SARCOPENIA IN GASTRIC CANCER AND BODY COMPOSITION CHANGES AFTER GASTRECTOMY

SARCOPÉNIA NO CANCRO GÁSTRICO E MODIFICAÇÕES DA COMPOSIÇÃO CORPORAL PÓS-GASTRECTOMIA

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ABSTRACT

Sarcopenia is the phenomenon of loss of muscle strength, muscle performance and muscle mass due to either age (primary sarcopenia) or other illnesses such as cancer (secondary sarcopenia). Sarcopenia has often been defined in the literature as low muscle mass. Sarcopenia among gastric cancer patients has been shown to carry a higher risk of post-operative complications and a higher overall and disease-specific mortality. Our study included 86 patients who underwent surgery for gastric cancer at our institution. Muscle mass was assessed by CT scan (L3 Muscle Index). A subgroup analysis was then performed of 39 patients who had had CT scans 12 months postoperatively. We collected demographic, clinical and body composition data. Sarcopenia was defined by the L3 Muscle Mass Index according to cut-off values previously defined in the literature. We found a prevalence of sarcopenia of 40.7% among gastric cancer patients undergoing gastrectomy. Sarcopenia was associated with a higher overall mortality. Nutritional risk and percentage of body weight lost did not identify sarcopenic patients. 51.4% of sarcopenic patients were overweight, 2.9% were obese. At 12 months post-operatively, 82.1% of patients lost weight and BMI and 76.9% of patients lost muscle mass (lower L3 muscle index) after gastrectomy. We did not find a significant association between the change in muscle mass, BMI or weight. We found that total gastrectomy was significantly associated to muscle mass loss compared to subtotal gastrectomy. We also found a significant association between advanced gastric cancer stage and muscle mass loss. We concluded that while sarcopenia is highly prevalent among gastric cancer patients after gastrectomy, the vast majority of patients lose weight and muscle mass. Since most patients will not improve muscle mass postoperatively it is crucial to implement prehabilitation strategies early on.

Keywords: Sarcopenia, L3 Muscle Index, Gastrectomy, Gastric Cancer, Nutrition.

RESUMO

A Sarcopénia é o fenómeno da perda de força, performance e massa muscular. Pode ser primário (relacionado com a idade) ou secundário (por exemplo a neoplasia) e tem sido definida na literatura como massa muscular baixa. A Sarcopénia nos doentes com cancro gástrico acarreta um aumento do risco de complicações pós-operatórias e da mortalidade específica e global. O nosso estudo incluiu 86 doentes submetidos a gastrectomia por cancro gástrico, cuja massa muscular foi avaliada por TC (Índice L3). Realizou-se uma subanálise de 39 doentes que tinham realizado TC também aos 12 meses pós-operatórios. Foram analisados



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dados demográficos, clínicos e de composição corporal. A Sarcopénia foi definida pelo Índice de Massa Muscular em L3, de acordo com valores previamente definidos na literartura. Verificámos uma prevalência de Sarcopénia de 40.7% em doentes submetidos a gastrectomia. A Sarcopénia relacionou-se com uma mortalidade global mais elevada. O Risco Nutricional e a percentagem de peso perdido não identificaram os doentes sarcopénicos. 51.4% dos doentes sarcopénicos tinham excesso de peso, 2.9% eram obesos. Aos 12 meses após gastrectomia, 82.1% dos doentes tinham diminuído de peso e IMC e 79.6% dos doentes tinham perdido massa muscular. Não encontrámos uma associação significativa entre a modificação na massa muscular e no peso ou IMC. Verificámos que a gastrectomia total se associava a uma perda de massa muscular significativamente superior à da gastrectomia subtotal. Verificámos que estadio avançado da neoplasia gástrica se associava a uma maior perda de massa muscular. Concluímos que a prevalência de Sarcopénia em doentes com cancro gástrico é elevada e que, após gastrectomia, a maior parte desses doentes perde peso e massa muscular. Dado que a maioria dos doentes não irão aumentar a sua massa muscular no pós-operatório, é crucial implementar estratégias de pré-habilitação precocemente.

Palavras-chave: Sarcopenia, Índice Muscular L3, Gastrectomia, Cancro Gástrico, Nutrição.

INTRODUCTION

Sarcopenia is defined as the loss of skeletal muscle mass. The term was first introduced by Rosenberg¹ in 1989 to describe the age-related loss of muscle mass as part of a discussion on the physical status of the elderly, namely the difference between biologic and chronological age.

In 2010 the European Working Group on Sarcopenia in Older People (EWGSOP) first published the European Consensus on Definition and Diagnosis of Sarcopenia². The 2010 definition introduced the concepts of sarcopenic obesity (loss of muscle mass with no decrease in fat mass) in cancer patients and the phenomenon of muscle marbling (fat infiltration of the muscle) as a condition that resulted in lower muscle quality and performance.

In 2018 the EWGSOP group shifted the focus to loss of muscle strength as the identifier of probable sarcopenia, which was then to be confirmed by the presence of low muscle mass or quality³.

Considering the association of weight loss and nutritional risk in patients with gastric cancer, these patients were deemed at a particularly high risk of muscle depletion and much research was done on the prevalence and impact of sarcopenia among gastric cancer patients⁴⁻²².

Interestingly, while much has been said on the prevalence and effect of preoperative Sarcopenia,

there is little information on the effects of gastrectomy on body composition and the postoperative prevalence of Sarcopenia. Gastrectomy may reduce food intake, lead to increased protein catabolism, insulin resistance, and metabolic changes which in turn may lead to weight loss and hypothetically to a higher prevalence of sarcopenia^{3,23}.

The aims of this paper were to determine the prevalence of sarcopenia assessed by CT scan (Cross Sectional Muscle Area at the L3 level) among patients undergoing gastrectomy for gastric cancer, to assess the impact of sarcopenia on the postoperative course and overall survival and to assess the changes in body composition after gastrectomy.

METHODS

Patient Selection and Study Design

All patients undergoing surgery for gastric cancer from January 2015 to May 2020 at our institution were reviewed. This was a retrospective cohort study of a prospectively built database. Only patients who had underwent a gastrectomy (total/subtotal) and had a pre-operative CT scan performed at our institution were included. A subgroup analysis was then performed of all the patients who had a



CT scan performed at our institution 12 months postoperatively.

Outcomes and covariates

Patient characteristics (including age, sex, weight, height, BMI, percentage of body weight lost, Nutrition Risk Screening 2012, comorbidities, ASA score), tumour stage (American Joint Committee on Cancer TNM staging and histology - 8th Edition), treatment characteristics (type of gastrectomy, chemotherapy regimen (adjuvant or neoadjuvant) were collected from the electronic medical record. Post-operative complications, hospital length of stay (LOS), and overall survival were the primary outcomes. Impact of comorbidities was stratified by the Charlson Comorbidity Index. Surgical complications were classified by the Clavien-Dindo Classification of Surgical Complications Scale. For the sub-group analysis, weight and BMI 12 months postoperatively were also collected.

Imaging studies and analysis

All included patients underwent CT scan of the abdomen and pelvis as part of the preoperative work-up. For the subgroup analysis, CT scans performed at 12 months post-operatively as part of the follow-up protocol were considered.

The CT scans were analyzed with the Osirix software by two radiologists.

Two consecutive axial images at the L3 level (with both transverse processes visible) were processed.

Skeletal muscle interest areas were selected using the -30 to +110 Hounsfield Units interval.

The automatic selections were manually corrected.

The total cross-sectional area (CSA) was automatically calculated for the two consecutive images and the average among the CSA of the two images was obtained. This final Cross-Sectional Area (cm²) was then adjusted to the squared height of the patient thereby yielding the L3 Muscle Index (cm²/m²).



FIGURE 1 – Corrected Skeletal Muscle Area at the L3 level

Patients were considered Sarcopenic if the L3 Muscle Index²¹ was:

- lower than $43 \text{ cm}^2/\text{m}^2$ in men with a BMI < 25;
- lower than $53 \text{ cm}^2/\text{m}^2$ in men with a BMI > 25;
- lower than $41 \text{ cm}^2/\text{m}^2$ in women.

Statistical analysis

Continuous variables are presented as median (minimum and maximum) and categorical variables as frequencies and percentages. Chi-squared or Fisher's exact tests were used to evaluate the association between two categorical variables. Comparisons between groups were performed using Mann–Whitney tests for continuous variables.

Overall survival was estimated by the Kaplan-Meier method. The log-rank test was performed to compare survival rates between groups. Risk factors were tested using a Cox-regression model. Hazard ratios (HRs) were calculated with 95% confidence intervals.

Statistical significance was considered at the level of p < 0.05. All statistical analysis was performed using the software R v4.0.1.



RESULTS

Sarcopenia in Gastric Cancer Patients undergoing Gastrectomy

A total of 86 patients were included in this study. The majority of patients were male (n=64, 74.4%) and median age was 71.5 (32-85) years old (Table 1).

Median follow-up time was 24.8 months. On preoperative assessment we found a prevalence of Sarcopenia of 40.7%.

There were no significant differences in age, gender, percentage of weight lost, nutritional risk, ASA score, Charlson comorbidity score or cancer stage between sarcopenic and non-sarcopenic patients.

Characteristics		Sarcopenia			
	Totat (N=86)	No (n=51)	Yes (n=35)	p-value	
Age	71.5 (32.0-85.0)	70.0 (42.0-85.0)	72.0 (32.0-83.0)	0.722	
Gender					
Male	64 (74.4%) 36 (70.6%)		28 (80.0%)	0.775	
Female	22 (25.6%)	15 (29.4%)	7 (20.0%)	0.465	
ВМІ					
Underweight	6 (7.0%)	0 (0.0%)	6 (17.1%)		
Normal Weight	37 (43.0%)	27 (52.9%)	10 (28.6%)	<0.001	
Overweight	32 (37.2%)	14 (27.5%)	18 (51.4%)		
Obese	11 (12.8%)	10 (19.6%)	1 (2.9%)	1 (2.9%)	
Weight Loss	5.5 (0.0-27.2)	5.7 (0.0-23.1)	4.9 (0.0-27.2)	0.703	
Unknown	8 (9.3%)	5 (9.8%)	3 (8.6%)		
Nutrition Risk Screening					
Low Risk	47 (54.7%)	25 (49.0%)	22 (62.9%)		
At Risk	13 (15.1%)	9 (17.6%)	4 (11.4%)	0.510	
High Risk	14 (16.3%)	9 (17.6%)	5 (14.3%)		
Unknown	12 (14.0%)	8 (15.7%)	4 (11.4%)		
ASA					
1	6 (7.0%)	3 (5.9%)	3 (8.6%)		
2	38 (44.2%)	23 (45.1%)	15 (42.9%)	0.071	
3	37 (43.0%)	22 (43.1%)	15 (42.9%)	0.971	
4	5 (5.8%)	3 (5.9%)	2 (5.7%)		
Charlson	4 (1-9)	4 (1-9)	4 (1-8)	0.798	
Stage					
1/11	45 (52.3%) 25 (49.0%) 2		20 (57.1%)	0.400	
III/IV	41 (47.7%)	26 (51.0%)	15 (42.9%)	0.602	
Hospital Stay	10 (6-122)	10 (7-82)	10 (6-122)	0.747	
Clavien-Dindo					
None/minor complications (\leq 2)	61 (70.9%)	35 (68.6%)	26 (74.3%)	0.7//	
Major complications (≥ 3)	25 (29.1%)	16 (31.4%)	9 (25.7%)	U./44	

TABLE 1 – Patient Characteristics



There were significant differences in BMI between sarcopenic and non-sarcopenic patients (p<0.001; Fig. 2). Non-sarcopenic patients, were mostly normal weight (52.9%), 27.5% were overweight and 19.6% were obese. Most sarcopenic patients were overweight (51.4%), 28.6% were normal weight, 17.1% were underweight and only 2.9% were obese.



FIGURE 2 – BMI distribution among sarcopenic and non-sarcopenic patients (p<0.001)

Sarcopenia was not associated with the occurrence of post-operative complications or a longer length of stay.

Sarcopenic patients had a worse overall survival than non-sarcopenic patients as shown by the Kaplan-Meyer (p=0.046; Fig. 3)

A Cox regression model showed a Hazard Ratio of 2.08 (95% CI: 1.01-4.32), showing that Sarcopenia was a risk factor for mortality. Sarcopenic patients are twice as likely to die than non-sarcopenic patients.

Body Composition changes after gastrectomy

For the subgroup analysis, 39 patients were included.

At 12 months post-operatively, 82.1% (n=32) of patients lost weight, 12.8% (n=5) gained weight and 5.1% (n=2) had no change in weight. The median difference in weight was -6Kg. The changes in BMI mirrored the weight changes, the median difference



FIGURE 3 - Overall survival in sarcopenic vs non-sarcopenic patients (p=0.046).



Sarcopenia in Gastric Cancer and Body Composition Changes after Gastrectomy

in BMI was -2.3 Kg/m². The median difference in Cross Sectional Area was -10.1cm² and the median difference in L3 Muscle index was: -3.6cm²/m². After their gastrectomy, 76.9% (n=30) patients lost muscle mass (as measured by the L3 muscle index).

Fourteen patients (35.9%) were sarcopenic preoperatively and 16 patients (41%) were sarcopenic post-operatively. After considering the BMIdependent cut-off values, we found that 7 patients "became" sarcopenic after gastrectomy: all of them had lost muscle mass, 6 of them had also lost weight, had 1 gained weight. Five patients became nonsarcopenic: while 4 increased their muscle mass, only one had gained weight. We did not find a significant association between the change in muscle mass and the change in BMI or weight.

Table 2 shows the changes in weight and muscle mass according the pre-operative BMI. The patients who became non-sarcopenic were either normal weight or overweight pre-operatively. All obese patients lost weight and muscle mass after gastrectomy, all lowered their BMI to overweight and some became sarcopenic, none improved their muscle mass. Despite some changes in weight and muscle mass no underweight patients were able to reach a normal weight or muscle mass.

There was a significant association between the muscle mass change and the type of surgery:



FIGURE 4 – Changes in Muscle Mass – On the left (1) are the preoperative values of the L3 Muscle Index, on the right (2) are the values of the L3 Muscle Index after gastrectomy.

Pre-Op Body Composition	n	CHANGE	Post-Op Body Composition
Underweight sarcopenic (n=3)	3	0	Underweight sarcopenic
Normal weight, sarcopenic (n=4)	2	↓ weight	Underweight sarcopenic
	2	1 muscle	Normal weight, non sarcopenic
Normal weight, non sarcopenic (n=13)	1	↓ weight ↓ muscle	Underweight sarcopenic
	3	↓ muscle	Normal weight, sarcopenic
	9	0	Normal weight, non sarcopenic
Overweight sarcopenic (n=6)	3	↓ weight	Normal weight, sarcopenic
	3	↓ weight, ↑ muscle	Normal weight, non sarcopenic
Overweight, non sarcopenic (n=7)	1	↓ weight ↓ muscle	Normal weight, sarcopenic
	4	↓ weight	Normal weight, non sarcopenic
	2	0	Overweight, non sarcopenic
Obese sarcopenic (n=1)	1	↓ weight	Overweight sarcopenic
Obese, non sarcopenic (n=5)	3	↓ weight	Overweight, non sarcopenic
	2	↓ weight ↓ muscle	Overweight sarcopenia

TABLE 2 – Distribution of Body Composition type before and after Gastrectomy. 0 = no change



total gastrectomy was significantly associated to muscle mass loss compared to subtotal gastrectomy (p=0.014). 88.9% of the patients submitted to a total gastrectomy had loss of muscle mass (lower L3 Muscle Index) at the 12-month evaluation, whereas only 50% of subtotal gastrectomy patients lost muscle mass. Changes in weight and BMI were not associated with the type of gastrectomy (total vs subtotal, p=0.307, p=0.028).

We found a significant association between advanced gastric cancer stage and muscle mass loss post-operatively (p=0.033): all patients with advanced gastric cancer (stages III and IV) suffered muscle mass loss as per the L3 Muscle Index.

Adjuvant chemotherapy was not associated with loss of muscle mass or weight loss.

DISCUSSION

Assessing muscle mass in Gastric Cancer and the impact of Sarcopenia

Rosenberg¹ (1989) argued that loss of muscle mass and function were of dramatic relevance to the fitness of the elderly, as it affected their ability to walk, breathe, their independence and nutritional intake. Rosenberg also pointed out a relationship between exercise and muscle loss and that there should be a focus on finding out how to rebuild muscle mass and recover function in elderly patients – the goal of the prehabilitation programs.

In the EWGSOP consensus (2010), for definition of Sarcopenia², both low muscle mass and loss of strength or performance were required to establish a diagnosis, as muscle strength does not depend on, or is related exclusively to muscle mass.

After the publication of this definition, many authors studied the prevalence and impact of Sarcopenia in various diseases and conditions. Sarcopenia was defined, in many of these studies, as low muscle mass on CT scans, as is the case of this report.^{21, 24-26} In the EWGSOP2 (2018) muscle strength was brought to the forefront³, as it seems to be a better predictor of frailty and decline in primary sarcopenia^{27,28} (whether this applies to prognosis of secondary sarcopenia is not yet clear). Besides, physical performance (muscle strength) is technically easier to assess in the clinical setting (SARC-F questionnaire, Grip strength and Chair Stand Test) and in cases of suspicion of sarcopenia, it should be confirmed by measurement of muscle quality and/or muscle mass.

As muscle mass is correlated to body size, the muscle mass estimated by the above-mentioned techniques should be adjusted to body size. This adjustement can be done using the squared height, squared weight ou BMI. Dernestine et al²⁹ have worked on the thresholds for Sarcopenia and how they correlate with height and weight but not BMI, their results suggest that the skeletal muscle index, used to identify sarcopenia, should be adjusted for BMI. There is currently no consensus on which adjustment is better or whether a particular adjustment is better suited to a specific population. There is not a consensus either on whether total body skeletal muscle mass, appendicular skeletal muscle mass or cross sectional areas have the same accuracy and meaning³.

CT scans are accurate in distinguishing body composition and provide consistent measures with little observer or machine variation. They allow assessment of muscle mass of specific muscles or body areas and the results are consistent even in individuals with low muscle mass and high weight.^{30,31}CT scans can provide various parameters such as muscle mass at the L3 level, mid-thigh muscle mass or psoas muscle mass. As most patients with gastrointestinal cancer undergo CT scans of the abdomen and pelvis, the L3 muscle mass has been extensively tested in these patient populations.

We have studied muscle mass and body composition using CT scans due to its high accuracy (even in underweight patients) and high availability of this information as all our patients undergo



preoperative and follow-up CT imaging. We also opted to use the L3 Muscle Index over the Psoas Muscle Index as it has been more thoroughly used in the literature.

In our study we opted for the cut-off values by Martin et al²¹, which have often been used in the literature and include different thresholds to account for BMI.^{5,10,15, 29, 32-37}

Muscle quality is a more recent parameter than muscle mass. It translates the changes in muscle composition (fat infiltration) associated with a worse muscle function.

This assessment may be done by MRI or CT and the two techniques are equally feasible and seem to be interchangeable³⁷. Muscle quality has been shown to have a prognostic relevance in gastrointestinal surgery³⁸⁻⁴⁰ but there is still no consensus on assessment methods and clinical aplicability³.

The impact of sarcopenia among gastric cancer patients (Table 1), submitted to gastrectomy in our department, was the focus of this work.

A 2020 meta-analysis of 15 studies⁴ (including a total of 4887 patients) on sarcopenia among gastric cancer patients, concluded that sarcopenic patients had a higher probability of post-operative complications (namely severe complications) and a higher overall and disease-specific mortality. However, Borggreve et al⁴ noted that the methods and cut-off values used to define Sarcopenia were remarkably variable among the various studies.^{5,6,8,10-20,41}

We found a prevalence of sarcopenia (assessed by CT scan) of 40.7% among gastric cancer patients undergoing gastrectomy. The prevalence of sarcopenia in preoperative gastric cancer ranges between 7% and 70% according to the patient population and the methods used to assess sarcopenia⁴². A previous study³⁵, on Portuguese gastric cancer patients undergoing chemotherapy, found a prevalence of sarcopenia of 23%. A Spanish study⁴³ reported a prevalence of sarcopenia, among gastric cancer patients, of 45.4%, quite similar to ours. While we did not find an association between postoperative complications and sarcopenia, we did find that sarcopenia was associated with a higher overall mortality.

It should also be noted that percentage of body weight lost and nutritional risk screening were not associated with sarcopenia. These parameters did not identify sarcopenic patients and do not seem to translate the risk of muscle depletion.

The EWGSOP³ also put a focus on sarcopenic obesity. This condition refers to the coexistence of muscle mass depletion (sarcopenia) and obesity. Diagnosis using CT scan in cancer patients was first introduced by Martin et al²¹ and this study is credited with establishing that loss of muscle (not loss of fat) portended a worse prognosis in these patients. In our study, sarcopenic obesity was only 2.9% of sarcopenic patients, however 51.4% of sarcopenic patients were overweight. We once again proved that sarcopenia can be present even with an excessive body weight and these overweight (sarcopenic) patients do have a higher risk than non-sarcopenic patients.

Body Composition Changes after Gastrectomy

Only a few reports have been published on sarcopenia before and after gastric cancer treatment.

Kouzo et al²³ studied 67 patients with recurrence after gastrectomy for gastric cancer. They found that a high reduction rate of the Psoas Muscle Index (PMI), between the preoperative and the "recurrence" PMI, was independently associated with a poor prognosis after recurrence. The L3 Muscle Index was not used in this study. It is worth mentioning that one of the findings of the study by Kouzo et al²³ was that a failure to complete more than 5 sessions of chemotherapy was also associated with a worse prognosis after recurrence.

In our study, we looked at body composition changes at 1 year postoperatively and we found that,



at 12 months post-operatively, 82.1% of patients lost weight, 12.8% gained weight and 5.1% had no change in weight (yielding a median change in weight of – 6Kg). The exact same pattern applied to the BMI after gastrectomy.

We also found that 76.9% of patients lost muscle mass (decreased their L3 muscle index) after gastrectomy. We did not find a significant association between the change in muscle mass, BMI or weight: as expected, muscle mass changes seem to be a phenomenon independent of BMI and weight.

After gastrectomy some patients "became" sarcopenic (most of whom had lost weight), a few however actually increased their muscle mass postoperatively and became non-sarcopenic. This increase in muscle mass was not followed by weight gain in most patients and we did not find a significant association between the change in muscle mass and the change in BMI or weight. The patients who increased their L3 muscle mass index postoperatively were mostly early stages gastric cancer patients who had undergone a subtotal gastrectomy. Accordingly, we found a significant association between the muscle mass change and the type of surgery: total gastrectomy was significantly associated to muscle mass loss compared to subtotal gastrectomy. We also found a significant association between advanced gastric cancer stage and muscle mass loss.

The patients who became non-sarcopenic post-operatively were either normal-weight or overweight pre-operatively. None of the preoperatively obese patients improved their muscle mass. So, despite apparently adequate nutritional intake, obese patients do not improve muscle mass post-operatively. We do not know whether this is due to previous deleterious eating habits, sedentary lifestyle or inadequate physical activity, or whether this may translate the effect of adipose tissue on anabolic and catabolic metabolism. Despite some changes in weight and muscle mass, no underweight patients were able to reach a normal weight or muscle mass. Pre-operative interventions on these patients seem mandatory.

Takahashi et al44 studied post-operative muscle mass among elderly patients undergoing distal gastrectomy. They found that patients lowered weight, muscle strength, muscle performance and appendicular muscle mass (BIA assessed) in the first six months postoperatively. But while weight and visceral fat area increased by 1 year postoperatively, the appendicular skeletal muscle mass index did not. Actually, the frequency of sarcopenia remained almost unchanged at 1 year postoperatively. Their analysis, however, was limited to elderly, stage I gastric cancer patients, submitted to a Bilroth-II type of reconstruction and who did not undergo adjuvant chemotherapy. Our results report on a much wider gastric cancer population undergoing both total and subtotal gastrectomy, with Rouxen-Y type of reconstruction, with and without adjuvant chemotherapy.

Lee et al⁴⁵ studied 247 patients submitted to gastric ressection and similarly they found that patients undergoing total gastrectomy suffered bigger reductions in hemoglobin, nutritional parameters, visceral fat and abdominal muscle mass.

Kugimiya et al⁴⁶ analysed the skeletal muscle mass at 6 months post-operatively of 119 patients and found that total gastrectomy was risk factor for a higher decrease in muscle mass. Their study also suggested that a loss in skeletal muscle mass $\geq 5\%$ (6 months post-operatively) was a risk factor for a shorter overall survival.

Park et al⁴⁷ (2020) had studied the L3 Skeletal Muscle Index of patients with gastric cancer before and after palliative chemotherapy. They found that sarcopenia at baseline was associated with a worse prognosis and that a greater decrease in skeletal muscle mass after chemotherapy portended a worse outcome with a shorter overall survival.

Other authors^{35,48} had already shown a negative association between sarcopenia and chemotherapy tolerance.

Thanks to these contributions, it seems increasingly clear that sarcopenic patients have a worse prognosis and this seems to be true for any step of



the way in gastric cancer treatment (pre and postoperatively, and before and after chemotherapy).

We do not yet know what determined the increase in muscle mass that we found in a few patients, whether their nutrition intake was improved or whether the increase in muscle mass is due to improved post-operative fitness and activity.

However, it should be noted that the vast majority of patients did not manage to improve their muscle mass after gastrectomy. Our study therefore suggests that interventions to improve patients muscle mass pre and post-operatively are necessary as patients do not easily overcome their low muscle mass alone. Nutritional management^{49,50} (optimal calorie and protein intake) and skeletal muscle mass loss prevention⁵¹ (physical activity) have been shown to decrease muscle depletion both pre- and post-operatively. The relevance of prompt identification of sarcopenia goes beyond adequate pre-operative risk stratification to actually enabling timely inclusion of these patients in prehabilitation programs, any time throughout the treatment process, thereby improving prognosis⁵².

Limitations

This study has a few limitations, it was a retrospective study, the sample for the subgroup analysis is relatively small. Likewise, the mean follow-up time is relatively short due to a number of patients included with little follow-up time. Increasing the number of patients in the subgroup analysis and their follow-up time would allow to properly study the long-term impact of postoperative sarcopenia and other categories of body composition.

CONCLUSION

Sarcopenia is highly prevalent among gastric cancer patients undergoing gastrectomy. Preoperative sarcopenia is associated with a worse overall survival.

After gastrectomy, the vast majority of patients lose weight and muscle mass. Total gastrectomy and advanced stage gastric cancer were associated with a higher muscle mass loss. Sarcopenic patients are not to likely to improve muscle mass after gastrectomy. These patients would particularly benefit from preoperative and post-operative interventions aimed at improving their nutritional status and fitness.

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Ethics approval

The Ethics Board at our institution approved this study (86/2020)

Conflict of Interest/Disclosures

None

REFERENCES

- 1. Rosenberg IH. Summary comments. The American Journal of Clinical Nutrition. 1989 Nov 1;50(5):1231-3.
- 2. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age and Ageing. 2010 Jul 1;39(4):412–23.
- 3. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age and Ageing. 2019 Jan 1;48(1):16–31.
- 4. Borggreve AS, den Boer RB, van Boxel GI, de Jong PA, Veldhuis WB, Steenhagen E, et al. The Predictive Value of Low Muscle Mass as Measured on CT Scans for Postoperative Complications and Mortality in Gastric Cancer Patients: A Systematic Review and Meta-Analysis. JCM. 2020 Jan 11;9(1):199.
- Tegels JJW, van Vugt JLA, Reisinger KW, Hulsewé KWE, Hoofwijk AGM, Derikx JPM, et al. Sarcopenia is highly prevalent in patients undergoing surgery for gastric cancer but not associated with worse outcomes: Sarcopenia Prevalent in Gastric Cancer. J Surg Oncol. 2015 Aug;112(4):403–7.



Margarida Ferreira, Ana Lúcia Barreira, Francisco Sardinha, João Costa, Jéssica Rodrigues, Afonso Gonçalves, Paulo Matos Costa

- 6. Mirkin KA, Luke FE, Gangi A, Pimiento JM, Jeong D, Hollenbeak CS, et al. Sarcopenia related to neoadjuvant chemotherapy and perioperative outcomes in resected gastric cancer: a multi-institutional analysis. J Gastrointest Oncol. 2017 Jun;8(3):589–95.
- Huang D-D, Cai H-Y, Chen X-Y, Dong W-X, Wangchuk D, Yan J-Y, et al. Value of Sarcopenia defined by the new EWGSOP2 consensus for the prediction of Postoperative Complications and Long-term Survival after Radical Gastrectomy for Gastric Cancer: A comparison with four common nutritional screening tools. J Cancer. 2020;11(19):5852–60.
- 8. Huang D-D, Chen X-X, Chen X-Y, Wang S-L, Shen X, Chen X-L, et al. Sarcopenia predicts 1-year mortality in elderly patients undergoing curative gastrectomy for gastric cancer: a prospective study. J Cancer Res Clin Oncol. 2016 Nov;142(11):2347–56.
- 9. Huang D-D, Zhou C-J, Wang S-L, Mao S-T, Zhou X-Y, Lou N, et al. Impact of different sarcopenia stages on the postoperative outcomes after radical gastrectomy for gastric cancer. Surgery. 2017 Mar;161(3):680–93.
- 10. Kudou K, Saeki H, Nakashima Y, Edahiro K, Korehisa S, Taniguchi D, et al. Prognostic Significance of Sarcopenia in Patients with Esophagogastric Junction Cancer or Upper Gastric Cancer. Ann Surg Oncol. 2017 Jul;24(7):1804-1810.
- 11. Nishigori T, Tsunoda S, Okabe H, Tanaka E, Hisamori S, Hosogi H, et al. Impact of Sarcopenic Obesity on Surgical Site Infection after Laparoscopic Total Gastrectomy. Ann Surg Oncol. 2016 Aug;23(S4):524–31.
- 12. Zhang Y, Wang JP, Wang XL, Tian H, Gao TT, Tang LM, et al. Computed tomography-quantified body composition predicts short-term outcomes after gastrectomy in gastric cancer. Curr Oncol. 2018 Nov 2;25(5).
- Wang S-L, Zhuang C-L, Huang D-D, Pang W-Y, Lou N, Chen F-F, et al. Sarcopenia Adversely Impacts Postoperative Clinical Outcomes Following Gastrectomy in Patients with Gastric Cancer: A Prospective Study. Ann Surg Oncol. 2016 Feb;23(2): 556–64.
- 14. Sierzega, M, Chrzan, R, Wiktorowicz, M, Kolodziejczyk, P, Richter, P. Prognostic and predictive implications of sarcopenia in Western patients undergoing gastric resections for carcinoma of the stomach. J Surg Oncol. 2019; 120: 473- 482.
- 15. Nishigori T, Tsunoda S, Obama K, Hisamori S, Hashimoto K, Itatani Y, et al. Optimal Cutoff Values of Skeletal Muscle Index to Define Sarcopenia for Prediction of Survival in Patients with Advanced Gastric Cancer. Ann Surg Oncol. 2018 Nov;25(12):3596–603.
- 16. Kuwada K, Kuroda S, Kikuchi S, Yoshida R, Nishizaki M, Kagawa S, et al. Sarcopenia and Comorbidity in Gastric Cancer Surgery as a Useful Combined Factor to Predict Eventual Death from Other Causes. Ann Surg Oncol. 2018 May;25(5):1160–6.
- 17. Lu J, Zheng Z-F, Li P, Xie J-W, Wang J-B, Lin J-X, et al. A Novel Preoperative Skeletal Muscle Measure as a Predictor of Postoperative Complications, Long-Term Survival and Tumor Recurrence for Patients with Gastric Cancer After Radical Gastrectomy. Ann Surg Oncol. 2018 Feb;25(2):439–48.
- 18. O'Brien S, Kavanagh RG, Carey BW, Maher MM, O'Connor OJ, Andrews EJ. The impact of sarcopenia and myosteatosis on postoperative outcomes in patients with inflammatory bowel disease. Eur Radiol Exp. 2018 Nov 21;2(1):37.
- 19. Zhuang C-L, Huang D-D, Pang W-Y, Zhou C-J, Wang S-L, Lou N, et al. Sarcopenia is an Independent Predictor of Severe Postoperative Complications and Long-Term Survival After Radical Gastrectomy for Gastric Cancer: Analysis from a Large-Scale Cohort. Medicine. 2016 Mar;95(13):e3164.
- 20. Sakurai K, Kubo N, Tamura T, Toyokawa T, Amano R, Tanaka H, et al. Adverse Effects of Low Preoperative Skeletal Muscle Mass in Patients Undergoing Gastrectomy for Gastric Cancer. Ann Surg Oncol. 2017 Sep;24(9):2712–9.
- 21. Martin L, Birdsell L, MacDonald N, Reiman T, Clandinin MT, McCargar LJ, et al. Cancer Cachexia in the Age of Obesity: Skeletal Muscle Depletion Is a Powerful Prognostic Factor, Independent of Body Mass Index. JCO. 2013 Apr 20;31(12):1539–47.
- 22. Nishigori T, Obama K, Sakai Y. Assessment of body composition and impact of sarcopenia and sarcopenic obesity in patients with gastric cancer. Transl Gastroenterol Hepatol. 2020 Apr;5:22–22.
- 23. Kouzu K, Tsujimoto H, Sugasawa H, Ishibashi Y, Itazaki Y, Tsuchiya S, et al. Impact of postoperative reduced skeletal muscle on prognosis after recurrence in gastric cancer. Mol Clin Oncol. 2020 Oct 30;14(1):1–1.
- 24. Moisey LL, Mourtzakis M, Cotton BA, Premji T, Heyland DK, Wade CE, et al. Skeletal muscle predicts ventilator-free days, ICUfree days, and mortality in elderly ICU patients. Crit Care.2013 Sep 19;17(5):R206.
- 25. Choi Y, Oh D-Y, Kim T-Y, Lee K-H, Han S-W, Im S-A, et al. Skeletal Muscle Depletion Predicts the Prognosis of Patients with Advanced Pancreatic Cancer Undergoing Palliative Chemotherapy, Independent of Body Mass Index. PLOS ONE. 2015 Oct 5;10(10):e0139749.
- 26. Lieffers JR, Bathe OF, Fassbender K, Winget M, Baracos VE. Sarcopenia is associated with postoperative infection and delayed recovery from colorectal cancer resection surgery. Br J Cancer. 2012 Sep 4;107(6):931-6.
- 27. Schaap LA, van Schoor NM, Lips P, Visser M. Associations of Sarcopenia Definitions, and Their Components, With the Incidence of Recurrent Falling and Fractures: The Longitudinal Aging Study Amsterdam. The Journals of Gerontology: Series A. 2018 Aug 10;73(9):1199–204.
- 28. Schaap LA, Koster A, Visser M. Adiposity, Muscle Mass, and Muscle Strength in Relation to Functional Decline in Older Persons. Epidemiologic Reviews. 2013;35(1):51–65.
- 29. Derstine BA, Holcombe SA, Ross BE, Wang NC, Su GL, Wang SC. Optimal body size adjustment of L3 CT skeletal muscle area for sarcopenia assessment. Sci Rep. 2021 Dec;11(1):279.



- 30. Prado CMM, Heymsfield SB. Lean Tissue Imaging: A New Era for Nutritional Assessment and Intervention. JPEN J Parenter Enteral Nutr. 2014 Nov;38(8):940-53.
- 31. Baracos V, Kazemi-Bajestani SMR. Clinical outcomes related to muscle mass in humans with cancer and catabolic illnesses. The International Journal of Biochemistry & Cell Biology. 2013 Oct;45(10):2302-8.
- 32. Su H, Ruan J, Chen T, Lin E, Shi L. CT-assessed sarcopenia is a predictive factor for both long-term and short-term outcomes in gastrointestinal oncology patients: a systematic review and meta-analysis. Cancer Imaging. 2019 Dec;19(1):82.
- 33. Park HS. Marked Loss of Muscle, Visceral Fat, or Subcutaneous Fat After Gastrectomy Predicts Poor Survival in Advanced Gastric Cancer: Single-Center Study from the CLASSIC Trial. Ann Surg Oncol. 2018 Oct;25(11):3222-3230.
- 34. Mosk CA, van Vugt JLA, de Jonge H, Witjes CD, Buettner S, Ijzermans JN, van der Laan L. Low skeletal muscle mass as a risk factor for postoperative delirium in elderly patients undergoing colorectal cancer surgery. Clin Interv Aging, 2018 Oct 24;13:2097-2106.
- 35. Palmela C, Velho S, Agostinho L, Branco F, Santos M, Santos MPC, et al. Body Composition as a Prognostic Factor of Neoadjuvant Chemotherapy Toxicity and Outcome in Patients with Locally Advanced Gastric Cancer. J Gastric Cancer. 2017;17(1):74.
- 36. Kudou K, Saeki H, Nakashima Y, Edahiro K, Korehisa S, Taniguchi D, Tsutsumi R, Nishimura S, Nakaji Y, Akiyama S, Tajiri H, Nakanishi R, Kurashige J, Sugiyama M, Oki E, Maehara Y. Prognostic Significance of Sarcopenia in Patients with Esophagogastric Junction Cancer or Upper Gastric Cancer. Ann Surg Oncol. 2017 Jul;24(7):1804-1810.
- 37. Faron A, Sprinkart AM, Kuetting DLR, Feisst A, Isaak A, Endler C, et al. Body composition analysis using CT and MRI: intraindividual intermodal comparison of muscle mass and myosteatosis. Sci Rep. 2020 Dec;10(1):11765.
- 38. Lee CM, Kang J. Prognostic impact of myosteatosis in patients with colorectal cancer: a systematic review and meta-analysis. J Cachexia Sarcopenia Muscle. 2020 Oct;11(5):1270-1282.
- 39. Srpcic M, Jordan T, Popuri K, Sok M. Sarcopenia and myosteatosis at presentation adversely affect survival after esophagectomy for esophageal cancer. Radiol Oncol. 2020 Mar 27;54(2):237-246.
- 40. Zhuang C-L, Shen X, Huang Y-Y, Zhang F-M, Chen X-Y, Ma L-L, et al. Myosteatosis predicts prognosis after radical gastrectomy for gastric cancer: A propensity score-matched analysis from a large-scale cohort. Surgery. 2019 Sep;166(3):297-304.
- 41. Zheng, Z.F.; Lu, J.; Zheng, C.H.; Li, P.; Xie, J.W.; Wang, J.B.; Lin, J.X.; Chen, Q.Y.; Lin, M.; Huang, C.M.; et al. A Novel Prognostic Scoring System Based on Preoperative Sarcopenia Predicts the Long-Term Outcome for Patients After R0 Resection for Gastric Cancer: Experiences of a High-Volume Center. Ann. Surg. Oncol. 2017, 24, 1795–1803.
- 42. Kamarajah SK, Bundred J, Tan BHL. Body composition assessment and sarcopenia in patients with gastric cancer: a systematic review and meta-analysis. Gastric Cancer. 2019 Jan;22(1):10-22.
- 43. Rodrigues V. Is Sarcopenic Obesity an Indicator of Poor Prognosis in Gastric Cancer Surgery? A Cohort Study in a Western Population. J Gastrointest Surg. :16.
- 44. Takahashi S, Shimizu S, Nagai S, Watanabe H, Nishitani Y, Kurisu Y. Characteristics of sarcopenia after distal gastrectomy in elderly patients. Mogi M, editor. PLoS ONE. 2019 Sep 11;14(9):e0222412.
- 45. Lee K, Kim KW, Lee J-B, Shin Y, Jang JK, Yook J-H, et al. Impact of remnant stomach volume and anastomosis on nutrition and body composition in gastric cancer patients. Surg Oncol. 2019 Dec;31:75-82.
- 46. Kugimiya N, Harada E, Oka K, Kawamura D, Suehiro Y, Takemoto Y, et al. Loss of skeletal muscle mass after curative gastrectomy is a poor prognostic factor. Oncol Lett. 2018 Jul;16(1):1341-1347.
- 47. Park SE, Choi JH, Park JY, Kim BJ, Kim JG, Kim JW, Park JM, Chi KC, Hwang IG. Loss of skeletal muscle mass during palliative chemotherapy is a poor prognostic factor in patients with advanced gastric cancer. Sci Rep. 2020 Oct 19;10(1):17683.
- 48. Shen Y, Hao Q, Zhou J, Dong B. The impact of frailty and sarcopenia on postoperative outcomes in older patients undergoing gastrectomy surgery: a systematic review and meta-analysis. BMC Geriatr. 2017 Dec;17(1):188.
- 49. Zanetti M, Gortan Cappellari G, Barazzoni R, Sanson G. The Impact of Protein Supplementation Targeted at Improving Muscle Mass on Strength in Cancer Patients: A Scoping Review. Nutrients. 2020 Jul 16;12(7):2099.
- 50. Prado CM, Purcell SA, Laviano A. Nutrition interventions to treat low muscle mass in cancer. J Cachexia Sarcopenia Muscle. 2020 Apr;11(2):366-80.
- 51. Steffl M, Bohannon RW, Sontakova L, Tufano JJ, Shiells K, Holmerova I. Relationship between sarcopenia and physical activity in older people: a systematic review and meta-analysis. Clin Interv Aging. 2017 May 17;12:835-845.
- 52. Molenaar CJL, Papen-Botterhuis NE, Herrle F, Slooter GD. Prehabilitation, making patients fit for surgery a new frontier in perioperative care. Innovative Surgical Sciences. 2019 Dec 18;4(4):132-8.

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