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Feasibility of Systematic Handgrip Strength Testing in Digestive Cancer Patients Treated With Chemotherapy: The FIGHTDIGO Study

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BACKGROUND: Handgrip strength (HGS) is a widely studied noninvasive test. Weak strength (dynapenia) seems to be associated with high morbidity and mortality in different populations, notably oncology populations. Despite this, HGS testing is not used in daily practice in oncology. The study was aimed at evaluating the feasibility and acceptability of HGS testing in patients with digestive cancer treated with ambulatory chemotherapy. **METHODS:** In this prospective, single-center study, enrolled patients were followed for 6 months. Two consecutive bilateral measures were performed with a Jamar dynamometer during each patient's appointments in the unit for intravenous treatment. A questionnaire was completed by patients and medical team members. **RESULTS:** There were 203 consecutive patients, and 201 were recruited. In all, 1704 of 1716 measurements (99.3%) were performed, and 201 patients (99.0%) performed at least 1 measure; 190 (94.5%) performed all expected measures. One hundred sixty-four of 171 participating patients (95.9%) found the test easy to perform, and 167 (97.7%) did not find the test restrictive. All of the 14 medical team members found the test easy to perform, unrestrictive, and undistruptive in their daily practice. **CONCLUSIONS:** HGS testing is routinely feasible, inexpensive, and well accepted by patients and medical teams in an ambulatory digestive cancer unit. *Cancer* 2018;124:1501-6. © 2017 American Cancer Society.

KEYWORDS: chemotherapy, digestive system neoplasms, dynapenia, feasibility study, muscle strength dynamometer, sarcopenia.

INTRODUCTION

Cancer and malnutrition became major concerns in developed and developing countries during the last century.^{1,2} Digestive cancers are particularly represented by bowel, stomach, and liver tumors, which are among the 10 most frequently diagnosed cancers.²

In this specific population, malnutrition is commonly found, and it is a concern with approximately 39% of colorectal cancers, 44% of esophageal and/or stomach cancers, and 67% of pancreatic cancers.³ It is responsible for higher morbidity and mortality rates, and this explains why its screening and treatment are important.

The current definition of malnutrition relies on a low body mass index, unintentional weight loss, and/or hypoalbuminemia without inflammatory syndrome.⁴ Those 3 criteria do not totally reflect the complex physiopathology of malnutrition and its impact.

For many years, investigations have been performed in the area of malnutrition, and more attention has been paid to muscle mass loss, which occurs in 80% of patients with cancer and is a first step toward malnutrition.⁵ However, muscle mass alone cannot be interpreted without its function, that is, muscle strength.

The evaluation of muscle strength with a handgrip dynamometer has been widely studied. Strength physiologically declines with age.⁶⁻⁸ Weak strength, known as dynapenia,⁹ is known to predict the risk of mortality from all causes when it is measured in middle-aged individuals in the general population.⁶ Dynapenia also appears to be a factor in disability,¹⁰ nosocomial infections,¹¹ and the length of hospital stays¹² for elderly people. In oncology, low handgrip strength (HGS) is associated with cancer-related fatigue,¹³ poor quality of life,¹⁴ postoperative complications,¹⁵ and high mortality.¹⁶ It was also recently included in the consensual definition of sarcopenia, which associates muscle mass loss and weak strength.¹⁷

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The HGS test was recently studied in large population samples including up to 140,000 patients,¹⁸⁻²⁰ and this suggests that it may be an easy test to perform. Despite this, the HGS test is not part of daily medical practice, notably in oncology, and the feasibility and acceptability of measuring grip strength in different medical services have not been yet established.²¹

The main objective of the current study was to determine whether routinely measuring HGS would be feasible for patients with digestive cancer treated with chemotherapy in an ambulatory digestive cancer unit. The other objectives were to evaluate the cost of this HGS test and its acceptability to patients and medical team members.

MATERIALS AND METHODS

Study Design and Participants

This prospective, single-center study was conducted in the Ambulatory Digestive Cancer Unit (Unit of Ambulatory Medicine, Oncology, and Hematology) of the Reims Teaching Hospital (University Hospital Center of Reims) in France. The patients were recruited from May 18, 2016, to November 18, 2016, and were followed for 6 months. They were asked to perform the HGS test at each of their appointments in the unit for their treatment (every week (eg, Gemcitabine), 2 weeks (eg, FOLFIRINOX), or longer (eg, VP16) according to the chemotherapy protocol). The measure could be performed before, during, or after the beginning of the perfusion. The test was conducted in the same way by a medical physician, a resident, a medical school student, or a nurse.

Patients were included in the study if they were older than 18 years and had a digestive cancer treated with cytotoxic chemotherapy and/or biotherapy in the unit. They were excluded if they could not give their consent, did not understand the test, had a neuromuscular disorder, and/or had appointed a health care proxy.

Ethical Approval

Informed written consent was obtained for each patient enrolled in the trial. The Feasibility of Systematic Hand-grip Strength Testing and Short-Term Changes in Muscle Strength in Digestive Cancer Patients Treated by Chemotherapy (FIGHTDIGO) study was approved by the ethics committee (Committee for the Protection of Persons EST I, Dijon, France; March 25, 2016) and was registered at ClinicalTrials.gov (NCT02797197).

Statistical Analysis

Data were described with means and standard deviations for quantitative variables and with numbers and

percentages for qualitative variables. All analyses were performed with SAS 9.4 (SAS Institute, Inc, Cary, North Carolina).

HGS Measurements

HGS was measured with a Jamar hydraulic dynamometer. Two dynamometers were available in the ambulatory unit. There were 5 possible positions, and the handle position used in this study was position 2. Every patient was seated comfortably in a chair. The shoulder of the upper limb holding the dynamometer was in an adduction position, the elbow was flexed to 90 degrees, and the forearm and wrist were in a neutral position. The other upper limb was placed alongside the body and relaxed. During the examination, verbal encouragement was given to the patients to obtain their best score. Four measurements were taken, and each one was supposed to last 3 seconds. Patients had to perform the first 2 measurements in a row: one with the dominant hand and the other with the non-dominant hand. Then, a 1-minute break was taken before the 2 measurements were repeated. The effective time needed to take the 4 measurements was approximately 15 seconds plus the 1-minute break used to proceed to the assessment of the side effects of the last treatment.

Primary Outcome

The feasibility of the HGS test was represented by the proportion of patients who performed at least 1 HGS test among all patients hospitalized in the unit for a digestive cancer treatment.

Secondary Outcomes

The total number of HGS measurements for each patient, the number of HGS measurements with respect to the number of hospitalizations in the unit, the number of patients who performed 100% of the HGS measurements, the number of patients who performed 50% to fewer than 100% of the HGS measurements, the number of patients who performed fewer than 50% of the measurements, and the mean number of measures per patient were evaluated.

The acceptability of the HGS test was determined initially with an anonymous questionnaire given to the patients after 3 months of follow-up and then with an anonymous questionnaire given to the medical team members who participated in the study at the end of the follow-up.

The HGS test cost was estimated as follows: cost estimates per hydraulic dynamometer, cost per patient, and cost per measurement. It was then compared with

other malnutrition markers such as weight and the modified Glasgow Prognostic Score (mGPS), which associates serum albuminemia and C-reactive protein.

RESULTS

Description of the Population

A total of 203 patients were consecutively hospitalized. Two patients were not included: 1 patient did not want to participate, and another patient was excluded because of limited cognitive function. Finally, 201 patients were analyzed (117 men [58.2%] and 84 women [41.8%]). Table 1 shows the participants' characteristics. The majority of the participants were right-handed (186 of 201 [92.5%]). Colorectal cancer was the most frequent ($n = 103$ [51.2%]). Sixty-nine percent of the patients came for an appointment for metastatic tumor treatment.

Feasibility

Among the 203 hospitalized patients, 201 (99.0%) performed at least 1 HGS test during the follow-up. A total of 1716 hospitalizations, corresponding to 1716 expected measurements, were registered. A total of 1704 measurements were performed, and 12 (0.7%) were missing for various reasons: 1 patient refused to perform the test on an occasion, 1 measure was forgotten, 7 others were missed because of time constraints, 1 was missed because of hand pain due to arthrosis, and 2 were missed for unknown reasons. Among the 201 patients, 190 (94.5%) performed 100% of the expected measures. Ten patients (5.0%) missed 1 measure, and 1 patient (0.5%) missed 2 measures. The mean number of measures per patient was 8.5 ± 4 , with a maximum of 19 measures per patient.

Acceptability

A total of 171 patients (85.1%) completed the questionnaire after 3 months of follow-up (Table 2). Some patients had already used the Jamar dynamometer before the study ($n = 11$ [6.4%]): 4 used it with a nutritionist, 1 used it with a digestive surgeon for another study, 1 used it with a medical physician at work, 1 used it during a checkup with the department of social insurance, 3 used it in our department for another study, and 1 used it for an unknown reason. The majority of the patients found the hand dynamometer easy to use ($n = 164$ [95.9%]). Difficulties met by the other patients ($n = 7$ [4.1%]) included the high weight of the instrument ($n = 2$ [28.5%]), the size of the instrument ($n = 1$ [14.3%]), and articular pains due to arthrosis ($n = 3$ [42.9%]). Almost all of the patients found the test not restrictive and estimated that their care quality was not altered ($n = 167$ [97.7%]).

TABLE 1. Baseline Characteristics (n = 201)

Characteristic	Value
Age, mean \pm SD, y	65.5 \pm 10.8
Sex, No. (%)	
Male	117 (58.2)
Female	84 (41.8)
Laterality, No. (%)	
Right-hander	186 (92.5)
Left-hander	15 (7.5)
Past medical history, No. (%)	
Neuropathy before chemotherapy	6 (3)
Neuropathy due to anterior chemotherapy	67 (33.3)
High blood pressure	73 (36.3)
Myocardial infarction	13 (6.5)
Stroke	4 (2)
Chronic obstructive pulmonary disease	3 (1.5)
Body mass index, mean \pm SD, kg/m ²	25.0 \pm 5.1
Previous oncologic surgery, No. (%)	128 (63.7)
mGPS, No. (%)	
0	99 (55.0)
1	68 (37.8)
2	13 (7.2)
G8 score, mean \pm SD	12.4 \pm 2.1
Primary tumor, No. (%)	
Colon and rectum	103 (51.2)
Esophagus	8 (4.0)
Stomach	22 (10.9)
Cholangiocarcinoma	11 (5.5)
Pancreas	44 (21.9)
Small intestine	3 (1.5)
Neuroendocrine tumor	8 (4.0)
Adenocarcinoma, unknown primitive tumor	2 (1.0)
Stage, No. (%)	
Local	40 (19.9)
Locally advanced	23 (11.4)
Metastatic	138 (68.7)
Type of treatment, No. (%)	
Chemotherapy	147 (73.1)
Biotherapy	4 (2.0)
Chemotherapy and biotherapy	50 (24.9)

Abbreviations: mGPS, modified Glasgow Prognostic Score; SD, standard deviation.

For mGPS, 180/201 patients were evaluated because 21 patients had no CRP and/or albuminemia at baseline.

During the study, 14 members of the medical team performed the test (Table 3): 5 medical residents, 1 MD/PhD, and 8 medical students. Only 1 (7.1%) had used it in a nutrition department before the beginning of the study, and Yes 3 (23.1%) and No 10 (76.9%) had heard about it. None of them found the test difficult to perform or restrictive. It did not disturb their daily medical practice or the quality of their provided care. All of them considered this test useful enough to perform routinely for patients with digestive cancer.

Economic Evaluation

Two hydraulic dynamometers were bought for approximately €200 each; this corresponded to €1.99 per patient (€400/201 patients) and €0.23 per measurement (€400/1704 measurements). Six weighing scales were used

TABLE 2. Patient Questionnaire

Question	Answer	No. (%)
Have you ever performed this test?	Yes	11 (6.4)
	No	160 (93.6)
	If yes, with	
	A nutritionist	4 (36.4)
	An endocrinologist	0
Did you find this test difficult to perform?	Your general practitioner	0
	Other	7 (63.6)
	Yes	7 (4.1)
	No	164 (95.9)
	If yes, could you explain why?	
Did you find this test restrictive to perform at the hospital?	The dynamometer was too heavy.	2 (28.5)
	The dynamometer was difficult to handle.	4 (57.1)
	Other	4 (57.1)
	Yes	2 (1.2)
After being informed about the purpose of this test, did you pay attention to the result?	No	167 (98.8)
	Yes	117 (69.2)
Did you feel that performing this test interfered with the usual medical care?	No	52 (30.8)
	Yes	2 (1.2)
	No	167 97.7

For the last 3 questions, 2 patients did to answer.

during the study. Each one cost approximately €50. Both C-reactive protein and serum albumin sampling cost €16 per sample, which corresponded to €27,264 for 1704 hospitalizations. Therefore, the HGS evaluation was almost the same price as the price of weighing patients and was far less expensive than the mGPS evaluation.

DISCUSSION

To our knowledge, this study is the first to show that HGS testing with a Jamar dynamometer is routinely feasible for oncology patients in an ambulatory unit.

We obtained a large number of measurements in a short period of time without interfering with medical care. Some patients had difficulties, which may have led to underestimations of their muscle strength. The first was articular pains due to arthrosis. This should be systematically considered before the test is performed. Another issue raised by 1 patient was the size of the dynamometer in comparison with her hand size. Position 2 was chosen on the handle of the dynamometer and is considered to be the most reliable of the 5 positions.²² In the future, more attention should be paid, and position 1 should be preferred for people with small hands, as already suggested in a previous study.²²

Few patients knew the HGS test before the study, and except for 1 patient who did not want to participate, the test piqued their interest and held their attention. A high degree of compliance and observance was observed during the entire period of the study. Other studies using the HGS test have mainly been vertical studies and have tended to collect only 1 to 2 measures per patient.^{16,18,23-}

²⁵ In our study, patients had to do it every week or every 2 weeks, and despite this high frequency, 98.8% did not find the test restrictive.

What was most surprising was the lack of knowledge about sarcopenia, dynapenia, and HGS testing among the medical staff. Only 1 medical student had used the Jamar dynamometer in a previous study. This observation highlights the fact that improvements could be made to our teaching in the area of malnutrition, especially because all participants showed a real interest and found this test useful enough to perform routinely in our population.

Another interesting aspect is the economic aspect because measuring HGS is affordable in comparison with an mGPS evaluation and costs almost the same as weighing patients. Hydraulic dynamometers are robust and can be used for several years if the manufacturer's recommendations are respected (the calibration of every new machine and annual or more frequent calibrations if the instrument is used on a daily basis).

Although this test was designed to be used in a daily medical and paramedical practice, nurses did not feel able to perform it on patients. The main reason invoked was a lack of time. The time needed to perform the HGS test was not evaluated with a chronometer but was estimated to be 2 minutes the first time (because of information given to the patient) and less than 1 minute 20 seconds the other time. This low involvement constituted a major bias in our study. Further training of the paramedical team seems fundamental to make them aware of the importance of this issue and to familiarize the team with the test.

TABLE 3. Medical Member Questionnaire

Question	Answer	No. (%)
Are you	A man?	8 (57.1)
	A woman?	6 (42.9)
How old are you?	Younger than 35 y	13 (92.9)
	Between 35 and 55 y	0
	Older than 55 y	1 (7.1)
You are a	PhD	1 (7.1)
	Medicine resident	5 (35.7)
	Medical student	8 (57.2)
	Nurse	0
Have you ever performed this test?	Yes	1 (7.1)
	No	13 (92.9)
	If no, have you ever heard about this test?	
	Yes	3 (23.1)
	No	10 (76.9)
Did you find this test difficult to perform?	Yes	0
	No	14 (100)
	If yes, could you explain why?	0 (0)
	The dynamometer was too heavy.	0 (0)
	The dynamometer was difficult to handle.	0 (0)
	The way the test works was difficult to explain to the patient.	0 (0)
	Other	0 (0)
Did you find this test restrictive to perform at the hospital?	Yes	0
	No	14 (100)
Did you find that performing this test disturbed your daily practice?	Yes	0
	No	14 (100)
Did you feel that performing this test interfered with your usual medical care?	Yes	0
	No	14 (100)
Did you meet difficulties during the study process? ^a	Yes	1 (7.1)
	No	13 (92.9)
Do you think that we should use this test routinely in oncology?	Yes	14 (100)
	No	0

^aA lack of time, difficulty with comprehending the dynamometer handle, and so forth.

Another limit was the fact that, mainly because of deaths before the third month of follow-up, questionnaires were not completed by all patients.

These results suggest that we can evaluate the strength of patients at each of their appointments or every time they are hospitalized in the same way that we weigh them. It can be done, especially because the Jamar dynamometer is an inexpensive, portable, and easy-to-use tool.

Nevertheless, several aspects of using the Jamar dynamometer may require further investigation. First, although more and more studies are attempting to determine cut points for weak grip strength with respect to age, sex, and ethnic group,^{8,17,20,25-29} the HGS dynamometer thresholds remain undetermined for patients with cancer. Second, we may need more standardization for the realization of the test: the number of attempts needed,³⁰ the hand chosen (the dominant hand vs the nondominant hand), and the value chosen (the best or mean of several values).²² Third, the consensual definition of sarcopenia includes low muscle mass, which suggests a computed tomography scan. However, a computed tomography scan is expensive, invasive, and difficult to perform, especially if a whole population

requires screening. If muscle strength declines before muscle mass loss and weight loss, as suggested by Norman et al,¹⁴ sarcopenia might be detected if we look for dynapenia first. Malnutrition could, therefore, be treated earlier, and its consequences could be limited. Further research will be necessary to clarify this. Finally, the correlations between dynapenia, chemotherapy toxicities, and other prognostic markers in malnutrition, such as the mGPS, body mass index, and performance status, are interesting and are being currently studied.

In conclusion, measuring grip strength with the HGS test is generally accepted, inexpensive, and feasible in routine practice. The measurement of grip strength with the HGS test presents minimal interference for both patients with digestive cancer treated by ambulatory chemotherapy and the medical professionals providing treatment. This study suggests that this test could be a part of our daily practice without affecting the quality of care or reducing medical care efficiencies. Further investigation is required to standardize the measurement for patients with cancer. Correlations between dynapenia and the performance status, nutritional data, and chemotherapy toxicities are being evaluated.

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CONFLICT OF INTEREST DISCLOSURES

Camille Mazza reports personal fees from Pierre Fabre outside the submitted work. Damien Botsen reports personal fees from Pierre Fabre and nonfinancial support from GlaxoSmithKline, Chugai, and Amgen outside the submitted work. Mathilde Brasseur reports personal fees from Bayer and nonfinancial support from Pierre Fabre, Novartis, Amgen, Roche, and AbbVie outside the submitted work. Olivier Bouché reports grants and personal fees from Roche and Pierre Fabre and personal fees from Amgen, Bayer, Lilly, Merck, and Novartis outside the submitted work.

AUTHOR CONTRIBUTIONS

Marie-Amélie Ordan: Conceptualization, methodology, validation, and writing—original draft. **Camille Mazza:** Conceptualization, investigation, validation, and writing—review and editing. **Coralie Barbe:** Data curation, formal analysis, methodology, software, supervision, validation, and writing—review and editing. **Marine Perrier:** Conceptualization, investigation, validation, and writing—review and editing. **Damien Botsen:** Conceptualization, investigation, validation, and writing—review and editing. **Yohann Renard:** Conceptualization, investigation, validation, and writing—review and editing. **Johanna Moreau:** Conceptualization, investigation, validation, and writing—review and editing. **Mathilde Brasseur:** Conceptualization, supervision, validation, and writing—review and editing. **Barbara Taillière:** Conceptualization, investigation, validation, and writing—review and editing. **Éric Bertin:** Conceptualization, supervision, validation, and writing—review and editing. **Olivier Bouché:** Conceptualization, investigation, methodology, supervision, validation, and writing—review and editing.

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