








# A HOME-BASED PREHABILITATION PROGRAM, DELIVERED THROUGH AN INTERNET-BASED PLATFORM, IN PATIENTS WITH LOCALLY ADVANCED GASTROESOPHAGEAL JUNCTION AND STOMACH ADENOCARCINOMA, UNDERGOING PERIOPERATIVE CHEMOTHERAPY: PROTOCOL FOR A FEASIBILITY AND ACCEPTABILITY STUDY

UM PROGRAMA DE PRÉ-HABILITAÇÃO DOMICILIAR, APLICADO ATRAVÉS DE UMA PLATAFORMA BASEADA NA INTERNET, EM DOENTES COM ADENOCARCINOMA LOCALMENTE AVANÇADO DA JUNÇÃO GASTROESOFÁGICA E ESTÔMAGO, ELEGÍVEIS PARA QUIMIOTERAPIA PERIOPERATÓRIA: PROTOCOLO PARA ESTUDO DE VIABILIDADE E DE ACEITABILIDADE

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## ABSTRACT

**Introduction:** Prehabilitation is a multimodal strategy implemented in the preoperative period, aiming to increase preoperative functional reserve, leading to better postoperative functional recovery and reduced incidence of complications. The majority of the prehabilitation programs are developed under supervision in an outpatient clinic, which might be an obstacle for those patients with geographical and/or travelling constraints. Home-based programs, with the support of telehealth resources, could be a convenient way to surpass these barriers. **Methods:** Patients with locally advanced, potentially resectable gastric or GEJ adenocarcinoma, undergoing perioperative chemotherapy with FLOT regimen will be recruited at IPO-Porto and Hospital Garcia de Orta. Patient will be invited to undergo a prehabilitation program (PREHAB) in addition to their usual (medical optimization, nutritional and psychological care). Exercise intervention will comprise aerobic and resistance training. An internet-based platform (iTherapy) via computer or mobile devices, will be used to deliver and monitor the intervention. The primary outcome of this study is to



test the acceptability, feasibility and safety of the intervention. As secondary outcomes, we intend to assess the impact of home-based prehabilitation on functional capacity, frailty status, quality of life, disability, postoperative complications and mortality, length of hospital stay, need of ICU, hospital readmission and place of discharge. **Conclusion:** This study will inform for a future randomized clinical trial to assess the role of prehabilitation to reduce postoperative morbidity and mortality in this population.

**Keywords:** Home-based prehabilitation; telehealth; cancer; surgery.

## RESUMO

**Introdução:** A pré-habilitação corresponde a uma intervenção multimodal, implementada no período pré-operatório, com o objetivo de aumentar a reserva funcional pré-operatória, acelerar a recuperação funcional pós-operatória e reduzir da incidência de complicações. A maioria dos programas de pré-habilitação é desenvolvida sob supervisão médica em ambulatório, o que pode ser um obstáculo para aqueles doentes com restrições geográficas e / ou de transporte. Programas domiciliares, com o apoio a recursos de telemedicina, poderão ser uma estratégia conveniente de superar essas barreiras. **Métodos:** Doentes com adenocarcinoma gástrico ou junção gastroesofágica localmente avançado, potencialmente ressecável, em quimioterapia perioperatória com regime FLOT serão recrutados no IPO-Porto e no Hospital Garcia de Orta. Os participantes serão convidados a realizar um programa de pré-habilitação com exercício físico (PREHAB) complementar aos cuidados habituais (otimização médica, atendimento nutricional e psicológico). A intervenção com exercício físico incluirá treino combinado (exercício aeróbio e resistido) e treino dos músculos inspiratórios. Uma plataforma digital (iTherapy), acessível via computador ou dispositivos móveis, será utilizada para implementar e monitorizar a intervenção. O objetivo principal deste estudo é testar a aceitabilidade, viabilidade e segurança da intervenção. Como objetivos secundários, pretendemos avaliar o impacto da pré-habilitação domiciliar na capacidade funcional, estado de fragilidade, qualidade de vida, incapacidade, complicações pós-operatórias e mortalidade, tempo de hospitalização, necessidade de UCI, readmissão hospitalar e local de alta. **Conclusão:** Este estudo servirá de base para um futuro ensaio clínico randomizado para avaliar o papel da pré-habilitação na redução da morbimortalidade pós-operatória nesta população.

**Palavras-chave:** pré-habilitação domiciliar; telemedicina; cancro; cirurgia.

## INTRODUCTION

Adenocarcinoma of the gastroesophageal junction (GEJ) and stomach are among the most common malignancies and causes of cancer death worldwide, including Portugal which has one of the highest incidence rates in Europe, predominantly occurring in patients > 65 years of age<sup>1</sup>. In patients with locally advanced disease, perioperative chemotherapy (PCT) is considered standard of care, as different clinical trials demonstrated its superiority in improving survival, when compared to surgery alone<sup>2</sup>. However, this multimodal therapy is not free of adverse effects. PCT promotes significant deconditioning and physiological deterioration<sup>2</sup>, impacting the patient's tolerance to surgery, which puts them at higher risk for

postoperative morbidity and mortality<sup>3</sup>. Even with the most recent PCT regimes, around 50-60% of patients develop postoperative complications<sup>2</sup>, with pulmonary complications on the top of the list. Postoperative complications can impose a significant burden by increasing morbidity and mortality, in-hospital length of stay, utilization of critical care and need for a greater level of care at discharge<sup>4,5</sup>. Moreover, postoperative complications may prevent or cause delays in the administration of adjuvant chemotherapy, which is associated to worse disease-free and overall survival<sup>6</sup>. Given the growing incidence of proximal gastric cancer and GEJ tumors and because these patients often present with age-related functional decline, comorbidities and geriatric syndromes (e.g. frailty), these patients are at greater risk for adverse postoperative



outcomes<sup>7</sup>. Presumed fear of greater postoperative morbidity and mortality often results in sub-optimal delivery of cancer surgery, which is the most efficient curative approach for solid tumors. Thus, it is mandatory to invest on strategies capable to minimize the negative effects of PCT and surgery by booting the patient's physiological reserve.

Interventions to improve postoperative outcomes have usually been intra- and postoperative, which might be too late for these high-risk patients. The preoperative period is now regarded as an excellent window of opportunity to optimize patients by intervening with factors known to contribute to postoperative outcomes. The process of enhancing the functional capacity in order to cope with an incoming stressor and optimize recovery has been termed prehabilitation<sup>8</sup>. Growing body of evidence supports the role of prehabilitation to improve postoperative outcomes such as physical fitness, quality of life, incidence of postoperative complications and length of hospital stay in cancer patients submitted to major surgery<sup>9-11</sup>. However, existing studies show a clear bias towards certain types of cancers (esophageal, colorectal, lung) and are underpowered to address major outcomes like postoperative complications. Moreover, the effectiveness of prehabilitation in high-risk patients for postoperative complications remains poorly addressed and these are the patients who are in greater need of better care. In addition, the majority of the prehabilitation programs are developed under supervision in an outpatient clinic, which might be an obstacle for those patients with geographical and/or travelling constrains<sup>12</sup>. Community-based programs, with the support of telehealth resources, were already shown to be a convenient way to surpass these barriers and provide safe and effective cardiac rehabilitation care<sup>13</sup>. Using this approach to deliver prehabilitation could be very useful to prepare cancer patients at higher risk for postoperative burden.

## 1.1. Objectives

The primary outcome of this study is to test the acceptability, feasibility and safety of a home-based prehabilitation program, delivered through an internet-based platform, in patients with locally advanced gastric or esophageal adenocarcinoma, undergoing perioperative chemotherapy with FLOT regimen.

As secondary outcomes, we intend to assess the impact of home-based prehabilitation on functional capacity, frailty status, quality of life, disability, postoperative complications and mortality, length of hospital stay, need of ICU, hospital readmission and place for discharge. This study will inform about a future multi-centre randomized clinical trial to reduce post-operative morbidity and mortality in this population.

## 1.2. Study design

This protocol is reported according to the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)<sup>14</sup>. We will conduct a prospective, single-group, pilot study investigating the feasibility and acceptability of a home-based prehabilitation program delivered through an internet-based platform. Patient recruitment is programmed to start in March 2021 until December 2021.

## 2. METHODS

### 2.1. Study setting and design

The study will be conducted in two Portuguese tertiary centres (Instituto Português de Oncologia do Porto Francisco Gentil, E.P.E, Porto (IPO-Porto) and Hospital Garcia de Orta, Lisbon (HGO-Lisbon)). All the assessments will take place in the aforementioned hospitals and the intervention will be home-based. An overview of the study design is shown in a schematic diagram (Figure 1).



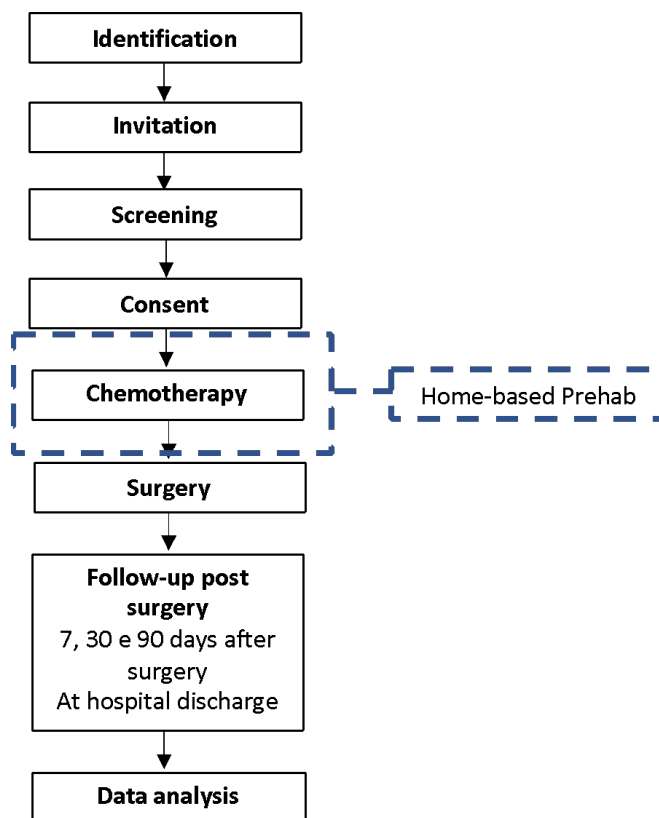


FIGURE 1 – Consort diagram of the study

## 2.2. Recruitment

Potential participants will be identified at the first hospital consultation or at the multi-disciplinary oncology meeting, where the management plan of the patient is decided. All consecutive patients with locally advanced, potentially resectable adenocarcinoma of the stomach or GEJ junction undergoing perioperative chemotherapy with FLOT regimen will be signaled. In the first clinic visit to discuss the therapeutic plan, a surgeon or medical oncologist, or anesthesiologist will ask the patient to consider participating in the study. Patients will receive a handout detailing the rationale of the study, what participation will implicate obligations and possible risks. After 24 hours, a team member will contact patients by phone to clarify any issue related to the study and to schedule the first research visit to complete the enrolment for those willing to voluntarily participate.

During the first research visit, participants will be screened for eligibility and sign the consent form. Only consenting patients will proceed to further evaluations. Participants will also be informed that they may discontinue and/or withdrawal the study at any time without compromising its standard care. The investigator or the medical team may discontinue a participant from the study due to the following reasons, but not limited to: i) withdrawal of consent; ii) not compliant with study arm and/or procedures; iii) development of a new medical illness limiting the participation in physical exercise; v) adverse events considered incompatible with the safe continuation in the study; vi) the investigator and/or the medical team decide it is for the best interest of the patient. The reasons for the participant's withdrawal and/or discontinuation from the study will be recorded.

## 2.3. Eligibility criteria

We will include consecutive patients with locally advanced, potentially resectable adenocarcinoma of the stomach or GEJ junction undergoing perioperative chemotherapy with FLOT regimen that fulfill the following criteria: i) >18 years old ii) with no contraindications for physical exercise<sup>15</sup>; iii) returning signed informed consent; iv) accepting to comply with the study procedures.

Patient treated for another cancer within 5 years (except basal cell skin carcinoma or carcinoma in situ of the cervix), with legal incapacity (person deprived of liberty or under guardianship), cognitive or severe psychiatric disorders, breastfeeding, pregnancy (or planning to become pregnant) will be excluded.

## 2.4. Intervention

We will use multimodal prehabilitation, which means combining exercise interventions with



nutritional and psychological care, on top of medical optimization. Since medical optimization, nutritional and psychological care are already part of usual care, a structured exercise program will be added. A clinical nutritionist evaluates the need of nutritional care through the Patient Generated Subjective Global Assessment (PG-SGA), where a score  $\geq 9$  indicates a critical need for nutrition intervention<sup>16</sup>. An individualized plan is then offered to the patients, which may include suggestions of meals and a list of foods to avoid/to favor, to help to obtain the recommended amount of protein intake (1.2-1.5 g/kg/d)<sup>17</sup>. A clinical psychologist evaluates the need of psychological care with the NCCN Distress Thermometer and Problem List (DTPL) (Version 2.2020). Patients indicate their level of distress over the course of the week prior to assessment. In those patients reporting high levels of distress (score  $>4$ ), the accompanying 40-item problem list, detailing common problems related to the cancer experience, will be reviewed and a personalized intervention is developed. This may include training on strategies to cope with stress and anxiety, relaxation exercises and good sleep hygiene, as needed.

In addition to usual care, patients will be asked to perform a specific exercise training program to be performed at home. The intervention will start as soon as possible after treatment decision and will be maintained until hospital admission for surgical resection. The exercise training program will consist of combined exercise training (aerobic exercise plus resistance exercise) and inspiratory muscle exercises, which was shown to be safe and effective to improve functional capacity in patients during chemotherapy<sup>11</sup>. Baseline fitness assessment will inform about the participant's fitness level and assist the tailoring of the exercise program, objectives and progression. Participants will be invited to perform, as tolerated, 3 sessions per week of combined exercise. For aerobic exercise (AEx), participants may opt for walking, jogging or cycling. After warming up for 5 minutes at their perceived

exercise intensity of "light" (9-11 Borg' scale), patients will be asked to engage on 30 min of Aex at "moderate" intensity (12-13 Borg' scale). Intensity and/or duration level will be adjusted through the intervention, if necessary. After Aex, the participant will be asked to start 1 set of 8 to 15 repetitions of the following exercises: i) chair squats (modified to the individual's level of function as squats); ii) wall press iii) seated row with resistance bands; iv) chair dips; v) bicep curls with resistance bands; vi) abdominal crunches (modified to be performed seated in a chair). When a participant completes the 15 repetitions before the point of muscle fatigue, the progressive addition of sets of exercises will be asked, as tolerated. This will take 10-15 minutes. At the end of each exercise session, participants will be asked to perform some stretch exercises. Patients will be recommended to walk in the remaining days (except on days of prescribed training sessions), for  $\geq 30$  minutes/day at moderate intensity. If the participant has a poor baseline conditioning, the day after their exercise session will be used to rest and allow recovery. As their fitness improves, rest days will be replaced by walking.

In order to deliver and monitor our home-based prehabilitation, participants will be assigned with individual credentials to access an internet-based platform (iTherapy) via computer or mobile devices. iTherapy is a responsive and customizable platform, with an embedded data collection system (e.g. Participants reported outcomes, questionnaires, etc.), that allows delivery of different treatment modalities (text, graphical content and video) and access to an end-to-end encrypted internal communication system (e-mail, chat and videoconference)<sup>18</sup>. This platform is currently being used by our team members to deliver a psychosocial intervention targeting breast cancer survivors<sup>19</sup>. iTherapy features will be used throughout the intervention to: i) deliver the tailored prehabilitation intervention (information about exercise prescription, instructions and videos exemplifying the exercises and with verbal



explanations of most important aspects to consider); ii) facilitate bi-directional communication in case of need; iii) measure the compliance and adherence to the program; iv) obtain information about the weekly progress and adjust the intervention; v) assess/report the occurrence of any adverse events; vi) clarify any issue and reinforce the importance of maintaining the prescribed program.

## **2.5. Assessments**

### **2.5.1. Demographic and clinical data**

Baseline demographic, clinical characteristics and physical activity levels of consented patients will be captured at the moment of their initial assessment during the first research visit. Clinical files might also be used in order to complete and/or confirm the patient's profile. The following information will be recorded: age, gender, marital status anthropometry, risk factors, chronic drug therapy, type and complexity of surgery, surgical risk with common tools (e.g. ASA score, ECOG, P-POSSUM, Charlson Comorbidity Index) and with the MyIPOscore<sup>20</sup>. MyIPOscore is a tool developed by us and is currently being prospectively validated at our institution. This stratification will not affect clinical decision but will be used for the purpose of sub-analysis to compare outcomes between high and low-risk patients. Clinical files might also be used in order to complete and/or confirm the patient's profile.

### **2.5.2. Outcome measurements**

Table 1 provides a timeline of assessments of the outcome measures.

#### **2.5.2.1. Primary outcomes**

##### **2.5.2.1.1. Feasibility**

The feasibility of the intervention will be measured by: i) assessing the willingness of clinicians to

recruit participants, ii) recruitment rate (number of patients recruited per month), iii) eligibility rate (number of patients fulfilling inclusion criteria per month), iv) retention (participants retained and assessed in the follow-up period), v) adherence rate to the prehabilitation program (the degree to which patients correctly follow prescription instructions) and vi) the generalizability of study participants (comparing their demographic and clinical features with all other patients submitted to surgery). Data will be collected during the entire period of the study.

##### **2.5.2.1.2. Acceptability**

Acceptability of the intervention will be measured by assessing the number of patients declining to participate in the study. Reasons for non-participation will be recorded.

##### **2.5.2.1.3. Safety**

The safety profile of the intervention will be assessed by measuring the number and severity of adverse events occurring during the exercise training sessions. The reporting period will be during the prehabilitation program. In the unlikely possibility of occurring, adverse events may be spontaneously reported by the participants or recorded by the team members during the weekly follow-up.

#### **2.5.2.2. Secondary outcomes**

##### **2.5.2.2.1. Physical and functional assessments**

These assessments will be made at 4 time-points: i) before starting chemotherapy (define baseline level), ii) after chemotherapy and iii) before surgery (comparison with baseline levels and test if the program mitigates functional decline), and iv) time



TABLE 1: Timeline of assessments

Assesement	Assessment measure	Baseline	Prehabilitation		Before surgery	After surgery			
			During Chemotherapy	After Chemotherapy		7 days	30 days	90 days	Discharge
<b>Demographic and clinical data</b>	With patient and clinical records	x			x				
<b>Primary outcomes</b>									
Feasibility	Willingness of clinicians to recruit participants	x							
	Willingness of patients to be randomized	x							
	Recruitment rate	x							
	Eligibility rate	x							
	Adherence rate		x	x					
Acceptability	Number of patients declining to participate	x							
Safety	Number and severity of adverse events		x	x					
<b>Secondary outcomes</b>									
Morphometry	Weight	x		x	x				x
	Height	x		x	x				x
	BMI	x		x	x				x
Body composition	Bioimpedance	x		x	x				x
Nutritional status	PG-SGA	x		x	x				x
Psychological assessment	NCCN Distress Thermometer and Problem List	x		x	x				x
Physical activity levels	Accelerometer	x		x	x				x
Physical fitness	6MWD	x		x	x				x
	30-second chair stand	x		x	x				x
	30-s arm curl	x		x	x				x
	Chair sit-and-reach	x		x	x				x
Frailty status	Fried's frailty phenotype	x		x	x				x
HRQoL	EORTC QLQ-C30, version 3	x		x	x				x
Disability	WHO Disability Assessment Schedule V.2.0	x		x	x				x
Morbidity	Postoperative Morbidity Survey					x	x	x	
	Clavien-Dindo					x	x	x	
	Comprehensive Complication Index					x	x	x	
Mortality	Death from any cause					x	x	x	
Health-care resources	In-hospital length of stay								X
	Need of intensive care					X	X	X	
	Readmissions					X	X	X	
	Place for discharge								X



of discharge (compare with previous levels and correlate with clinical outcome measures). It will include measuring morphometry (weight, height and BMI), body composition (bioimpedance), physical activity levels, physical fitness and frailty status. The Senior Fitness Test measures basic mobility-related parameters: aerobic endurance (6 min walking distance test, 6MWD), lower and upper body strength (30-second chair stand and 30-s arm curl, respectively), lower and upper body flexibility (chair sit-and-reach and back scratch, respectively), and agility/dynamic balance (8-foot up-and-go). This is a valid instrument that provides fitness standards (performance cut points) to identify individuals at greater risk of premature loss of mobility and independence<sup>21,22</sup>. Moreover, the performance at the 6MWD was previously shown to be independently predictive of post-operative complications and recovery in cancer patients<sup>23-25</sup>. Regarding frailty status, in the absence of a well-accepted gold standard tool to assess frailty, we will use the phenotype model proposed by Fried<sup>26</sup>. Fried's frailty phenotype considers the analysis of five physical health items: unintentional weight loss; exhaustion; low energy expenditure (or inactivity status); slowness; and weakness. Deterioration of each of these domains is scored as 1 if present or 0 if absent, giving a potential score spanning from 0 to 5. Ultimately, three phenotypical categories will be obtained: fit (no deterioration); pre-frail (one or two items); or frail (three or more items). Multiple epidemiological studies have found that frailty diagnosis with this tool was predictive of postoperative complications and mortality in older surgical patients<sup>27,28</sup>.

#### **2.5.2.2.2. Patient-reported outcomes**

Patient-reported outcomes will be measured in the same 4 time-points previously defined for functional capacity. Health-related quality of life will be assessed by European Organization for

Research and Treatment of Cancer Quality of Life Questionnaire Core-30 (EORTC QLQ-C30, version 3). The EORTC QLQ-C30 is a reliable and valid measure of the perceived health-related quality of life of patients diagnosed with cancer in multicultural clinical research setting<sup>29</sup>. Patient-reported disability will be measured using WHO Disability Assessment Schedule V.2.0, which is a questionnaire that assesses activity limitations and participation restrictions (ie. disability) in the prior month [30]. It covers 6 domains of functioning, including 1) understanding and communication; 2) self-care; 3) mobility (getting around); 4) interpersonal relationships (getting along with others); 5) work and household roles (life activities); and 6) community and civic roles (participation). This tool was validated in a variety of disease states, including surgery<sup>31</sup>, and was found to be as responsive to change as disorder-specific functional measures<sup>32</sup>.

#### **2.5.2.2.3. Postoperative burden**

These outcomes will be measured at 7, 30 and 90 days postsurgery. Data will be collected by an outcome assessor blinded to the intervention and with no role in any other part of the study or in the patient's clinical care pathway. Data will be retrieved from the hospital clinical information system as well as from the patient's files, clinical notes and caregivers. If needed, the discharged patient will be contacted by telephone and interviewed around day 90 after surgery. The Postoperative Morbidity Survey (POMS) will be used to describe postoperative morbidity<sup>33</sup>. The POMS contain 18 items that address nine domains of postoperative morbidity (pulmonary, infectious, renal gastrointestinal, cardiovascular, neurological, hematological, wound and pain). For each domain, either presence or absence of morbidity is recorded on the basis of objective criteria. The severity of the complications will be graded by using the Clavien-Dindo classification system<sup>34</sup> and the Comprehensive





Complication Index [35]. The outcome assessor will record the number of events per participants as well as the number of participants with a complication. Death from any cause will be recorded until day 90 after surgery. Health-care resource utilization will be assessed by measuring in-hospital length of stay (number of days in hospital after the surgery, with the day of surgery counting as day 0), need of intensive care (number of days in intensive care unit), readmissions (number of hospital admittance after discharge, with the day of discharge counting as 0) and place for discharge after leaving the hospital (institution versus home).

## 2.6. Data collection, management and monitoring

Patients will be informed and explicitly authorize the collection, storage and use of data for the research purpose in the signed consent form.

Data will be collected from clinical records and database systems at the hospital or assessed with the patients (e.g. questionnaires and physical fitness). All documents will be stored securely in confidential conditions where only the principal investigator has key access. In all other project-specific documents (including any database), other than the signed consent, the participant will be referred by the study participant number and subject number (if applicable), not the name. A cloud-based platform (Azure) will be designed and open to all project members, to centralize data into a repository. Security and privacy will be granted according to The European Union General Data Protection Regulation (approved by the European Parliament in 14/4/2016; Enforcement date: 25/5/2018).

## 2.7. Ethics and dissemination

The project will be conducted in accordance with Declaration of Helsinki and National Legislation.

Team members are committed to work according to the Good Clinical Practices, in agreement with the Declaration of Helsinki and respecting patients' confidentiality. The local Ethical Authorities already approved the study protocol and informed consent (CES IPO: 145A/020).

Adverse events caused by prehabilitation exercises are rare and of minor impact [11]. We will minimize this by screening the patients for the presence of absolute and relative contraindications to exercise<sup>15</sup> and by following the exercise guidelines for cancer patients<sup>36</sup>. Participants will be submitted to the standard procedures related to their treatment plan, decided at the multi-disciplinary oncology meeting, as usual. Thus, participants in the study will have the risks associated with the procedures they are normally submitted (e.g. collection of blood and urine samples, imaging for disease staging, adverse effects of chemotherapy and surgery), which excludes the need for additional study insurances.

Research findings will be disseminated through peer reviewed journals with impact to the scientific community, and public presentations (to clinicians, to academic audiences, and in national and international meetings). Data produced will be made available to the scientific community and to the society according to the ethical and social rules of involved institutions and government. The rules on open access publications (Green or Gold) will be complied. All academic publications (e.g. final articles or manuscripts accepted for publication, thesis) will be deposited into the institutional repository of the involved research institutions respecting the embargo period.

## 2.8. Statistics

No sample size calculation was pre-established as we are primarily interested in precise estimates of feasibility and acceptability, as well as outcome variability that will aid in the planning of a larger, sufficiently powered efficacy trial to compare the



effectiveness of prehabilitation to reduce post-operative morbidity and mortality. This exploratory pilot study will enable us to collect the preliminary data we require to perform an accurate sample size calculation for the full study.

Analysis will be conducted with SPSS, version 28 (IBM Corp., USA). Normality of data will be determined by using the Shapiro-Wilk test. Baseline features will be described as mean±SD or median (interquartile range) for continuous data and as frequency and percentage for categorical data. Comparison between pre and post intervention data will be analyzed using Student's t test or Mann-Whitney's test for continuous data. A two-sided p value <0.05 will be considered to indicate statistical significance.

### 3. DISCUSSION







This study is investigating whether a home-based prehabilitation program, delivered through

an internet-based platform, can be implemented in order to prepare patients for surgery. The results will inform about a future multi-centre randomized clinical trial to reduce post-operative morbidity and mortality in patients with locally advanced gastric or esophageal adenocarcinoma, undergoing perioperative chemotherapy with FLOT regimen. This could have a major impact by allowing to offer prehabilitation to a greater number of patients who, due to geographical and/or travelling constraints, would not benefit from this intervention.

#### Financial support

CIAFEL is funded by the European Regional Development Fund (ERDF) through the Operational Programme for Competitiveness and Internationalization (COMPETE) and by Fundação para a Ciência e a Tecnologia (FCT) grant (UIDB/00617/2020). This work was supported by FCT (grant PTDC/SAU-DES/7945/2020).

#### Supplementary Material (Videos)

- |                         |   |
|-------------------------|---|
| 1) Lower limb exercises |  <a href="https://youtu.be/mmOfYqTne30">https://youtu.be/mmOfYqTne30</a> |
| 2) Chest exercises      |  <a href="https://youtu.be/_RunaMsS7go">https://youtu.be/_RunaMsS7go</a> |
| 3) Back exercises       |  <a href="https://youtu.be/mhxXjBG_0_M">https://youtu.be/mhxXjBG_0_M</a> |
| 4) Triceps exercises    |  <a href="https://youtu.be/ruSNowHlptc">https://youtu.be/ruSNowHlptc</a> |
| 5) Biceps exercises     |  <a href="https://youtu.be/tGeIQ045Ce4">https://youtu.be/tGeIQ045Ce4</a> |
| 6) Abdominal exercises  |  <a href="https://youtu.be/McPRkaTiUvs">https://youtu.be/McPRkaTiUvs</a> |

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**Data de recepção do artigo:**

24/02/2021

**Data de aceitação do artigo:**

20/04/2021

