

Study Protocol

Title: From Prehabilitation to Rehabilitation: A Feasibility Trial for Digitally Supported Prehabilitation in Major Visceral Oncologic Surgery

Short title: Prehab2Rehab-OncoVis

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Abstract

Introduction: Major visceral oncologic surgery is associated with high morbidity and mortality, often aggravated by pre-existing comorbidities, reduced functional capacity, malnutrition, and sarcopenia. Postoperative complications and delayed recovery contribute to prolonged hospitalization, increased healthcare costs, and may compromise the initiation of adjuvant oncologic therapies. Prehabilitation has been shown to optimize physical, nutritional, and psychological status before surgery to support postoperative recovery and rehabilitation. However, its implementation in routine perioperative care in Austria is currently lacking, and the feasibility of a digitally supported prehabilitation-to-rehabilitation pathway for patients undergoing major visceral surgery remains insufficiently evaluated. **Objectives:** The primary objective of the Prehab2Rehab-OncoVis trial is to evaluate the feasibility of implementing a multimodal prehabilitation intervention, including a digital support system for patients scheduled to undergo major visceral oncologic surgery. In addition, historical clinical and rehabilitation cohorts will be used to contextualize surgical and rehabilitation outcomes. **Methods:** Prehab2Rehab-OncoVis will be conducted at the University Hospital Salzburg and the University Institute of Sports Medicine, Prevention and Rehabilitation, coordinated by the Paracelsus Medical University and implemented in cooperation with the Ludwig Boltzmann Institutes for Rehabilitation Research and for Digital Health and Prevention within the Prehab2Rehab consortium. The rehabilitation center St. Veit serves as a secondary study center. A prospective, non-randomized feasibility cohort study will enroll a consecutive convenience sample of 30 adult patients (up to 50 if feasible). Feasibility outcomes will be evaluated within the prospective cohort. Two historical comparator groups will be used to contextualize outcomes: a local hospital cohort of patients who previously underwent similar surgery without prehabilitation, to contextualize in-hospital outcomes at discharge, and a national rehabilitation cohort derived from routine rehabilitation datasets, matched for diagnosis, sex, and age, to contextualize rehabilitation outcomes. The study will follow the perioperative care pathway from a four-week prehabilitation phase through surgery, post-discharge transition, and inpatient rehabilitation, with predefined assessments conducted at prehabilitation start and end (PRE1, PRE2), rehabilitation admission and discharge (REH1, REH2), and at 7 days after REH2 follow-up. **Outcomes:** The primary outcome will be feasibility, assessed through recruitment and retention rates, adherence and fidelity to the prehabilitation intervention, safety, data collection and management performance, and acceptability and usability of the digital tools. Secondary outcomes will include clinical recovery indicators, functional independence, psychological well-being, and health-related quality of life, broader functional and rehabilitation needs, hematological and metabolic variables, and functional and physiological outcomes. Clinical recovery will be described as time to functional recovery, number of postoperative complications, length of intensive care unit and hospital stay, readmission rates, and short-term mortality. Functional and physiological outcomes will include body composition, cardiorespiratory fitness, functional exercise capacity, and muscle strength. **Ethics and dissemination:** The study protocol will be submitted to the responsible ethics committee for approval. Written informed consent will be obtained from all participants. Findings will be disseminated through peer-reviewed publications and conference presentations.

Trial registration number: To be completed before enrollment.

Keywords: Digital interventions; Surgical oncology; Rehabilitation pathways; Hepato-biliary surgery; digital health

Introduction

Surgical resection of visceral cancers remains the only chance for long-term survival or cure, with an estimated 80% of cancer patients requiring surgery during their illness [1, 2]. Despite its central role, only 20-30% of patients qualify for potentially curative surgery procedures, largely due to poor general health, nutritional status, and physical fitness [3-5]. These factors represent substantial patient-related limitations for surgery. Even when surgery is feasible, major visceral surgeries continue to carry significant risks, remaining one of the leading causes of in-hospital mortality [1, 2, 6].

In patients undergoing oncologic surgery of the pancreas, liver, esophagus, or stomach, postoperative morbidity (defined as any postoperative medical or surgical complication) remains high, ranging from 30% to 60%, and mortality can be as high as 20% in extended liver surgery [7-10]. Patients in the perioperative phase are exposed to multiple stressors, including the surgical trauma itself, the physiological impact of anesthesia, and the psychological burden associated with major surgery [11]. As such, strategies to mitigate postoperative complications and to optimize recovery are needed. Resilience to surgery stressors is influenced by age, comorbidities, and acute physiological deterioration due to the underlying disease. In this context, physical fitness and nutritional status play a pivotal role in determining postoperative outcomes and are linked to disease-associated factors such as cancer-related cachexia, malabsorption, and myopathy [12]. Nutritional aspects of prehabilitation address these needs by strengthening nutritional status before surgery, creating potential to buffer postoperative catabolism [13], which is supported by the latest European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines. They confirm that nutritional status substantially influences postoperative complications and mortality [14], where malnourished patients with cancer experience higher complication and mortality rates, longer hospital stays, more frequent readmissions, and thus cause higher treatment costs [15-17].

Given the high postoperative morbidity rates following major oncological surgery, there is a need for strategies that reach beyond intraoperative and postoperative care. Many existing interventions miss the critical preoperative window to enhance patients' functional reserves [6, 7, 10]. Postoperative interventions often fail to prevent poor outcomes, reinforcing the need for preoperative strategies. Ideally, these measures should be accessible and easy to integrate into everyday life to ensure high adherence [18].

Furthermore, postoperative functional decline can delay or prevent the initiation of adjuvant treatments, which are critical for improving long-term survival in cancer patients [19]. This limitation becomes particularly relevant when considering that only patients who recover adequately from surgery are eligible to begin or complete oncologic treatment [20]. Even more, only those who regain a high level of functional capacity can proceed with intensified chemotherapy regimens, which are associated with greater survival benefits [21]. Therefore, enhancing fitness before surgery may be a decisive step for accessing the full therapeutic benefit of cancer treatment care [22]. Thus, prehabilitation may not only reduce surgical risk but also enhance access to potentially life-prolonging oncologic therapies [23].

Prehabilitation aims to improve the patient's functional capacity before surgery through targeted physical training, nutritional support, and psychological preparation [12]. Studies from prehabilitation programs in major visceral oncology surgery demonstrate that these interventions are safe and well-tolerated, reporting no intervention-related serious adverse events but high adherence to both supervised and home-based prehabilitation programs [19, 22, 24]. Furthermore, these studies also supported that prehabilitation is a low-risk strategy to enhance fitness without adding clinical risk. However, for patients in Austria undergoing major oncologic surgeries, prehabilitation is not implemented in the health care system. Further, content and duration of prehabilitation programs remain heterogeneous and poorly defined, also on an international level. Consequently, standardized guidelines currently do not exist regarding the extent of nutritional support or the level of physical activity required [25, 26].

Evidence: Preoperative physical fitness is a key predictor of clinical outcome after surgery or other oncologic treatments. Low physical fitness correlates with higher rates of complications, longer hospital stays, and mortality [27, 28]. Also, sarcopenia, frequently seen in patients with cancer, contributes substantially to a poor prognosis [29]. A Cochrane review evaluating multimodal prehabilitation showed that functional capacity can improve before surgery, although the effects on postoperative complications and several other clinically relevant endpoints remain uncertain because of small sample sizes, methodological variability, and incomplete outcome reporting [30]. These limitations are consistent with broader inconsistencies in prehabilitation research, including variation in the assessment of physical fitness,

uncertainty regarding the most effective training intensity, and unclear prioritization of endurance or strength components [31]. Together with the heterogeneity of patient populations, these challenges restrict the ability to derive clear conclusions for specific clinical groups, such as patients undergoing major visceral surgery.

Local Context: In Austria, around two-thirds of the population live with chronic diseases or health problems affecting both physical and/or mental health, largely driven by unhealthy lifestyles and social determinants [32]. Further improvements are unlikely without addressing modifiable risk factors such as low fitness, obesity, and frailty [33]. Prehabilitation remains absent from routine care due to financial, infrastructural, and organizational barriers [30]. Moreover, coordination and continuity between prehabilitation and rehabilitation are often lacking, and digital tools remain underutilized in delivering continuous care [34, 35]. Digital applications have shown potential in increasing patient engagement, enabling self-management, and improving adherence, even in larger patient populations [36].

The Prehab2Rehab-OncoVis-Trial evaluates the feasibility and potential effectiveness of a structured, four-week, multimodal exercise program for patients undergoing major visceral oncologic surgery. The intervention combines supervised, center-based training with strategies to support home-based physical activity, utilizing digital tools throughout the preoperative period and beyond. The study will also assess the contribution of these digital tools to patient engagement and the continuity of care from prehabilitation through rehabilitation. Additionally, the trial aims to determine whether this integrated approach improves postoperative recovery (measured by clinical and functional outcomes) as well as postoperative morbidity, defined by the incidence and severity of complications, and overall rehabilitation outcomes.

Methods

Study design

Prehab2Rehab-OncoVis is a prospective, single-arm feasibility cohort study designed to assess the feasibility of implementing a digitally supported prehabilitation intervention for patients scheduled to undergo major visceral oncologic surgery, as presented in Figure 1. While the feasibility objectives are addressed within the prospective cohort, two historical comparison groups will be referenced to provide preliminary estimates of efficiency and efficacy: i) a historical comparator group from

the same hospital, consisting of patients who did not receive prehabilitation, to evaluate the effects of prehabilitation on clinical outcomes at hospital discharge; and ii) a cohort from the Ludwig Boltzmann Institute for Rehabilitation Research (LBI-RR), including national rehabilitation datasets [37–39], matched for diagnosis (ICD), sex, and age to assess potential effects on rehabilitation outcomes.

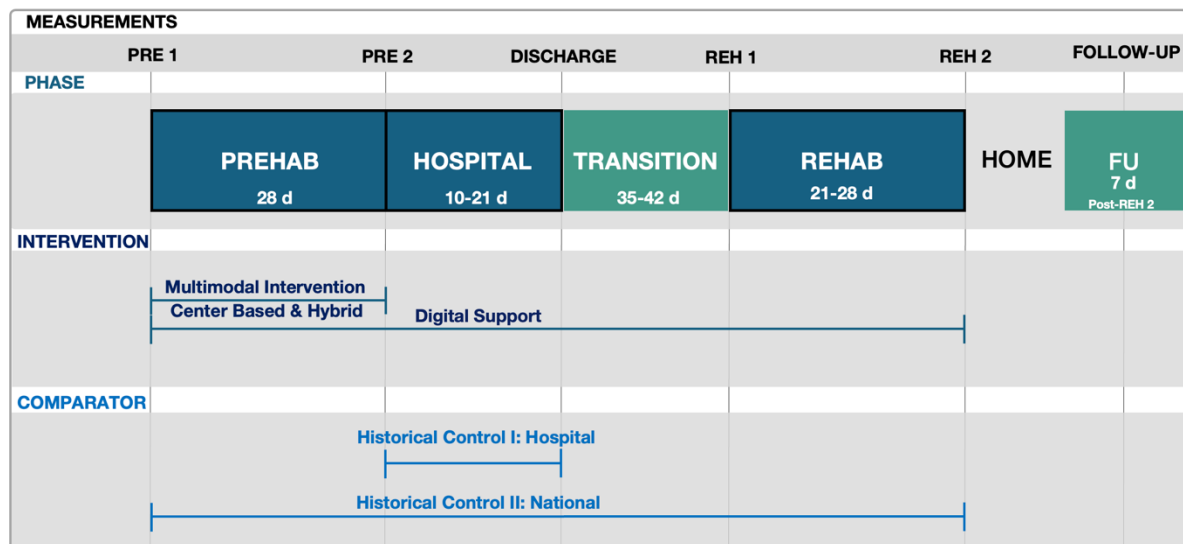


Figure 1: Study design. Illustration of the study phases, time points of assessment, interventions, and comparisons to historical control groups.

Abbreviations: Prehabilitation (PREHAB); start of prehabilitation (PRE1); end of prehabilitation (PRE2); rehabilitation (REHAB); start of rehabilitation (REH1); end of rehabilitation (REH2); Follow-up (FU).

Note: Duration of transition phase depends on individual health conditions.

A mixed-methods approach will be employed, combining quantitative and qualitative data derived from participant questionnaires and structured feedback to evaluate the feasibility of implementation, patient experience, adherence, and clinical outcomes. The study structure follows the entire perioperative care pathway. It begins with a four-week prehabilitation phase, including a center-based supervised intervention and complementary home-based physical activity, and ends with rehabilitation.

Assessments will be conducted at two predefined time points: at the start (PRE1) and at the end (PRE2) of the prehabilitation period. This is followed by hospitalization for surgery, lasting approximately 10 to 21 days (approx. 2 to 3 weeks), depending on the individual clinical course. After discharge, a 35 to 42 days (approx. 5 to 6 weeks) transition phase at home occurs. Subsequently, Rehabilitation Phase II

begins, lasting 21 days, optionally 28 days (approx. 3 to 4 weeks), with assessments at its start (REH1) and end (REH2). REH2 marks the end of the study. A follow-up assessment is conducted approximately 7 days after REH2 to evaluate long-term recovery and patient-reported experiences. The study is designed to ensure continuity across all phases, with coordinated prehabilitation, transitional support, and rehabilitation forming a connected patient pathway. Participation in the prehab program will likely create no delay or not more than one week, since due to mandatory preoperative cardiac and pulmonary evaluation, surgery is routinely delayed by at least 3 to 4 weeks. According to the literature, a delay of even more than 30 days does not negatively affect recurrence-free or overall survival [37]. For the historical rehabilitation group, routine rehabilitation assessment data (REH1 and REH2) will be used for comparison.

The study protocol follows guidance from Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) [38]. A SPIRIT schedule of enrollment, interventions, and assessments is provided in Table 1, and a SPIRIT checklist is provided in Supplementary File S1. A flowchart of study design, including the historic control group, is presented in Figure 2.

Ethics and Regulatory Approvals

The study will be conducted in accordance with the Declaration of Helsinki [39] and the principles of Good Clinical Practice (GCP) [40]. Ethical approval will be obtained from the Local Ethics Committee of the state of Salzburg (Landesethikkommission Salzburg) before the study onset. Any substantial amendments to the protocol will be submitted for review and approval by the Ethics Committee before implementation.

All procedures related to data collection, storage, and analysis will comply with the European General Data Protection Regulation (GDPR/DSGVO). Personal data will be pseudonymized and handled confidentially in accordance with the applicable data protection laws. All digital tools will be implemented in a study-specific configuration, with functionalities and access rights adapted to the requirements of the Prehab2Rehab-OncoVis trial and in accordance with applicable data protection and regulatory standards. Study findings will be disseminated through peer-reviewed scientific publications, conference presentations, and stakeholder meetings.

Summaries of aggregated results will be made available to participants upon request. No individual-level data will be publicly disclosed to ensure participant confidentiality. Any data sharing will be limited to anonymized and aggregated datasets, in consideration of both GDPR requirements and applicable Findable, Accessible, Interoperable, and Reusable (FAIR) data principles. Authorship will follow the recommendations of the International Committee of Medical Journal Editors (ICMJE), and the investigators will retain full independence in data analysis, interpretation, and publication. The funder will have no authority over the decision to publish or the content of the resulting manuscripts.

Study setting

The study will be conducted at the University Hospital Salzburg (UKS), Department of General and Visceral Surgery (UKDS), and the University Institute of Sports Medicine, Prevention and Rehabilitation (UISM). The study is coordinated by the Paracelsus Medical University (PMU), conducted in tight cooperation with the Ludwig Boltzmann Institutes for Rehabilitation Research (LBI-RR) and Digital Health and Prevention (LBI-DHP), executed under the research and innovation project umbrella of the Prehab2Rehab consortium (publicly available project information: <https://www.prehab2rehab.at>). Within the Prehab2Rehab, related site-specific feasibility and implementation studies are planned in patients undergoing total knee replacement at the Rehabilitation Centre Bad Vigaun and in patients undergoing cardiac surgery at the Medical University of Vienna. Each study will be designed, submitted for ethical approval, and conducted independently, while sharing a common conceptual framework.

Participants will be recruited from the hepato-biliary outpatient clinic of the UKDS. Before the prehabilitation program onset, all participants will undergo a sports-medical examination conducted by a licensed sports medicine physician of the UISM, who will perform the baseline assessment and confirm participants' medical eligibility for medical training therapy. The Co-Investigator representing the UISM will be responsible only for the clinical oversight of the exercise intervention, while overall study responsibility, including safety oversight beyond the training intervention, will remain with the surgical Principal Investigator.

An accredited training therapist will supervise the prehabilitation under oversight and according to the physician-approved training plan at the UIS. On days without scheduled training, participants will be encouraged to maintain an active lifestyle, such as low-intensity activities (short walks). This home-based physical activity component will be supported by a digital training diary to document and support home-based activity. To include an evaluation of the feasibility of a predominantly tele-prehabilitation intervention, patients with a travel time of more than 40 minutes one-way are offered the option of combining center-based training with tele-prehabilitation. Tele-prehabilitation has already proven effective in other contexts [41].

Most participants are planned to complete their postoperative rehabilitation at the Rehabilitation Center St. Veit (Rehabilitationszentrum St. Veit im Pongau Betriebs-GmbH). The center is affiliated with the Salzburg State Hospitals (SALK) and functions as a secondary study site for all participants who undergo rehabilitation there. Standard rehabilitation procedures remain unchanged; however, study-related assessments (REH1 and REH2) will be coordinated within this setting.

Sample size

For this feasibility cohort trial, we plan to recruit a convenience sample of 30 patients consecutively, with the possibility of enrolling up to 50 patients if possible. To contextualize the observed changes and provide preliminary estimates of efficiency and efficacy, the local clinical comparator group from the Department of General and Visceral Surgery, UKS, consisting of patients who previously underwent major visceral surgery without prehabilitation, and the national rehabilitation comparator group derived from the LBI-RR routine rehabilitation registry will be used. This structure allows for both within-group comparison (pre-post cohort comparison) and between-group contextual comparison (cohort vs. historical groups). Patient enrolment is planned to commence upon receipt of a positive ethical approval and will continue until 6 weeks before the end of the funding period, currently scheduled for 30 April 2027.

Participant eligibility

Inclusion and exclusion criteria

The prospective cohort, non-randomized feasibility study will include adults aged 18 years or older with a clinical diagnosis requiring major surgery of the

pancreas, liver, bile ducts, stomach, or esophagus, performed with curative intent at the Department of General and Visceral Surgery. A confirmed indication for surgery must be documented by the multidisciplinary tumor board. Participation requires medical stability and clearance by a licensed physician to engage in a prehabilitation exercise program. In addition, patients must be willing and able to attend center-based prehabilitation exercise training sessions three times per week, or once per week if travel time is longer than 40 min (one way), and to engage in home-based physical activities. Sufficient proficiency in German language, digital literacy, and access to a smartphone or tablet device with an internet connection are required to ensure comprehension of study-related information and appropriate use of the digital application. If participants have insufficient German language skills or limited digital literacy, the study permits, upon participant consent, the installation of the study applications on the smartphone of a close relative or accompanying family member. The provision of written informed consent is mandatory for participation.

Patients will be excluded if they are younger than 18 years, if they present with a physical disability or mental impairment that precludes safe and adequate participation in the study, or if they are under a health care medical power of attorney that does not permit independent consent. Further exclusion criteria include non-elective, emergency, or revision surgery, as well as any acute medical condition that contraindicates participation in a structured prehabilitation program.

Participant Recruitment and Informed Consent

Recruitment will take place at the specialized outpatient clinic of UKDS, as outlined in Figure 1. During the outpatient consultation, the study physician will screen patients according to the predefined eligibility criteria. Those meeting the criteria will receive an initial verbal explanation of the study. Patients who express interest will then be referred to the research team for detailed study information and clarification of any further questions. Written informed consent will be obtained before enrolment and before any study-related procedures.

Multimodal prehabilitation intervention

The prehabilitation intervention will be implemented as a multimodal, digitally supported program combining exercise training, health literacy promotion, structured

nutritional, laboratory, and psycho-oncological distress screening. Digital technologies will support structured delivery, remote supervision, information provision, and continuous engagement along the patient pathway. Screening results may lead to therapeutic measures if clinically indicated.

Exercise intervention

The exercise intervention will be delivered in two formats: (i) standard - three supervised center-based prehabilitation sessions per week plus encouragement of an active lifestyle including physical activity; or (ii) hybrid - one supervised center-based prehabilitation session per week plus two tele-prehabilitation sessions per week, again with encouragement of an active lifestyle, offered to patients whose travel distance to the prehabilitation center exceeds approximately 40 minutes one way, to reduce travel burden, improve feasibility and adherence.

The center-based prehabilitation exercise program will be conducted at the UISM and structured according to the Frequency, Intensity, Time, and Type (FITT) principles [42, 43]. Each session will follow a standardized four-phase format: warm-up, endurance training, resistance training, and cool-down. The details of these components will be personalized based on the initial evaluation, medical assessment, and the expertise of the therapist, but can be described on a general level as follows: the warm-up will consist of light cardiovascular activity on a stationary cycle ergometer for approximately 5 minutes at low intensity (RPE 1 to 2 (on a modified Borg scale of 0-10)). Endurance training will be performed on a cycle ergometer at moderate intensity for 10-15 minutes. Resistance training will be performed using machines and/or elastic bands at moderate intensity for 15-20 minutes. The cool-down phase will focus on light static stretching and breathing exercises and will last 5 minutes. For an exemplary training plan, see Table 1.

During all supervised endurance exercise sessions at UISM, safety will be ensured through electrocardiogram (ECG) monitoring if indicated. Exercise therapists and/or physicians will be present during each session component. Emergency equipment, including a defibrillator, emergency phone access, and a predefined medical emergency response protocol, will be in place.

For patients who live more than approximately 40 minutes from the training center, the hybrid training option will include one supervised on-site session per week

at UISM, and two tele-rehabilitation home-based sessions conducted via the CAATS telecommunication platform (<https://caats.io>). These tele-rehabilitation sessions will not fully replicate the center-based training structure, as patients do not have access to an ergometer or treadmill. The endurance component will therefore be limited to safe and accessible walking as a part of daily life, while the resistance component will follow a progressive plan aligned with the overall prehabilitation goals and will consist of chair-based and elastic band exercises. During tele-prehabilitation sessions, patients will receive guidance on how to position their smartphones to allow continuous visual supervision by the therapist, ensuring correct technique and maintaining minimum safety throughout by enabling the timely initiation of the medical emergency response chain if required. If real-time video supervision cannot be established, the tele-rehabilitation session will not be conducted.

Irrespective of whether patients are allocated to the standard center-based or the hybrid tele-rehabilitation approach, they will be encouraged to maintain an active lifestyle on days without scheduled training. On these days, patients will be advised to engage in both indoor and outdoor activities, particularly walking, twice per week at light to moderate intensity (RPE, 1 to 3), starting with 10 to 15 minutes in week 1 and ideally progressing to 20-30 minutes by week 4.

Nutritional Counseling

Nutritional counseling will be initiated after the outpatient clinic visit and study inclusion of the patient by the staff of the Department of General and Visceral Surgery. It will run in parallel with the exercise program intervention. The counseling will follow the recommendations of the ESPEN practical guideline *Clinical nutrition in surgery* [14] and will be delivered by experienced dietitians and physicians to optimize nutritional status before surgery. Each patient will undergo a structured screening for malnutrition risk using the Nutritional Risk Screening score (NRS-2002) [44]. The NRS-2002 score follows a standardized two-step approach. An initial screening evaluates a potential nutritional risk indicator, including low body mass index, recent unintended weight loss, reduced dietary intake, or increased metabolic stress related to the underlying disease. If nutritional risk is suspected, a main screening is performed that quantitatively assesses two domains: (i) impairment of nutritional status, based on weight loss, body mass index, and recent reduction in food intake or general condition;

and (ii) disease severity, reflecting the degree of metabolic stress and increased nutritional requirements associated with the planned surgical intervention. Each domain is scored on an ordinal scale from 0 (no impairment) to 3 (severe impairment), and the domain scores are summed to obtain a total NRS-2002 score. A total score of ≥ 3 points is considered indicative of clinically relevant nutritional risk and supports the need for nutritional optimization. Based on these assessments, individualized recommendations will be provided to ensure adequate energy and protein intake. The general target is an energy intake of at least 25 to 30 kcal/kg/day and protein intake of 1.2 to 2.0 g/kg/day, as recommended by ESPEN. When dietary intake is insufficient due to the underlying disease, oral nutritional supplements will be prescribed, which patients pay for at cost. Counseling will primarily take place during face-to-face sessions at the Department of General and Visceral Surgery, while patients who cannot attend in person will be supported via video consultation through the CE-certified CAATS platform. Additional written information and practical resources will be provided to help patients implement the platform in daily life. Nutritional status will be monitored throughout the prehabilitation period by an advanced practicing nurse, and counseling will be adapted according to tolerance, clinical progress, and the surgical timeline.

Psycho-oncological distress screening

The psycho-oncological distress screening will be conducted in accordance with the certification requirements of the German Cancer Society (*Deutsche Krebsgesellschaft*, DKG) and the S3 guideline on psycho-oncological diagnostics, counseling, and treatment of adult cancer patients [45]. Patients will undergo standardized screening by using the NCCN Distress Thermometer and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, Core 30 (EORTC-QLQ-C30) to evaluate life quality. Screening results will be documented, and patients exceeding the established thresholds or expressing a need for support will be referred to psycho-oncological care by the primary treating unit. Interventions may include individual or group counseling and family-oriented support. Feedback will be provided to the oncology team to ensure integration into the overall treatment pathway. Screening coverage, referral rates, and uptake will be monitored to ensure compliance with DKG recommendations.

Health literacy

Health literacy will be assessed and promoted as part of the prehabilitation program to support patients before and after surgery. Patients' health literacy will be measured using validated instruments such as the European Health Literacy Questionnaire (HLS-EU-Q) [46] and the Brief Health Literacy Screening Tool (BRIEF) [47]. Structured education delivered via the HERO app will provide information on surgical procedures, anesthesia, prehabilitation strategies, and postoperative recovery. Content will be adapted to plain language standards and supported by visual and digital resources to enhance comprehension [48].

Digital support

HERO (originally: Herz-Reha-Informationstool), developed by the Ludwig Boltzmann Institute for Digital Health and Prevention in collaboration with REDOX GmbH, is a digital information resource designed to promote health literacy and provide orientation to patients and, where appropriate, their relatives throughout the entire treatment pathway, including prehabilitation, hospital stay, transition, and rehabilitation. It provides structured, evidence-based information, including disease-specific background, general guidance, and motivational resources, thereby promoting patient understanding, facilitating self-management, and reducing uncertainty, particularly in the period before formal rehabilitation begins. Patients and their relatives or caregivers have access to tailored content at each stage of care, ensuring ongoing support and understanding. HERO is an educational, motivational, and potentially self-efficacy-fostering tool and does not constitute a diagnostic instrument or therapeutic intervention. Content in the application will be specifically adapted to the described use case, reflecting the needs of both health care professionals and patients. The HERO app serves as an adjunct digital tool to routine clinical follow-up and is not intended to replace medical assessment or therapeutic decision-making.

aktivplan, developed by the Ludwig Boltzmann Institute for Digital Health and Prevention in collaboration with alphaport OG, will be used as a digital training diary and exercise planner, allowing participants to keep an overview of prescribed sessions, document adherence, and receive reminders. It serves as the central

organizational interface for online training, helping patients manage their prehab appointments efficiently. Additionally, aktivplan supports patients on non-training days in maintaining an active lifestyle by providing guidance and motivation for everyday physical activity. The tool also allows the clinical team to monitor fidelity and engagement in real time.

The CAATS-platform, developed by Loidl Consulting, is a video communication tool, providing video-based supervision for participants who are unable to attend all training sessions in the UISM due to overlong travel distances. It also facilitates remote delivery of educational consultations.

Together, these digital tools form an integrated framework that supports patient education, encourages structured participation in the prehabilitation program, and enables safe and consistent guidance throughout the whole intervention period.

Rehabilitation

Rehabilitation within the study will be delivered as usual care, without any study-specific intervention or modification of standard rehabilitation procedures. However, patients who undergo rehabilitation at the affiliated center Rehabilitationszentrum St. Veit im Pongau Betriebs-GmbH will be systematically included in the observation period in order (a) to explore the impact of prehabilitation on subsequent rehabilitation outcomes and course, and (b) to evaluate the feasibility and acceptance of the digital support tools from the patients' perspective across the entire treatment pathway, including the rehabilitation phase. During this period, patients will retain access to the digital support tools.

Outcomes

Primary outcomes

Feasibility outcomes are summarized in Table 2. They include recruitment rate, retention rate, communication with participants, data collection and entry, adherence, fidelity, safety, and acceptability of the digitally supported prehabilitation intervention. The recruitment rate refers to the proportion of all patients screened for eligibility who meet the inclusion criteria and subsequently provided informed consent to participate in the study. The retention rate refers to the proportion of enrolled participants who complete the study as planned. Communication with participants considers the

schedule and duration of communication between the team members and study staff to address operational issues. Data collection and entry assess the time and system performance related to data handling. Adherence represents the average proportion of prehabilitation sessions attended by the patients, and fidelity describes the extent to which the intervention is implemented as intended, in adherence to the protocol and consistency of delivery. Safety, as a feasibility outcome, will be assessed based on the number and type of serious and non-serious adverse events considered related or possibly related to the intervention or study procedures. Serious adverse events are defined as events causing death, life-threatening conditions, hospitalization or its prolongation, or persistent disability; non-serious adverse events refer to all other unfavorable medical occurrences. All adverse events and serious adverse events will be monitored, documented, and reported in accordance with Good Clinical Practice (GCP) guidelines. Acceptability of digital technologies (including use experience and usability) is evaluated using standardized instruments, including the Unified Theory of Acceptance and Use of Technology 2 (UTAUT-2) [49], the mHealth App Usability Questionnaire (MAUQ) [50], the Mobile Application Rating Scale (MARS) [51], AttrakDiff [52], and the Affinity for Technology Interaction (ATI) [53].

Secondary outcomes

Clinical outcomes

Clinical outcomes will be assessed in this feasibility study to provide preliminary data on the effectiveness and safety of the prehabilitation intervention. The outcomes will include: i) clinical recovery indicators; ii) functional independence; iii) psychological well-being; iv) broader functional and rehabilitation needs, v) hematological status and patient blood management, and vi) metabolic control.

i) Clinical recovery indicators

Secondary outcomes will be assessed to further characterize the potential effectiveness and safety of the intervention. The Time to Functional Recovery (TtFR) will serve as the primary indicator of postoperative recovery. This will be defined as the period from surgery until all of the following criteria are fulfilled: adequate pain control achieved with oral analgesics and discontinuation of intravenous opioids, tolerance of oral or enteral nutrition, return of lower gastrointestinal function evidenced

by the passage of flatus or stool, restoration of independent mobility and self-care, and the absence of complications that require additional medical or surgical treatment.

Postoperative complications will be recorded and graded according to the Clavien-Dindo classification ($\geq$ grade 3a), thereby capturing clinically relevant morbidity. In addition, the Comprehensive Complication Index (CCI) will be calculated to provide a continuous, weighted measure of the overall postoperative morbidity burden. The length of intensive care unit stay and complete hospital stay, defined as the number of days from surgery to discharge, will serve as a measure of postoperative recovery and healthcare resource utilization. All-cause 30-day and 90-day mortality will be assessed to evaluate short-term survival. Finally, the 30-day readmission rate, defined as the proportion of participants requiring unplanned rehospitalization within 30 days after discharge, will be determined.

ii) Functional independence

The Barthel Index (BI) is a validated, 10-item ordinal scale used to measure functional independence in activities of daily living, including feeding, bathing, dressing, continence, and mobility. Scores range from 0 to 100, with higher scores indicating greater independence [54]. In this study, the BI will be administered at baseline (admission) and post-intervention (discharge from the rehabilitation phase) to evaluate potential changes in self-care and mobility performance before surgery.

The Eastern Cooperative Oncology Group Performance Status (ECOG) will be used to evaluate patients' overall performance capacity and disease-related functional impairment. The ECOG scale ranges from 0 (fully active and able to carry on all pre-disease activities without restriction) to 5 (death), with higher scores indicating greater functional limitation [55].

The Rapid Assessment of Physical Activity (RAPA) is a brief, validated physical activity self-report [56]. It includes items covering aerobic activity, strength, and flexibility, providing a quick categorization of participants' activity levels.

The Exercise Self-Efficacy Scale (ESES) is a validated instrument developed to measure confidence in performing regular exercise under various circumstances [57]. It includes 10 items rated on a 4-point scale, where higher scores reflect greater perceived self-efficacy for exercise.

iii) Psychological well-being

The Patient Health Questionnaire-4 (PHQ-4) is an ultra-brief screening instrument designed to assess symptoms of anxiety and depression, comprising the two-item Generalized Anxiety Disorder scale (GAD-2) and the two-item Patient Health Questionnaire depression scale (PHQ-2) [58]. Each item is scored from 0 (“not at all”) to 3 (“nearly every day”), producing a total score from 0 to 12, with higher scores indicating greater psychological distress.

The Hospital Anxiety and Depression Scale (HADS) will be used to provide a more detailed assessment of anxiety and depressive symptoms throughout the perioperative period [59]. It consists of 14 items divided into two subscales, HADS-A and HADS-D, each ranging from 0 to 21. Higher scores indicate greater emotional distress. HADS is widely applied in oncology and surgical settings and is sensitive to changes in psychological well-being across treatment stages.

The EuroQol-5 Dimensions-5 Levels (EQ-5D-5L) is a standardized, generic measure of health-related quality of life that evaluates five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension is rated on five levels of severity, from “no problems” to “extreme problems,” and the instrument also includes a visual analogue scale (VAS) for self-rated health [60].

The NCCN Distress Thermometer will be used as a rapid screening tool to identify psychological distress and supportive care needs. It includes a visual analogue scale ranging from 0 (“no distress”) to 10 (“extreme distress”) and an associated problem list covering physical, emotional, practical, and spiritual concerns [61].

Health-related quality of life will also be assessed using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC-QLQ-C30) [62]. This 30-item questionnaire assesses global health status, functional domains (physical, emotional, cognitive, role, and social), and symptom burden.

iv) Broader functionality and rehabilitation needs.

Broader rehabilitation needs, including psychosocial and vocational aspects relevant for participation, will be assessed at admission within an International Classification of Functioning, Disability and Health (ICF) based framework [63], in accordance with the Austrian PVA medical performance profile for inpatient

rehabilitation (MLP) [64]. The assessment includes structured documentation of occupational and social history and screening using the Screening Instrument for Medical-Vocational Oriented Measures - Clinical Version (SIMBO-C) [65]. Through the integrated evaluation of these components, special vocational problem situations (besondere berufliche Problemlagen; BBPL) are identified as a diagnostic classification to inform individualized rehabilitation planning and the indication of targeted work-oriented rehabilitation measures.

v) Hematological status and patient blood management

The patient blood management (PBM) program strictly follows current clinical guidelines as issued by the Austrian Society of Anaesthesiology, Resuscitation and Intensive Care Medicine (ÖGARI) [66], as well as European [67, 68] and international [69] consensus statements. Accordingly, all diagnostic and therapeutic decisions within PBM are exclusively based on hemoglobin concentrations and iron status to optimize oxygen-carrying capacity before surgery and minimize transfusion requirements. All participants will undergo laboratory screening, including hemoglobin, ferritin, and transferrin saturation, with additional tests (vitamin B12, folate) if indicated. Iron deficiency will be treated, preferably with intravenous iron in the limited preoperative window, while oral supplementation will only be considered when surgery is scheduled more than four weeks ahead. Erythropoiesis-stimulating agents may be prescribed selectively with adequate thromboprophylaxis. Perioperative measures such as careful anticoagulation management, maintenance of normothermia, and antifibrinolytic therapy when indicated will complement this approach, while transfusions are generally applied restrictively and considered supportive therapy only.

vi) Metabolic control (glycemic control)

Glycemic control will be conducted in accordance with current evidence and international recommendations [70]. All patients scheduled for surgery will undergo screening of fasting plasma glucose and glycated hemoglobin (HbA1c). HbA1c ≥ 42 mmol/mol ($\geq 6.0\%$) will prompt further evaluation, and HbA1c ≥ 48 mmol/mol ($\geq 6.5\%$) will be considered diagnostic for diabetes [71]. Patients with abnormal glucose metabolism will receive individualized counseling on nutrition and physical activity and,

when indicated, pharmacological optimization. In patients with known diabetes, current regimens will be reviewed and adjusted as required. The perioperative glucose target will be 140 to 180 mg/dl. On the day of surgery and in the immediate postoperative period, structured glucose monitoring will be performed. Blood glucose >180 mg/dl will be treated with insulin according to standardized protocols[72]. Monitoring will continue during the hospital stay, with therapy adapted to metabolic status and surgical course.

Functional outcomes

Functional outcomes will be evaluated in this feasibility study to explore the potential effects of the prehabilitation intervention on participants' physical capabilities and mobility. These outcomes will include: i) anthropometrics and body composition; ii) cardiorespiratory fitness; iii) functional exercise capacity; and iv) muscle strength.

i) Anthropometrics and body composition

Anthropometric measurements will be assessed using standardized procedures. Body mass (kg) will be measured using a calibrated digital scale, and height (cm) will be measured using a stadiometer. Body mass index (BMI) will then be calculated as body mass in kilograms divided by height in meters squared (kg/m^2).

Body composition will be assessed using bioelectrical impedance analysis (BIA). This method allows the estimation of lean mass (kg), fat mass (kg), and phase angle ($^\circ$), providing a noninvasive and time-efficient evaluation [73]. Body composition assessment is clinically relevant in the preoperative evaluation of patients with liver, pancreas, and biliary tract system diseases [74]. Malnutrition and altered body composition, such as sarcopenia or fluid imbalance, are common in this patient population and are strongly correlated with adverse surgical outcomes, including increased morbidity, prolonged hospital stay, and reduced overall survival [75].

ii) Cardiorespiratory fitness

Cardiopulmonary exercise testing (CPET) will be performed preoperatively to objectively assess patients' functional capacity and physiological reserve before the prehabilitation program. CPET evaluates the integrated response of the cardiovascular, pulmonary, and muscular systems during exercise, providing

parameters such as peak oxygen uptake ($\dot{V}O_{2peak}$, L/min), maximum mechanical power output (W), and the first and second ventilatory thresholds (VT1 and VT2). These measures are established as predictors of postoperative morbidity and mortality. Tests will be conducted on an electronically braked cycle ergometer using an established incremental ramp protocol [76] to the limit of tolerance, with continuous 12-lead ECG monitoring, blood pressure, and oxygen saturation. CPET will be performed in accordance with perioperative clinical guidelines to ensure validity, reproducibility, and patient safety [77] in the UISM.

iii) Functional exercise capacity

The six-minute walk test (6MWT) is used to objectively assess functional exercise capacity [78]. This test is widely used in clinical and research settings due to its simplicity, safety, and reproducibility. Participants will be instructed to walk at their own pace along a flat, straight, 30-meter indoor corridor for a total duration of six minutes to cover the greatest possible distance within the allotted time. Following established guidelines, standardized encouragement and instructions will be given [78]. The total distance walked will be measured in meters (m) for analysis.

The timed Up and Go (TUG) test will be used to assess basic functional mobility and screen for impairments that may affect recovery in patients scheduled for elective visceral cancer surgery. During the test, the participant is instructed to rise from a standard armchair, walk 3 meters at a comfortable and safe pace, turn, return to the chair, and sit down. The total time taken to complete the task is recorded in seconds (s) [79]. Both tests will be conducted in the UKS.

iv) Muscle strength

Handgrip (HG) strength will be assessed using a manual hydraulic dynamometer, following the standardized procedures [80]. Participants will be seated in an armless chair with the trunk maintained in an upright position. The lower limbs will be positioned to ensure a knee flexion angle of 90 degrees. The upper limb on the testing side, positioned with the shoulder in adduction and neutral rotation, the elbow flexed at 90 degrees, the forearm in a semi-pronated position, and the wrist in a neutral posture, permitting up to 30 degrees of extension. Before testing, a familiarization trial will be conducted to determine the most ergonomically appropriate position for each

participant and to adjust the grip size of the dynamometer as needed. Following familiarization, handgrip strength will be measured by instructing participants to apply maximal voluntary contraction for five seconds in a single repetition for each hand. The highest value obtained (HGpeak) expressed in kilograms (kg) will be recorded and used for subsequent analysis.

Rehabilitation outcomes

Rehabilitation outcomes will be assessed during Rehabilitation Phase II, according to the schedule in Table 3, at the secondary study site (Rehabilitation Center St. Veit). These assessments follow routine rehabilitation procedures and are complemented by study-specific evaluations described in the protocol. Clinical routine endpoints captured during the rehabilitation phase or available from hospital records will include - depending on the length of the transition phase - the 30-day readmission rate (30dRR), 30-day mortality rate (30dMR), and 90-day mortality rate (90dMR), Barthel-index (BI), Eastern Cooperative Oncology Group Performance Status (ECOG), Rapid Assessment of Physical Activity (RAPA), Exercise Self-Efficacy Scale (ESES), Patient Health Questionnaire-4 (PHQ-4), EORTC-QLQ-C30, NCCN Distress Thermometer, International Classification of Functioning, Disability and Health (ICF), Hospital Anxiety and Depression Scale (HADS), SIMBO-C, and EQ-5D-5L. Functional and physiological assessments will include body mass, body mass index, and Six-minute Walk Test (6MWT). Together, these routine measures will provide a detailed description of recovery during Rehabilitation Phase II.

Timing and procedures for outcome data collection

Outcome data will be collected at predefined time points along the prehabilitation and rehabilitation pathway to capture changes from baseline through post-surgery recovery, as shown in Figure 1 and Table 3. During the prehabilitation phase, data will be obtained at enrolment and repeated after completion of the 4-week intervention but before surgery. These assessments will follow the standardized procedures defined in the outcomes section and will allow characterization of baseline status and the short-term effects of prehabilitation.

After surgery, outcome data will be collected during the inpatient period of Rehabilitation Phase I at the University Hospital Salzburg, where routine clinical

documentation will provide information on length of stay, intensive care utilization, complications, and readmissions. Standardized outcome data will again be collected at admission and discharge of Rehabilitation Phase II. This point marks the end of the study. A final assessment will be gathered at the 3-month follow-up visit. This approach will allow for an extended view of the perioperative course and will support the evaluation of feasibility, safety, and recovery trajectories.

In addition, semi-structured interviews will be conducted with a subset of participants to explore their experiences with prehabilitation and the digital support components throughout the patient pathway. These interviews will be scheduled at the end of the digital support phase, either at REH2 (online, via CAATS, or phone) or at the follow-up visit (in person), with timing individually coordinated to ensure flexibility. With the participants' consent, interviews will be audio-recorded to enable accurate transcription; audio files will be deleted immediately after transcription, and any personal identifiers (e.g., names of people or places) will be substituted to preserve anonymity. This approach provides a richer qualitative dataset compared to contemporaneous interviewer notes. The qualitative findings will complement quantitative outcomes by providing deeper insights into user perception, satisfaction, and barriers or facilitators of digitally supported prehabilitation.

Patient data will be pseudonymized at the point of collection. A separate identification log linking personal identifiers to study IDs will be maintained under restricted access at the study site. This log will include the study ID, family name, given name, date of birth, sex, contact information, date of informed consent, enrolling site, and any notes relevant to study conduct. Access to the identification log will be limited to authorized study personnel only. The pseudonymization key will consist of a study ID in the format ****P2R-SALK-XXXX****, where XXXX is a pre-generated sequential number. These IDs will be listed on a master allocation list and assigned consecutively at inclusion. The study ID will be used in all study documents and datasets instead of direct personal identifiers.

Harms and safety monitoring

Participant safety will be systematically monitored throughout the study, including prehabilitation, surgery, and rehabilitation. Any adverse event or serious adverse event that occurs from enrollment until the end of the study will be

documented and evaluated for its possible relation to the intervention or study procedures.

An adverse event is defined as any unintended medical occurrence in a participant, meaning any new symptom or worsening of an existing condition during the study period, regardless of its causal relationship to the intervention. A serious adverse event is defined as any event that results in death, is life-threatening, requires or prolongs hospitalization, or leads to a significant or lasting disability. The severity, expectedness, and potential causality of each event will be assessed by the responsible study physician. Based on extensive clinical experience at the executing UKDS, the expected rate of serious adverse events during the four-week preoperative time window (between surgical indication and the scheduled operation) is zero.

During supervised prehabilitation and rehabilitation sessions, participants will be continuously observed by exercise therapists and/or physicians. Exercise sessions will be terminated according to current guidelines. For the hybrid tele-prehabilitation sessions, correct smartphone placement will be required to ensure continuous visual monitoring by the therapist, and sessions will not be conducted if adequate visual supervision cannot be established. All adverse events and serious adverse events will be reported to the principal investigator within twenty-four hours of recognition. Serious adverse events that are related or possibly related to the intervention will be reported to the Ethics Committee of the Land Salzburg and the University Clinic Salzburg in accordance with institutional and national requirements. Regular safety reviews will be conducted by the study team to evaluate the frequency, severity, and nature of adverse events and to assess the feasibility of the implemented safety monitoring procedures.

Statistical analysis

Statistical analyses will be conducted to describe feasibility and implementation outcomes and to explore changes in clinical, functional, and patient-reported outcomes across the perioperative pathway, as detailed below.

i) Design and primary objective (feasibility focus)

This study is designed as a prospective, single-arm feasibility cohort trial. The primary objective is to evaluate the feasibility, acceptability, and safety of a digitally supported multimodal prehabilitation intervention in patients undergoing curatively

intended major visceral oncologic surgery. The study is not powered to formally test clinical hypotheses regarding the effectiveness of the intervention.

ii) Sample size and implications for inference

The planned sample size of approximately 30 patients (with the option to include up to 50 participants if feasible) is primarily based on practical and methodological considerations typical for feasibility trials, rather than on a formal power calculation for clinical endpoints. The sample is intended to allow robust assessment of feasibility parameters (e.g. recruitment and retention rates, adherence, acceptability, safety signals) and to provide preliminary estimates of effect sizes for key clinical and functional outcomes that can be used to design subsequent, adequately powered randomized controlled trials.

iii) Primary analysis: descriptive and feasibility parameters

The primary analysis will focus on feasibility outcomes and implementation metrics. These will be summarized using descriptive statistics (e.g. counts and proportions, means and standard deviations, medians and interquartile ranges, as appropriate). Confidence intervals may be reported to quantify the precision of key feasibility estimates (e.g. recruitment and completion rates, adherence to the intervention, frequency and nature of adverse events). No formal hypothesis testing will be conducted for feasibility outcomes.

iv) Secondary / exploratory analyses and group comparisons

Secondary and exploratory analyses will examine changes in clinical, functional, psychological, and patient-reported outcomes over time within the intervention cohort, as well as comparisons with historical control groups. For these analyses:

- Outcomes will be summarized descriptively for each time point and, where applicable, for each comparison group.
- Exploratory inferential methods (e.g. paired or unpaired tests, regression models) may be used to estimate potential effect sizes and to investigate trends and associations.

- Any p-values and confidence intervals reported for these exploratory analyses will be interpreted cautiously and exclusively for hypothesis-generating purposes.

The study is not designed or powered to provide definitive evidence of effectiveness, and no conclusions about efficacy will be based solely on statistical significance. Instead, the results of these exploratory analyses will inform the refinement of the intervention and the planning (including sample size calculations) of future confirmatory trials.

v) Handling of missing data

Given the feasibility nature of the trial, patterns and reasons for missing data will be described in detail as part of the feasibility assessment. Where appropriate, sensitivity analyses may be performed to explore the robustness of descriptive and exploratory findings.

Publication Strategy

The results of this clinical trial will be published in peer-reviewed scientific journals and may also be presented at scientific conferences. Any publication or presentation of study results requires prior review and approval by the Sponsor. Data protection and confidentiality of all participant information will be strictly maintained; only pseudonymized or aggregated data will be reported. The reporting of the protocol and primary outcomes will follow the recommendations of the CONSORT Statement, including the extension for randomized pilot and feasibility trials (www.consort-statement.org).

At least two scientific publications in international peer-reviewed journals are planned:

1. Publication of the study protocol.
2. Publication of the main trial results (primary and secondary outcomes may be published separately).

Any additional or subsequent publications (e.g., subgroup analyses or complementary investigations) must be discussed with and approved by the Sponsor

before submission. The publication of interim results is not intended. Authorship will be based on the recommendations of the International Committee of Medical Journal Editors (ICMJE, <https://www.icmje.org>). The Principal Investigator will ensure adherence to these guidelines and coordinate the publication strategy in collaboration with the Sponsor and project partners. Detailed provisions on authorship, publication rights, and related responsibilities are defined in the consortium agreement and the internal governance procedures agreed upon within the consortium board of the Prehab2Rehab Project (www.prehab2rehab.at).

Author Contributions

Giorjines Boppre and Gunnar Treff drafted the initial study protocol, revised subsequent versions, and coordinated the overall revision process. Together with Stefan Löb, they contributed to the conceptualization and design of the study. Stefan Löb, Clemens Schmutzhart, and Josef Niebauer provided additional clinical expertise and reviewed the protocol for medical and procedural accuracy. Daniela Wurhofer, Jan Smeddinck, and Vincent Grote provided methodological input and supported the development of the study design and outcome assessments. Andrea Planatscher coordinated the preparation of study materials, documentation, and revisions across multiple sections. Jan Smeddinck also contributed the original research concept for the overarching project and critically reviewed and helped refine the final protocol manuscript. All authors read and approved the final version of the study protocol.

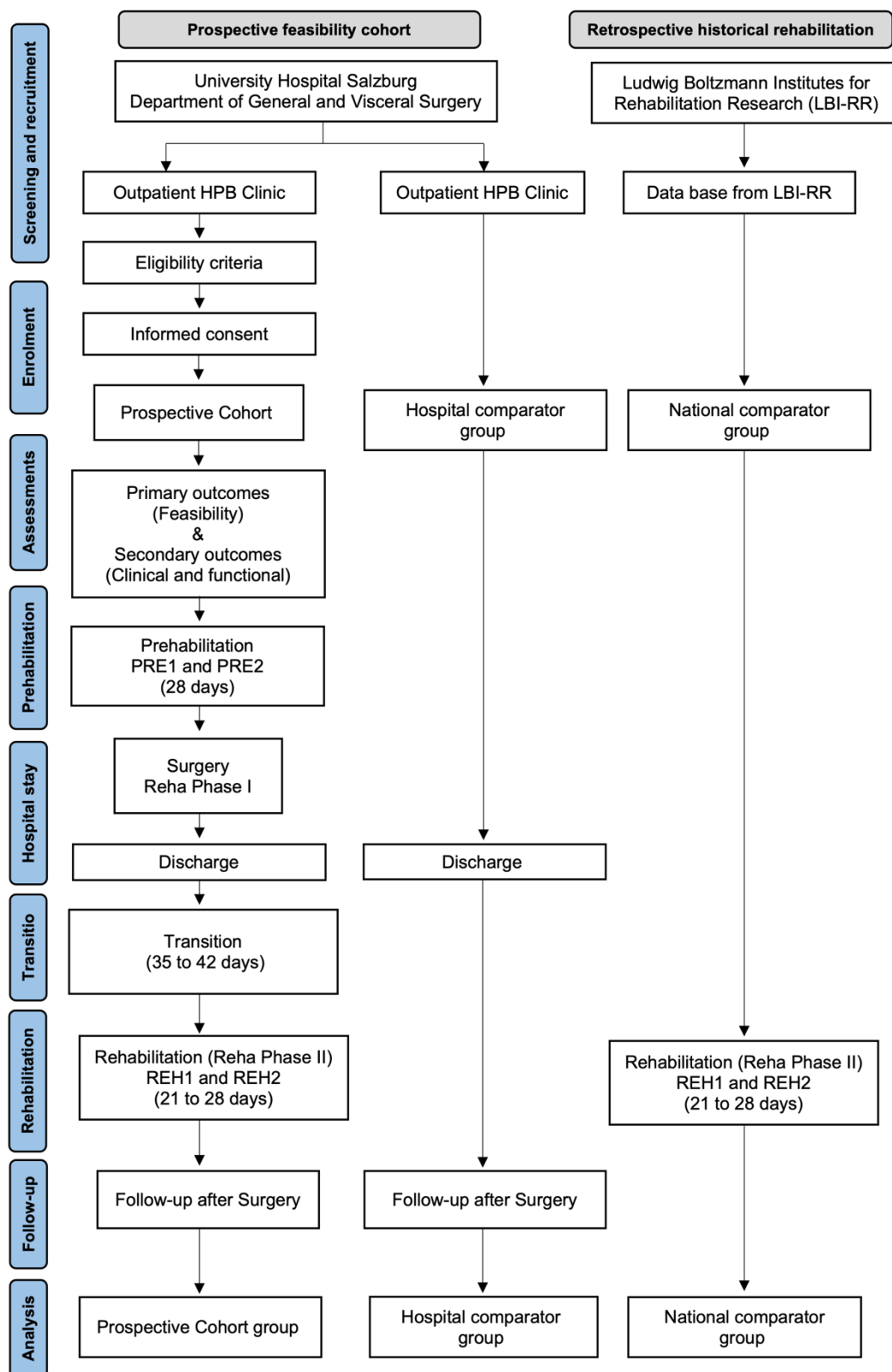


Figure 2: Study design flow chart

Abbreviations: Start of prehabilitation (PRE1); end of prehabilitation (PRE2); start of rehabilitation (REH1); end of rehabilitation (REH2)

Table 1. Exemplary overview of center-based and home-based physical activity prehabilitation program

Periodization (Weeks)	Standard Center-based prehabilitation exercise session				Home-based Physical Activity
	Initial part	Main part		Final part	
	Warm-up	Endurance	Resistance	Cool-down	
Week 1	Intensity: Light • Equipment: Stationary cycling • Intensity: RPE 2 • Time: 5 min	Intensity: Moderate • Equipment: Stationary cycling • Intensity: RPE 3 (50 to 60% $\dot{V}O_{2peak}$) CPET • Time: 10 min ECG monitored	Intensity: Moderate • Equipment: Machines or elastic bands (5 to 6 exercises) • Exercises: Major muscle groups • Sets/Reps: 1 x 10 to 12 • Rest: 30s • Intensity: RPE 3 • Time: 15 min	Intensity: Light • Exercises: static stretching for major muscle groups. Focusing on breathing and relaxation • Time: 5 min	Light physical activity, e.g., walking • Time: 10 to 15 min • Frequency: 2x/week
Week 2	Intensity: Light • Equipment: Stationary cycling • Intensity: RPE 2 to 3 • Time: 5 min	Intensity: Moderate • Equipment: Stationary cycling • Intensity: RPE 3 to 4 (60% $\dot{V}O_{2peak}$) CPET • Time: 10 to 15 min ECG monitored	Intensity: Moderate • Equipment: Machines or elastic bands • Exercises: Major muscle groups (5 to 6 exercises) • Sets/Reps: 1 or 2 x 10 to 12 • Rest: 30s • Intensity: RPE 3 to 4 • Time: 15 to 20 min	Intensity: Light • Exercises: static stretching for major muscle groups. Focusing on breathing and relaxation • Time: 5 min	Light physical activity, e.g., walking • Time: 15 min • Frequency: 2x/week
Week 3	Intensity: Light • Equipment: Stationary cycling • Intensity: RPE 3 • Time: 5 min	Intensity: Moderate • Equipment: Stationary cycling • Intensity: RPE 4 (60 to 65% $\dot{V}O_{2peak}$) CPET • Time: 10 to 15 min ECG monitored	Intensity: Moderate • Equipment: Machines or elastic bands • Exercises: Major muscle groups (5 to 6 exercises) • Sets/Reps: 2 x 10 to 12 • Rest: 30s • Intensity: RPE 4 • Time: 15 to 20 min	Intensity: Light • Exercises: static stretching for major muscle groups. Focusing on breathing and relaxation • Time: 5 min	Light physical activity, e.g., walking • Time: 15 to 20 min • Frequency: 2x/week
Week 4	Intensity: Light • Equipment: Stationary cycling • Intensity: RPE 3 • Time: 5 min	Intensity: Moderate • Equipment: Stationary cycling • Intensity: RPE 4 to 5 (60 to 65% $\dot{V}O_{2peak}$) CPET • Time: 10 to 15 min ECG monitored	Moderate resistance • Equipment: Machines, elastic bands • Exercises: Major muscle groups (5 to 6 exercises) • Sets/Reps: 2 x 12 • Rest: 30s • Intensity: RPE 4 • Time: 15 to 20 min	Intensity: light • Exercises: static stretching for major muscle groups. Focusing on breathing and relaxation • Time: 5 min	Light physical activity, e.g., walking • Time: 15 to 20 min • Frequency: 2x/week
Abbreviations: Electrocardiogram (ECG); Cardiopulmonary exercise testing (CPET); Rating of perceived exertion (RPE); seconds (s); repetitions (reps).					

Table 2: Outcomes of the study

Metric	Objectives	Measure
Primary outcomes		
Feasibility	i) Recruitment rate	A proportion of eligible patients who are recruited and give informed consent to participate in the study.
	ii) Retention rate	The proportion of patients who consent to take part in the study.
	iii) Communication with participants	Schedule and duration of communication between team members and study staff to address operational issues.
	iv) Data collection and entry	Time and system assessment.
	v) Adherence	Average proportion of the prehabilitation sessions attended by the patients.
	vi) Fidelity	Extent to which the intervention is implemented as intended, in adherence to the protocol and with consistency of delivery.
	vii) Safety	The number and type of serious and non-serious adverse events that are related or possibly related to the intervention or study procedures
	viii) Acceptability	Acceptance: Unified Theory of Acceptance and Use of Technology 2 (UTAUT-2); Usability: mHealth App Usability Questionnaire (MAUQ); User experience: Mobile Application Rating Scale (MARS); AttrakDiff; and Affinity for Technology Interaction (ATI).
Secondary outcomes		
Clinical and Functional	i) Clinical recovery indicators	Time-to-functional recovery (TtFR); Length of hospital stay (LOHS); Length of intensive care unit (LoICU); Comprehensive complication Index (CCI); 30-day readmission rate (30dRR) 30- and 90-days mortality rate (30d/90dMR)
	ii) Functional independence	Barthel Index (BI); Eastern Cooperative Oncology Group Performance Status (ECOG); Rapid Assessment of Physical Activity (RAPA); and Exercise Self-Efficacy Scale (ESES).
	iii) Psychological distress, well-being, and quality of life	Patient Health Questionnaire-4 (PHQ-4); Hospital Anxiety and Depression Scale (HADS) and EuroQol-5 Dimensions-5 Levels (EQ-5D-5L); NCCN Distress Thermometer; European Organization for Research and Treatment of Cancer Quality of Life Questionnaire, Core 30 (EORTC-QLQ-C30); European Health Literacy Questionnaire (HLS-EU-Q); Brief Health Literacy Screening Tool (BRIEF).
	iv) Broader functional and rehabilitation needs	Screening Instrument for Medical-Vocational Oriented Measures - Clinical Version (SIMBO-C).

	v) Hematological status and patient blood management	Ferritin ($\mu\text{g/L}$); Transferrin saturation (%), vitamin B12 (pmol/L); Folate (nmol/L); Hb concentration (g/dl); hematocrit (%)
	vi) Metabolic control	Glycated hemoglobin (HbA1c, mmol/mol)
	vii) Anthropometric and body composition	Nutritional Risk Screening score (NRS-2002); body mass (kg); body height (cm); body mass index (kg/m^2); Phase angle ($^\circ$); body fat and lean mass (kg , %)
	viii) Cardiorespiratory fitness	Assessed by Cardiopulmonary exercise testing (CPET) and considering the following measures: $\dot{V}\text{O}_{2\text{peak}}$ (l/min) and mechanical work output (P_{max} , W)
	ix) Functional exercise capacity	Six-Minute Walk Test (6-MWT, m); Timed Up and Go (TUG, s)
	x) Strength.	Handgrip strength (kg)

Table 3: Schedule and timing of outcomes assessments throughout the Prehabilitation to Rehabilitation

Outcomes	Prehabilitation		Hospital Stay			Transition	Rehabilitation Phase II		Follow-up
	PRE1	PRE2	Surgery	Rehabilitation Phase I	Discharge		REH1	REH2	
Duration	4 weeks		Approx. 10 to 21 days			Approx. 35 to 42 days	21 (28) days		Approx. 7 days after REH 2
Digital acceptability									
Unified Theory of Acceptance and Use of Technology 2 (UTAUT-2)								X*	
mHealth App Usability Questionnaire (MAUQ)								X*	
Mobile Application Rating Scale (MARS)								X*	
Perceived hedonic and pragmatic quality questionnaire (AttrakDiff)								X*	
Affinity for Technology Interaction (ATI)	X								
Clinical recovery indicators									
Time to Functional Recovery (TtFR)					o				
Length of Hospital Stay (LOHS)					o				
Length of Intensive Care Unit (LoICU)					o				
Comprehensive Complication Index (CCI)					o				
30-day re-admission rate (30dRR)						o	o		
30-day mortality rate (30dMR)					o	o	o		
90-day mortality rate (90dMR)					o	o	o	o	o
Functional independence									
Barthel-index (BI)	X						X	X	
Eastern Cooperative Oncology Group Performance Status (ECOG)	X	X							X
Rapid Assessment of Physical Activity (RAPA)	X							X*	
Exercise Self-Efficacy Scale (ESES)	X	X						X*	
Psychological distress, well-being, and quality of life									
Patient Health Questionnaire-4 (PHQ-4)	X	X					o	o	
Hospital Anxiety and Depression Scale (HADS)	X	X					o	o	
EuroQol-5 Dimensions-5 Levels (EQ-5D-5L)	X	(X)					o	o	
NCCN Distress Thermometer	X	X			X				X
European Health Literacy Questionnaire (HLS-EU-Q)	X							X*	
Brief Health Literacy Screening Tool (BRIEF)	X							X*	
European Organization for Research and Treatment of Cancer – Quality of Life Questionnaire Core 30 (EORTC-QLQ-C30)	X						o	o	X

Table 3 (continued): Schedule and timing of outcomes assessments throughout the Prehabilitation to Rehabilitation

Outcomes	Prehabilitation		Hospital Stay			Transition	Rehabilitation Phase II		Follow-up
	PRE1	PRE2	Surgery	Rehabilitation Phase I	Discharge		REH1	REH2	
Duration	4 weeks		Approx. 10 to 21 days			Approx. 35 to 42 days	21 (28) days		Approx. 7 days after REH 2
Broader functional and rehabilitation needs									
Nutritional Risk Screening (NRS)	X	X							X
International Classification of Functioning, Disability and Health (ICF)							o		
Screening Instrument for Medical-Vocational Oriented Measures – Clinical Version (SIMBO-C)	X						o	o	
Hematological status and patient blood management									
Ferritin (µg/L); Transferrin saturation (%), vitamin B12 (pmol/L); Folate (nmol/L); Hb concentration (g/dl); hematocrit (%)	X	X							
Metabolic control									
Glycated hemoglobin (HbA1c)	X	X							
Anthropometrics and body composition									
Body Mass (kg)	X	X			o		o	o	X
Body Height (cm)	X								
Body Mass Index (kg/m2)	X	X			o		o	o	X
Bioelectrical impedance analysis (BIA) Phase Angle (°), Body Fat and Lean Mass (kg, %)	X	X			X				X
Cardiorespiratory fitness									
Cardiopulmonary exercise testing (CPET) ṠO ₂ peak (l/min) and Maximum Work Capacity (Pmax, W)	X	X							
Functional exercise capacity									
Six-minute Walk Test (6MWT, m)	X	X					o	X	X
Timed Up and Go (TUG, s)	X	X							
Handgrip strength (kg)	X	X							
Notes: Start of prehabilitation (PRE1); end of prehabilitation (PRE2); start of rehabilitation (REH1); end of rehabilitation (REH2). o indicates routine measurements (independent of the study); X indicates additional measurements (due to study participation); () indicates optional measurements; * indicates measurements not coordinated by the rehabilitation center but completed by participants around the time of REH2, with support from the study team (either paper-based or digital).									

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