed for the diagnosis of this condition, but there is no validated cut-off point.

Our study aimed to assess the role of TPAI as a marker for sarcopenia and to compare the utility of previously proposed cut-off values for predicting post-operative complications in patients with digestive cancers undergoing surgery.

Methods. We retrospectively included all adult patients with digestive cancers admitted to a tertiary center for elective surgery between January and December 2019. Sarcopenia was considered based on TPAI evaluated on abdominal computed tomography (CT) and for analysis we used different cut-off points published by various authors. The primary endpoint was the occurrence of any complications as defined by the Clavien-Dindo classification. The secondary endpoints were fistula development, low- versus high-grade Clavien-Dindo post-operative complications, moderate or severe anemia at discharge, major bleeding, hypoalbuminemia at discharge, and decrease in albumin levels by at least 1g/dL.

Results. We included 155 patients with a mean age of 64.78 ± 11.40 years, of which 59.35% were males; 58.06% developed postoperative complications. TPAI evaluated as a continuous variable was not a predictor for the development of post-operative complications neither in the general study sample, nor in the gender subgroups of patients. Sarcopenia defined by previously proposed cut-off values was not a predictor of the secondary end-points either.

Conclusion. TPAI as a sole parameter for defining sarcopenia was not a predictor for postoperative complications in patients undergoing surgery for digestive neoplasia.

Keywords: sarcopenia, total psoas index, digestive cancer, post-operative complications

Background and aims

Sarcopenia represents a progressive and generalized loss of skeletal muscle mass and strength. It has been identified as an important healthcare target in both the general population and specific subgroups of patients suffering from chronic illnesses [1]. Among these subsets of diseases, cancer remains one of the leading causes of death worldwide, despite continuous progress in its

diagnosis and treatment [2]. Up to 89% of oncologic patients associate low muscle mass with a significant impact on morbidity [3]. With sarcopenia being a potential therapeutic target, its correlation with prognosis across the malignancy spectrum is a subject of increasing interest [4]. More than that, sarcopenia may be a predictor for postoperative complications in cancer patients, either in curative or palliative surgery [5,6].

DOI: 10.15386/mpr-2539

Manuscript received: 25.04.2022

Accepted: 10.05.2022

Address for correspondence:
catalin.buzea@umfcd.ro

This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License <https://creativecommons.org/licenses/by-nc-nd/4.0/>

In this setting, the possibility to easily assess its presence is an attractive goal for clinical practice, to implement its use in the routine evaluation of these patients. The 2019 Revised European consensus on the definition and diagnosis of sarcopenia proposed the use of the SARC-F questionnaire, the clinical evaluation of muscle strength, and the imaging modalities to confirm the low quantity or quality of muscle mass, the main modality for this evaluation being the measurement of total skeletal muscle area index (SMAI) [1]. Looking for an accessible alternative to calculating SMAI, recently published data suggested that total psoas area index (TPAI) alone might be a viable option for the diagnosis of sarcopenia [4]. TPAI is obtained more conveniently by indexing only the psoas muscle area measured at the level of the third lumbar vertebra on computed tomography imaging normalized for height and gender, with a resulting figure for TPAI in cm^2/m^2 [4].

However, the majority of reported studies assessing TPAI included only one type of malignancy, and each study group proposed a different cut-off level. The variety of methods used for the evaluation of sarcopenia, among other factors, may be responsible for the conflicting data regarding its impact on the risk of complications after surgery in neoplastic patients [7,8].

Since no consensus was reached regarding the role of TPAI as a marker of sarcopenia for predicting postoperative complications in cancer patients, our study aimed to assess this association in a heterogeneous cohort of patients with digestive malignancies undergoing surgery. We also intended to evaluate the utility of previously proposed cut-off levels of TPAI to define sarcopenia and to forecast post procedural complications.

Methods

Type of study

This was a retrospective, observational cohort study.

Population

We included all adult patients with digestive cancers admitted to the Oncological Surgery and

Transplant Department of the Fundeni Clinical Institute, Bucharest, Romania, for which an elective surgery was planned. The period of inclusion was from January to December 2019.

Emergency surgery, in-hospital mortality, lack of abdominal CT evaluation at admission, and lack of histopathological definitive diagnosis represented the exclusion criteria. Patients with CT scans performed in other radiological centers were also excluded due to the impossibility to retrieve and analyze the images. All patient data were extracted from the electronic health records.

Definitions

By the scope of this paper, sarcopenia was defined using various cut-off levels of the total psoas index, as proposed by different authors (Dodson et al. [9], Jung et al. [10], Kasahara et al. [11], Kayano et al. [12], Nakayama et al. [13], Williet et al. [14], Xu et al. [15]) listed in table I.

Anemia was defined according to WHO Guidelines, as hemoglobin (Hb) levels lower than 12 g/dL in women, respectively lower than 13 g/dL in men. Moderate and severe anemia was diagnosed when hemoglobin levels were below 11 g/dL, and respectively below 8 g/dL, regardless of gender.

TPAI protocol

CT scans were performed for each patient during the index admission, according to the local screening protocol for digestive tract malignancy. Imaging was obtained using a 64-slice General Electric Healthcare Optima™ CT660 Medical System (Buckinghamshire, UK) with helical reconstruction technology. An experienced radiologist analyzed all CT scans, running the same reconstruction algorithm for all patients.

The L3 (third lumbar vertebra) transverse image that best displayed both vertebral transverse processes was selected for analysis. Clear differentiation between muscles and surrounding tissue, completely visible muscle area without cuts, and lack of artifacts were the required criteria for the selected images to comply with quality indicators.

Table I. Cut-off values for TPAI.

	Female patients (cm^2/m^2)	Male patients (cm^2/m^2)
Cut-off 1 - Dodson et al. [9]	3.38	4.77
Cut-off 2 - Jung et al. [10]	4.43	8.18
Cut-off 3 - Kasahara et al. [11]	2.07	2.49
Cut-off 4 - Kayano et al. [12]	2.89	4.75
Cut-off 5 - Nakayama et al. [13]	3.92	6.36
Cut-off 6 - Williet et al. [14]	4.37	5.73
Cut-off 7 - Xu et al. [15]	3.46	4.78

The margins of the skeletal muscles at the level of the third lumbar vertebra (L3) were manually outlined: spinal erector muscles, lumbar square muscles, transverse, internal oblique, external and abdominal right, bilateral.

After the manual selection of the mentioned muscles, the software of the CT workstation (Advantage Workstation 4.7) elaborated the values of the selected muscles: area, perimeter, mean, and SD of the skeletal muscle radiation attenuation.

The total psoas area index (TPAI) was calculated using the equation: $TPAI = \text{total psoas muscle area (cm}^2\text{)} / \text{height (m}^2\text{)}$.

Endpoints

The primary end-point was the development of any post-operative complications, as defined by the Clavien-Dindo classification [16].

Secondary end-points included fistula development, low- versus high-grade Clavien-Dindo post-operative complications [16], moderate or severe anemia at discharge, major bleeding defined by a decrease in hemoglobin levels by at least 2g/dL [17], hypoalbuminemia at discharge, and decrease in albumin levels by at least 1g/dL [18].

Statistics

Continuous variables with normal distribution were expressed as mean \pm standard deviation. Continuous variables with non-normal distribution were expressed as median [interquartile range]. Qualitative variables were expressed as absolute numbers and percentages.

ROC analysis was used in univariate analysis to correlate TPAI as a continuous variable with the selected outcomes.

Chi-square corrected test was used to evaluate if sarcopenia defined by different TPAI cut-off levels was

linked the post-operative results in patients with digestive cancers.

A p-value <0.05 was considered statistically significant.

IBM SPSS Statistics 23 (IBM Corp. Armonk, NY, U.S.A.) and Epi Info 7 (CDC, U.S.A.) were used for statistical analysis.

Ethics Committee

The study protocol was approved by the Research Ethics Committee of the *Fundeni Clinical Institute*.

Results

Our study sample included 155 patients (Figure 1), predominantly male, with a mean age of 64.78 ± 11.40 years. The most prevalent type of cancer was colorectal, followed by pancreatic. Two-thirds of patients had T3 or T4 extension, and almost a quarter had metastases. Diabetes mellitus and anemia were the most prevalent comorbidities (Table II).

A percentage of 58.06% of patients developed at least one complication as defined per protocol. Postoperative complications were more frequent in colorectal cancers, less frequent in biliary malignancies, and had similar distribution among patients with hepatic, gastric and pancreatic tumors (Table II).

TPAI evaluated as a continuous variable in ROC analysis was not a predictor for the development of post-operative complications neither in the general study sample nor in the gender subgroups of patients (Table III, Figure 2). The only significant correlation of TPAI in the entire population was with moderate or severe anemia at discharge (Figure 2C), however, in the gender subgroups this association lost the statistical significance (Table III).

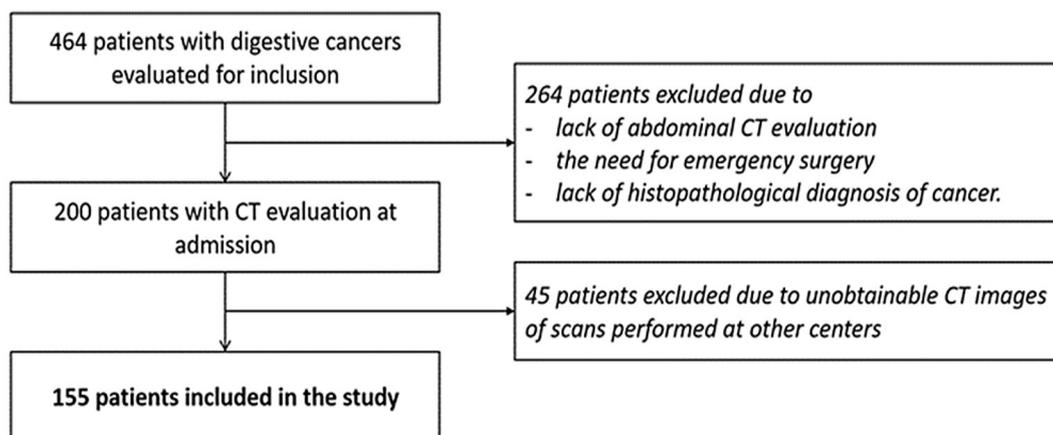


Figure 1. Flow-chart of patients' selection.

Table II. General characteristics.

	All patients N=155 patients	Without complications N=65 patients	With complications N=90 patients	p value [#]
Demographics				
Age (years-old)	64.78 ± 11.40	63.95 ± 13.04	65.37 ± 10.08	0.44
Male gender	92 (59.35%)	41 (63.07%)	51 (55.43%)	0.52
Neoplastic disease characteristics				
Type of cancer				
Biliary	17 (10.97%)	6 (9.23%)	11 (12.22%)	0.55
Colorectal	60 (38.71%)	34 (52.31%)	26 (28.89%)	0.03
Gastric	23 (14.84%)	7 (10.77%)	16 (17.78%)	0.22
Hepatic	23 (14.84%)	4 (6.15%)	19 (21.11%)	0.01
Pancreatic	32 (20.65%)	14 (21.54%)	18 (20.00%)	0.81
Extension				
T1-T2*	44 (33.85%)	16 (27.59%)	28 (38.89%)	0.17
T3-T4*	86 (66.15%)	42 (72.41%)	44 (61.11%)	0.17
Metastasis*	31 (23.85%)	13 (22.03%)	18 (25.35%)	0.65
Comorbidities				
IHD	12 (7.74%)	8 (12.31%)	4 (4.44%)	0.12
Heart failure	10 (6.45%)	7 (10.77%)	3 (3.33%)	0.12
CKD	5 (3.23%)	2 (3.08%)	3 (3.33%)	0.93
Diabetes	37 (23.87%)	16 (24.62%)	21 (23.33%)	0.85
Cirrhosis	7 (4.52%)	2 (3.08%)	5 (5.56%)	0.73
Anemia	82 (52.90%)	41 (63.08%)	41 (45.56%)	0.03
BMI	21.71 ± 5.40	21.97 ± 5.44	21.54 ± 5.40	0.63
Laboratory parameters on admission				
White blood cells	7490 [5950-9030]	7700 [6180-9440]	7355 [5860-9000]	0.46
Hemoglobin	12.22 ± 2.07	11.81 ± 1.91	12.53 ± 2.13	0.03
Creatinine	0.96 [0.82 – 1.20]	0.97 [0.85 – 1.20]	0.93 [0.81 – 1.20]	0.63
AST	25 [20 – 52]	24 [17 – 42]	27 [21 – 52]	0.10
Total protein	6.64 ± 0.98	6.74 ± 1.12	6.57 ± 0.90	0.54
Albumin	3.89 ± 0.71	3.74 ± 0.73	3.99 ± 0.68	0.03
CT measurements				
Right psoas area	6.10 ± 2.25	6.21 ± 2.10	5.98 ± 2.38	0.55
Left psoas area	6.36 ± 2.43	6.62 ± 2.16	6.20 ± 2.60	0.28
Total psoas area	12.46 ± 4.55	12.83 ± 4.10	12.19 ± 4.86	0.38
Total psoas index	4.31 ± 1.58	4.43 ± 1.43	4.23 ± 1.69	0.42

*Data available for 130 patients; [#]Comparison of patients with and without complications
 N – number of patients, T – tumor staging, IHD – ischemic heart disease, CKD – chronic kidney disease, BMI - body mass index, AST – aspartate aminotransferase.

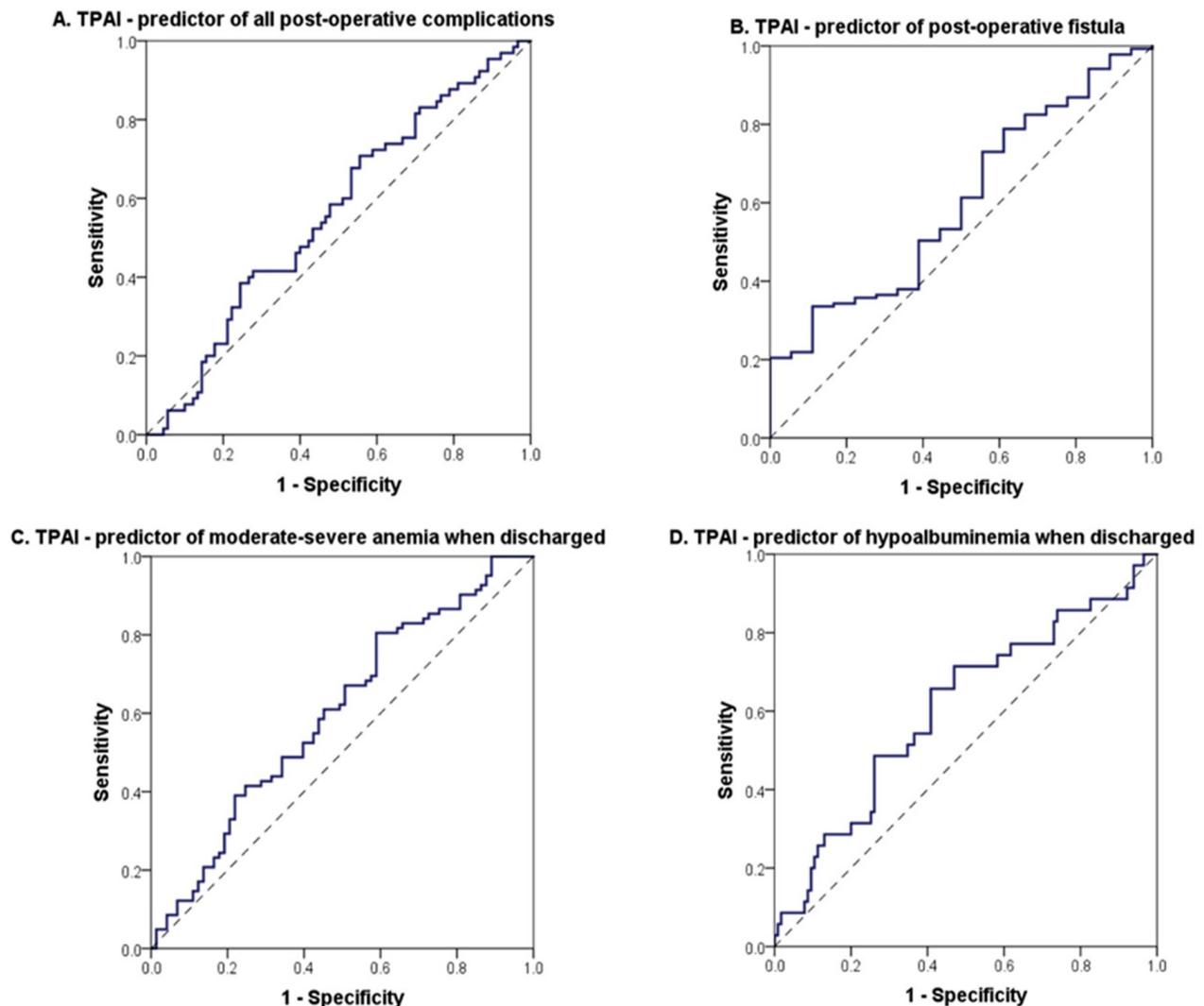


Figure 2. ROC analysis of TPAI for predicting post-operative complications.

Table III. TPAI – Predictor of postoperative outcome in all patients and based on gender.

	All patients N=155	Male patients N=92	Female patients N=63
	AUC, 95%CI	AUC, 95%CI	AUC, 95%CI
Any complication	0.562, 0.471 – 0.653 p=0.191	0.508, 0.390 – 0.627 p=0.891	0.598, 0.451 – 0.746 p=0.193
Fistula	0.601, 0.469 – 0.734 p=0.163	0.610, 0.424 – 0.796 p=0.335	0.481, 0.283 – 0.679 p=0.842
Low-grade Clavien-Dindo	0.580, 0.487 – 0.673 p=0.091	0.554, 0.430 – 0.678 p=0.378	0.644, 0.507 – 0.781 p=0.054
High-grade Clavien-Dindo	0.530, 0.416 – 0.643 p=0.630	0.518, 0.353 – 0.682 p=0.844	0.433, 0.272 – 0.595 p=0.439
Hemoglobin decrease > 2g/dl	0.538, 0.445 – 0.630 p=0.421	0.471, 0.350 – 0.592 p=0.635	0.622, 0.484 – 0.761 p=0.096
Anemia when discharged	0.606, 0.491 – 0.721 p=0.127	0.492, 0.346 – 0.638 p=0.916	0.667, 0.453 – 0.881 p=0.333
Moderate-severe anemia when discharged	0.599, 0.509 – 0.689 p=0.034	0.531, 0.411 – 0.652 p=0.612	0.639, 0.501 – 0.776 p=0.060
Hypoalbuminemia when discharged	0.607, 0.497 – 0.716 p=0.056	0.640, 0.508 – 0.773 p=0.049	0.545, 0.359 – 0.730 p=0.622
Albumin decrease >1mg/dl	0.514, 0.421 – 0.606 p=0.773	0.439, 0.320 – 0.558 p=0.315	0.605, 0.463 – 0.747 p=0.155

N – number of patients, AUC – area under the curve, CI – confidence interval.

In univariate analysis, using the different previously proposed cut-off values for TPAI to defining sarcopenia (Table I), no relation could be established with the development of the post-operative complications for any of the definitions (Table IV).

Of the secondary endpoints, sarcopenia defined

by Dodson et al. [9] was correlated to a higher risk of developing moderate or severe anemia at discharge, while sarcopenia defined by Williet et al. [14] and by Xu et al. [15] was correlated with hypoalbuminemia at discharge. All other cut-off levels were not predictors of postoperative complications (Table IV).

Table IV. Different cut-off points of TPAI for predicting postoperative complications.

General complications			
Sarcopenia defined by	Any complication	High-grade complications*	Post-operative fistula
	OR, 95%CI	OR, 95%CI	OR, 95%CI
Cut-off 1 [9]	1.14, 0.93 – 1.40 p=0.28	0.98, 0.85 – 1.13 p=0.95	1.03, 0.93 – 1.16 p=0.71
Cut-off 2 [10]	1.09, 0.79 – 1.50 p=0.86	0.93, 0.68 – 1.26 p=0.86	0.95, 0.75 – 1.21 p=0.66
Cut-off 3 [11]	1.17, 0.75 – 1.82 p=0.64	0.87, 0.74 – 1.04 p=0.49	1.14, 0.86 – 1.50 p=0.44
Cut-off 4 [12]	1.07, 0.87 – 1.32 p=0.63	0.94, 0.82 – 1.08 p=0.56	1.003, 0.89 – 1.13 p=0.96
Cut-off 5 [13]	1.06, 0.84 – 1.34 p=0.77	0.97, 0.81 – 1.16 p=0.91	1.01, 0.88 – 1.15 p=0.91
Cut-off 6 [14]	1.19, 0.97 – 1.46 p=0.21	1.02, 0.86 – 1.20 p=0.82	1.09, 0.99 – 1.22 p=0.29
Cut-off 7 [15]	1.12, 0.91 – 1.37 p=0.38	0.97, 0.84 – 1.12 p=0.84	1.03, 0.92 – 1.15 p=0.79
Anemia related complications			
	Hb decrease ≥ 2g/dL	Anemia at discharge	Moderate-severe anemia at discharge
	OR, 95%CI	OR, 95%CI	OR, 95%CI
Cut-off 1 [9]	1.13, 0.84 – 1.51 p=0.51	1.18, 0.52 – 2.68 p=0.87	1.37, 1.02 – 1.84 p=0.05
Cut-off 2 [10]	1.15, 0.73 – 1.81 p=0.79	1.21, 0.32 – 4.66 p=0.78	1.02, 0.60 – 1.73 p=0.94
Cut-off 3 [11]	1.57, 0.76 – 3.22 p=0.24	N/A	1.93, 0.83 – 4.49 p=0.10
Cut-off 4 [12]	1.21, 0.89 – 1.630 p=0.27	1.17, 0.51 – 2.71 p=0.89	1.22, 0.89 – 1.66 p=0.26
Cut-off 5 [13]	1.03, 0.74 – 1.44 p=0.85	0.58, 0.18 – 1.87 p=0.51	1.21, 0.88 – 1.66 p=0.35
Cut-off 6 [14]	1.06, 0.76 – 1.47 p=0.86	0.79, 0.28 – 2.24 p=0.88	1.09, 0.79 – 1.53 p=0.73
Cut-off 7 [15]	1.18, 0.89 – 1.58 p=0.31	1.02, 0.45 – 2.32 p=0.96	1.31, 0.97 – 1.76 p=0.11
Albumin related complications			
	Albumin decrease by > 1 mg/dL	Hypoalbuminemia at discharge	
	OR, 95%CI	OR, 95%CI	
Cut-off 1 [9]	1.02, 0.75 – 1.38 p=0.89	1.81, 0.99 – 3.28 p=0.07	
Cut-off 2 [10]	1.03, 0.61 – 1.75 p=0.91	1.75, 0.82 – 3.74 p=0.31	
Cut-off 3 [11]	1.39, 0.69 – 2.82 p=0.45	1.01, 0.36 – 2.86 p=0.98	
Cut-off 4 [12]	1.05, 0.78 – 1.43 p=0.74	1.71, 0.91 – 3.24 p=0.09	
Cut-off 5 [13]	1.08, 0.77 – 1.52 p=0.79	1.71, 0.95 – 3.08 p=0.13	
Cut-off 6 [14]	0.98, 0.68 – 1.39 p=0.89	2.03, 1.16 – 3.58 p=0.02	
Cut-off 7 [15]	1.07, 0.79 – 1.45 p=0.76	1.91, 1.05 – 3.46 p=0.04	

* Defined by Clavien-Dindo classification [16]; OR – odds ratio, CI – confidence interval.

Discussion

Our research is among the first studies to compare different TPAI cut-off levels for defining sarcopenia and for predicting postoperative complications of patients with digestive cancers. In a heterogeneous population with diverse gastrointestinal malignancies, TPAI levels were not correlated with the established endpoints.

Previous reports had concordant conclusions regarding the risk of mortality correlated with sarcopenia assessed by TPAI [4]. However, when examining the association with perioperative complications, different authors reached divergent results [4]. A meta-analysis focused on patients undergoing esophageal cancer surgery found no correlation between sarcopenia and the rate of postoperative complications [8]. Recently, Benedek et al. correlated the psoas muscle index as a continuous variable to the severity of postoperative complications in patients with colorectal cancer [19]. When examining the psoas index as a dichotomous variable, using distinct cut-off values, various authors proposed cut-off values linked to specific outcomes in diverse clinical settings. Jung et al. found no correlation between TPAI and the incidence of perioperative neurological complications in patients undergoing single-level lateral lumbar interbody fusion [10]. Kasahara et al. proved that sarcopenia evaluated by the psoas muscle index was a predictor of overall survival in patients with advanced urothelial carcinoma undergoing chemotherapy [11]. In patients undergoing surgery for lower gastrointestinal perforation, the low psoas muscle index was a predictor of in-hospital mortality and prolonged hospitalization [12]. Using the cut-off for sarcopenia proposed by Hamaguchi et al. [20], Nakayama and colleagues found the psoas muscle index to be a predictor of overall and event-free survival in patients with esophageal cancer undergoing neoadjuvant therapy [13]. Williet et al. found TPAI to be a strong predictor of overall as well as progression-free survival in patients with metastatic pancreatic cancer [14]. Xu et al. studied Chinese patients undergoing open pancreatoduodenectomy [15]. The sarcopenia defined by TPAI index was associated with the occurrence of major complications and adverse outcomes, while the nutritional assessment was not [15]. A meta-analysis performed by Simonsen et al. demonstrated sarcopenia as a predictor for complications in gastrointestinal oncologic surgery [7]. However, the meta-analysis included only 5 studies in which sarcopenia was defined by TPAI only. Interestingly, Tamura et al. [21] found no impact of sarcopenia on non-infectious complications rate in patients with gastric cancer. However, in their study, sarcopenia was evaluated based on a different parameter, namely skeletal muscle mass index.

By analyzing TPAI as a continuous as well as a dichotomous variable with various cut-off levels, we aimed to cover a variety of possibilities and to discover the most feasible cut-off level for sarcopenia and the prediction of postoperative complications. We used the TPAI values

proposed by the above-mentioned authors, in the attempt to validate preexisting cut-offs. However, we could not prove their viability for a broader use outside the clinical scenario for which they were initially tested. The negative results of our study could be explained by a few hypotheses.

The 2019 Revised European consensus on the definition and diagnosis of sarcopenia proposed an integrative approach using the SARC-F questionnaire, alongside the clinical assessment of muscle strength and the imaging modalities to confirm low quantity or quality of muscle mass [1]. Some authors argue that patient performance tests alone could be subjective [9], and others proved that integrating clinical and tomographic criteria for diagnosing sarcopenia increased the predictive probability for complications post pancreaticoduodenectomy [22]. The 2019 consensus mentions the use of the 3rd lumbar vertebra imaging by computer tomography as a potential alternative tool for sarcopenia assessment, pointing that validity, reliability, and accuracy are still in the research spotlight [1]. We could therefore argue that the measurement of muscle mass alone is insufficient to diagnose sarcopenia.

Should the muscle mass appraisal be sufficient for the diagnosis, another debate focuses on which measurement is more reliable: the total skeletal muscle or the psoas muscle alone. In a recent review, Weerink et al. concluded that low psoas mass evaluated before surgery was a strong predictor of postoperative complications, while low total skeletal muscle mass had less accuracy as an indicator of morbidity [23]. Contradictory results were presented by Shi et al, in patients with gastric cancer, concluding that skeletal muscle index may be a more accurate method for sarcopenia assessment, reducing the rate of misdiagnosis and predicting postoperative complications [24].

Should the psoas muscle be enough for diagnosing sarcopenia, another discussion refers to the method used to quantify muscle mass. In a study of 264 older adults undergoing emergency laparotomy, Simpson et al concluded that the method of choice should be the psoas muscle to L3 vertebra ratio (PML3) [25]. After comparing the psoas muscle index, PML3, and the psoas muscle to body area ratio, they obtained the strongest correlation to post-operative mortality for PML3 [25]. After assessing 763 patients with pancreatectomy for adenocarcinoma, Amini et al found that the use of total psoas volume to define sarcopenia was correlated to both short- and long-term outcomes, as opposed to the use of TPAI that was not correlated to postoperative complications [26].

Discrepancies also exist regarding the use of muscle quality versus quantity. Tankel et al concluded that Hounsfield unit average calculation obtained from CT imaging had higher prognostic accuracy compared to TPAI in a cohort of 185 patients undergoing laparoscopic right hemicolectomy [27]. These findings were recently confirmed by Carvalho et al in patients with gastric and colorectal tumors [28]. Comparing skeletal muscle

index with skeletal muscle radiodensity, they proved the latter was the only independent risk factor for major postoperative complications [28].

Another hypothesis is that most of the cut-off values that we evaluated were proposed for predicting mortality and not post-operative complications, since they were not all studied in patients undergoing surgery [11,13,14]. However, we might retaliate that our assessment included TPI values as a continuous variable as well as dichotomous, therefore if a significant correlation with post-operative complications existed, the ROC analysis would prove it. Even if for some isolated end-points the ROC curve analysis reached statistical significance, the values of the AUC as well as the limits of the 95%CI were well beyond the conventional threshold of 0.800 for clinical significance.

Limitations

Our study has several limitations. The presented study includes a retrospective analysis of patients with a heterogeneous set of digestive cancers, about a quarter of them having metastases. The sample population is relatively small and collected from a single tertiary center, which may limit the power and representativity of the study. However, patients from neighboring cities are often referred to this center, which may diminish the selection bias.

We acknowledge the heterogeneity of digestive neoplastic diseases included in the study, in different stages and with various surgical procedures performed. While this could be considered a limiting factor, in view of previous studies focusing on single types of malignancy, it was our aim to study diverse patients since a universal definition for sarcopenia applicable to all patients regardless of neoplastic etiology should be sought out.

The definition of sarcopenia was based on a single factor, namely TPAI. A larger definition including other factors like the presence of low muscle strength, and low muscle function may lead to more definitive conclusions.

Conclusions

Total psoas area index as the sole parameter for defining sarcopenia was not a predictor for post-operative complications in patients undergoing surgery for digestive neoplasia, regardless of the cut-off values used. Considering the identified limitations, as well as the existing controversy in previously published data, a prospective study is needed to evaluate the use of TPAI for defining sarcopenia and for predicting post-operative complications in oncologic patients.

References

1. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48:16–31.
2. Mattiuzzi C, Lippi G. Current Cancer Epidemiology. *J Epidemiol Glob Health*. 2019;9:217–222.
3. Rier HN, Jager A, Sleijfer S, Maier AB, Levin MD. The Prevalence and Prognostic Value of Low Muscle Mass in Cancer Patients: A Review of the Literature. *Oncologist*. 2016;21:1396-1409.
4. Haiducu C, Buzea A, Mirea LE, Dan GA. The prevalence and the impact of sarcopenia in digestive cancers. A systematic review. *Rom J Intern Med*. 2021;59:328-344.
5. Sehouli J, Mueller K, Richter R, Anker M, Wopen H, Rasch J, et al. Effects of sarcopenia and malnutrition on morbidity and mortality in gynecologic cancer surgery: results of a prospective study. *J Cachexia Sarcopenia Muscle*. 2021;12:393–402.
6. Fukuda Y, Yamamoto K, Hirao M, Nishikawa K, Nagatsuma Y, Nakayama T, et al. Sarcopenia is associated with severe postoperative complications in elderly gastric cancer patients undergoing gastrectomy. *Gastric Cancer*. 2016;19:986–993.
7. Simonsen C, de Heer P, Bjerre ED, Suetta C, Hojman P, Pedersen BK, et al. Sarcopenia and Postoperative Complication Risk in Gastrointestinal Surgical Oncology: A Meta-analysis. *Ann Surg*. 2018;268:58–69.
8. Schizas D, Frountzas M, Lidoriki I, Spartalis E, Toutouzas K, Dimitroulis D, et al. Sarcopenia does not affect postoperative complication rates in oesophageal cancer surgery: a systematic review and meta-analysis. *Ann R Coll Surg Engl*. 2020;102:120–132.
9. Dodson RM, Firoozmand A, Hyder O, Tacher V, Cosgrove DP, Bhagat N, et al. Impact of sarcopenia on outcomes following intra-arterial therapy of hepatic malignancies. *J Gastrointest Surg*. 2013;17:2123–2132.
10. Jung JM, Chung CK, Kim CH, Yang SH, Won Y II, Choi Y. Effects of Total Psoas Area Index on Surgical Outcomes of Single-Level Lateral Lumbar Interbody Fusion. *World Neurosurg*. 2021;154:e838-e845.
11. Kasahara R, Kawahara T, Ohtake S, Saitoh Y, Tsutsumi S, Teranishi JI, et al. A Low Psoas Muscle Index before Treatment Can Predict a Poorer Prognosis in Advanced Bladder Cancer Patients Who Receive Gemcitabine and Nedaplatin Therapy. *Biomed Res Int*. 2017;2017:7981549.
12. Kayano H, Nomura E, Abe R, Ueda Y, Machida T, Fujita C, et al. Low psoas muscle index is a poor prognostic factor for lower gastrointestinal perforation: a single-center retrospective cohort study. *BMC Surg*. 2019;19(1):181.
13. Nakayama T, Furuya S, Kawaguchi Y, Shoda K, Akaike H, Hosomura N, et al. Prognostic value of preoperative psoas muscle index as a measure of nutritional status in patients with esophageal cancer receiving neoadjuvant therapy. *Nutrition*. 2021;90:111232.
14. Williet N, Fovet M, Maoui K, Chevalier C, Maoui M, Le Roy B, et al. A Low Total Psoas Muscle Area Index Is a Strong Prognostic Factor in Metastatic Pancreatic Cancer. *Pancreas*. 2021;50:579–586.
15. Xu JY, Li C, Zhang H, Liu Y, Wei JM. Total Psoas Area Index is Valuable to Assess Sarcopenia, Sarcopenic Overweight/Obesity and Predict Outcomes in Patients Undergoing Open Pancreatoduodenectomy. *Risk Manag Healthc Policy*.

- 2020;13:761–770.
16. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.* 2004;240:205–213.
 17. Schulman S, Angerås SU, Bergqvist D, Eriksson B, Lassen MR, Fisher W, et al. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in surgical patients. *J Thromb Haemost.* 2010;8:202–204.
 18. Labgaa I, Joliat GR, Kefleyesus A, Mantziari S, Schäfer M, Demartines N, et al. Is postoperative decrease of serum albumin an early predictor of complications after major abdominal surgery? A prospective cohort study in a European centre. *BMJ Open.* 2017;7:e013966.
 19. Benedek Z, Todor-Boér S, Kocsis L, Bauer O, Suciú N, Coroş MF. Psoas Muscle Index Defined by Computer Tomography Predicts the Presence of Postoperative Complications in Colorectal Cancer Surgery. *Medicina (Kaunas).* 2021;57:472.
 20. Hamaguchi Y, Kaido T, Okumura S, Kobayashi A, Hammad A, Tamai Y, et al. Proposal for new diagnostic criteria for low skeletal muscle mass based on computed tomography imaging in Asian adults. *Nutrition.* 2016;32:1200–1205.
 21. Tamura T, Sakurai K, Nambara M, Miki Y, Toyokawa T, Kubo N, et al. Adverse Effects of Preoperative Sarcopenia on Postoperative Complications of Patients With Gastric Cancer. *Anticancer Res.* 2019;39:987–992.
 22. Sur MD, Namm JP, Hemmerich JA, Buschmann MM, Roggin KK, Dale W. Radiographic Sarcopenia and Self-reported Exhaustion Independently Predict NSQIP Serious Complications After Pancreaticoduodenectomy in Older Adults. *Ann Surg Oncol.* 2015;22:3897–3904.
 23. Weerink LBM, van der Hoorn A, van Leeuwen BL, de Bock GH. Low skeletal muscle mass and postoperative morbidity in surgical oncology: a systematic review and meta-analysis. *J Cachexia Sarcopenia Muscle.* 2020;11:636–649.
 24. Shi B, Liu S, Chen J, Liu J, Luo Y, Long L, et al. Sarcopenia is Associated with Perioperative Outcomes in Gastric Cancer Patients Undergoing Gastrectomy. *Ann Nutr Metab.* 2019;75:213–222.
 25. Simpson G, Manu N, Magee C, Wilson J, Moug S, Vimalachandran D. Measuring sarcopenia on pre-operative CT in older adults undergoing emergency laparotomy: a comparison of three different calculations. *Int J Colorectal Dis.* 2020;35:1095–1102.
 26. Amini N, Spolverato G, Gupta R, Margonis GA, Kim Y, Wagner D, et al. Impact Total Psoas Volume on Short- and Long-Term Outcomes in Patients Undergoing Curative Resection for Pancreatic Adenocarcinoma: a New Tool to Assess Sarcopenia. *J Gastrointest Surg.* 2015;19:1593–1602.
 27. Tankel J, Yellinek S, Vainberg E, David Y, Greenman D, Kinross J, et al. Sarcopenia defined by muscle quality rather than quantity predicts complications following laparoscopic right hemicolectomy. *Int J Colorectal Dis.* 2020;35:85–94.
 28. Carvalho ALM, Gonzalez MC, Sousa IM, das Virgens IPA, Medeiros GOC, Oliveira MN, et al. Low skeletal muscle radiodensity is the best predictor for short-term major surgical complications in gastrointestinal surgical cancer: A cohort study. *PLoS One.* 2021;16:e0247322.