Multidisciplinary prehabilitation clinic to improve frailty and functional capacity in high-risk elective surgical patients: a pilot retrospective observational study

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Background

Traditionally in surgical practice, the decision to proceed to surgery is made between the surgeons and the patients. Whenever necessary, the patients are sent to other specialties (eg. anaesthesiologists, physicians, dietitians, physiotherapists) for consultation and optimization before elective surgery. This approach is acceptable for the majority of fit patients, it can however be unsatisfactory for high-risk frail patients undergoing major surgical procedures. Hong Kong is facing an aging population. According to the 2016-based population projections published by the Census and Statistics Department, the pace of population aging in Hong Kong will keep on ramping up in the coming 20 years or so. Between 2018 and 2038, the size and share of the elderly population will almost double from 1.27 million and 17.9% to 2.44 million and 31.9% respectively[1]. With aging, there is an increase in frailty and a loss in functional and physiological reserve and adaptability, putting a patient that is exposed to a stressor, such as a major operation, at a higher risk of adverse outcomes[2]. Frailty is associated with two to six- fold increased risk of major adverse cardiac and cerebrovascular events, longer stays in intensive care unit and hospital, a 1-year mortality[3]. Pre-frail patients are also at risk of poor outcomes. Compared to non-frail patients, pre-frail patients (Clinical Frailty Score 4) had longer ICU stays, longer hospital stays, higher risk of postoperative stroke and a high risk of in-hospital mortality[4]. Malnutrition and sedentary lifestyle are common in frail elderly patients. These have been demonstrated to be a recognizable risk factor of poor postoperative outcomes[11]. It is therefore necessary to have a multidisciplinary team to manage frailty preoperatively.

Prehabilitation is a multidisciplinary and multimodal approach involving anaesthesiologists, physicians, physiotherapists, occupational therapists and dietitians that aims to optimize functional capacity, nutritional status and emotional resilience before surgery, so as to enable the patients to better withstand perioperative

stress. It encompass individualized aerobic and resistance training to enhance cardiopulmonary fitness, dietary interventions to counteract the catabolic state of surgery, emotional support to improve resilience and advice on behavioural changes such as cessation of smoking and alcohol abuse. In the literature, prehabilitation has well been reported to enhance functional capacity before and after surgery. In particular, exercise training has been shown to improve various aspects of physical function of the frail elderly (eg. muscle strength, body composition, mobility, functional status and fall prevention)[5]. Tailored exercise training is therefore expected to improve physical fitness and increase functional capacity so that patients can better withstand the stress of surgery[6]. In a systematic review, prehabilitation before orthopaedic surgery have beneficial effects in improving strength, flexibility, balance and speed in 5 out of 7 randomized controlled trials[7]. Regarding postoperative clinical outcomes such as length of stay, readmission rate and postoperative complications rate, evidence demonstrated an association between physical fitness improvement and a lower rate and severity of complications[8-9]. Despite the heterogenicity in study design and modalities of prehabilitation program, the positive effect of prehabilitation on perioperative functional fitness has been shown across a wide variety of surgical procedures, including abdominal aortic aneurysm repair, esophagectomy, cystectomy, liver resection and colorectal surgery. In general, individuals who have been frail and having a sedentary activity level would benefit the most from prehabilitation program. Preoperative malnutrition can be due to inadequate intake and high requirements from the disease process that results in reduced body mass, strength and function and a reduced ability to mount an immunological defense. All these can be significant in the high catabolic state perioperatively for the healing process and the systemic inflammatory response to surgery. Preoperative malnutrition is associated with many adverse outcomes. After adjusting for active smoking status, preoperative malnutrition was associated with postoperative complications after pneumonectomy and hepatectomy[12-13], a longer length of stay in hospital, higher readmissions within 28 days and a higher mortality up to 90 days after surgery[14-16]. Nutritional prehabilitation therefore helps prepare and optimize the patients' nutritional status for surgery and recovery.

The timing and duration of prehabilitation program can affect the risk of postoperative outcomes. An ideal duration of prehabilitation has not been established and there is a large heterogenicity in duration from the literature. But in general, a minimum of three to four weeks is required to have an effect of physical fitness[17]. Despite the need for novel resources, economic evaluation suggested that prehabilitation could be a cost-effective approach[10], the resulting benefits in short- and medium-term outcomes offset the costs of additional resources.

Most of the "fast-track" surgical pathways focus on intraoperative and postoperative measures to enhance recovery, and the traditional rehabilitation approach is to operate first and then intervene. However, postoperative pain, fatigue and wound care impede the efficiency of rehabilitation measures such as physiotherapy and nutritional program. Therefore, it would be more ideal to start intervention before surgery while patients can be more actively engaged in the process of perioperative care and functional improvement. The earlier the patients can be engaged, the greater the likelihood of having a meaningful

impact and the less likely to affect the surgical schedule. The waiting time for surgery creates a window of opportunity to prepare the patients for prehabilitation by addressing problems of physical fitness, nutritional status and emotional distress. By re-engineering our preoperative assessment clinic and integration within the prehabilitation clinic, we are more able to risk stratify and identify high-risk patients at the time of preoperative evaluation. A common and one-stop platform can be shared by a multidisciplinary perioperative team with seamless communications, which reduces the chance of high-risk patients being bounced between independent consultations.

Changing the present structure and logistics of preoperative assessment clinic requires active participation of the stakeholders involved in perioperative care. Surgeons need to refer patients to anaesthesiologists as early as possible for further screening into prehabilitation program. Anaesthesiologists need to have new assessment strategies for functional capacity that are not traditionally used in routine preoperative assessment clinic. Physiotherapist, occupational therapist and dietitians should ideally set up a one-stop service model to minimize patient travel. Effective implementation requires buy-in from hospital administrators, investing resources to support this value-based approach. Therefore, we will conduct a pilot retrospective observational study to evaluate the feasibility and impact of prehabilitation on our patients before major elective surgery. In particular, for the feasibility part, we aim to (1) estimate recruitment, attrition and adherence rate, and (2) ensure safety of prehabilitation. For the pilot part, we aim to identify if there are any changes on the outcomes after the prehabilitation intervention, and (2) identify estimates of variance for sample size calculation for future randomized trials.

Materials and Methods

Trial design

This is a single centered, unblinded, single-arm retrospective study.

Setting and preoperative care pathway

The study is conducted at the Prince of Wales Hospital, a tertiary centre and a university teaching hospital with 1650 bed in Hong Kong. In the usual preoperative care pathway, referred patients are seen in preoperative assessment clinic. If the patients need medical optimization, consultations will be sent to corresponding medical specialty for further workup and assessment. Physiotherapy and dietitians referrals are initiated by surgeons at the time of decision for surgery. No adjustment is made between the schedule of surgery and the date to be seen at preoperative assessment clinic. Functional capacity assessment is based on subjective estimation of metabolic equivalent based on exercise tolerance. A metabolic equivalent of less than 4 and inability to climb 2 flights of stairs have been used to identify patients with poor functional capacity. There are no screenings for anaemia and malnutrition in the routine preoperative care pathway, and no preoperative interventions are prescribed to patients with baseline anaemia, malnutrition and poor functional capacity.

Prehabilitation clinic

New preoperative care pathway has been implemented since August 2019. In the new preoperative care pathway (Fig 1), referred patients are screened by anaesthesiologists for inclusion into prehabilitation clinic, with the date of the clinic session at least 5 weeks before the estimated operation date. Eligible patients will have the baseline blood samples taken on the same day of clinic attendance. The blood samples include routine bloods plus the investigations necessary for anaemia screening (ferritin, iron profile, C-reactive protein, vitamin B_{12} and folate level). Anaemia is defined by the World Health Organization as a circulating haemoglobin concentration below 13g/dL for men and 12g/dL for non-pregnant women[21]. Patients found to have absolute iron deficiency anaemia (ferritin <30mcg/L, or ferritin <100mcg/L with transferrin saturation <20%) will be admitted to day surgery centre on the same day for a single dose of intravenous ferric carboxymaltose (20mg/kg for body weight <50kg, 1000mg for body weight >50kg) at least 3 weeks prior to the estimated operation date. The intravenous iron infusion will be given over 30 minutes under close monitoring. Patients will also be screened for malnutrition in the prehabilitation clinic using the Malnutrition Screening Tool (MST). Patients with MST score of more than one will be referred to dietitians for nutritional prehabilitation. Furthermore, functional capacity and frailty of patients will be assessed using Duke Activity Status Index (DASI) questionnaire, 6-mintue walk test (6MWT) and Clinical Frailty Scale (CFS). Patients with DASI score <34 or 6MWT distance <400m will be recruited into the prehabilitation program.

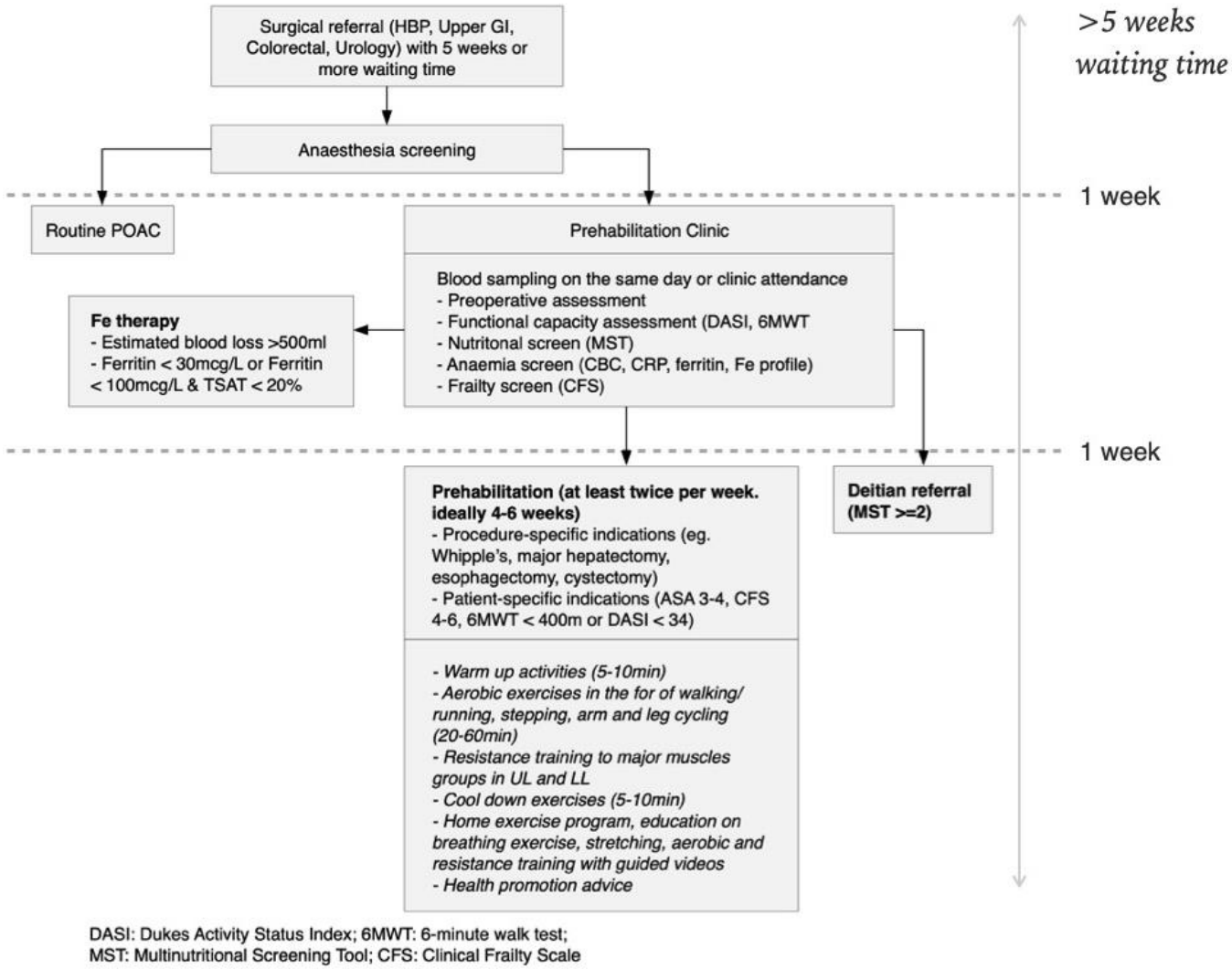

Fig 1. Workflow of prehabilitation clinic

Exercise prehabilitation

Collaboration was made with the Geriatric Day Hospital (GDH) of the same hospital cluster for the prehabilitation service. The GDH at Shatin provides a seamless one-stop service in medicine and geriatrics, physiotherapy, occupational therapy and dietitians. Patients screened eligible for recruitment are sent to GDH within one week after the prehabilitation clinic attendance for further holistic care and assessments. Patients will undergo a structured preoperative exercise training of 3 or more weeks, depending on the schedule of surgery, to optimize the physical and psychosocial fitness of patients with underlying frailty syndrome before surgery by physiotherapists at GDH. The result of the submaximal exercise test from the 6MWT will be used as an estimation of individual peak oxygen uptake and hence oxygen uptake reserve (VO_2R) for exercise prescription[22]. Each patient's prehabilitation program will be individualized and symptom limited, in which exercise prescription and progression will be based on the results of the exercise test, individual health status, exercise performance and training response. Based on the American College of Sport Medicine guidelines on exercise prescription, the exercise protocol comprise of 75-90min of supervised

exercises at least twice per week (3 times per week for the first 2 weeks). There is a combination of moderate-intensity aerobic exercise and resistance training, with the exercise intensity 3-6 according to the modified Borg Scale. In the aerobic exercise, the patients will be asked to perform treadmill walking, stepping exercises and ergometer for 30min. For the resistance training, patients will be asked to perform 10 repetitions per major muscle group of upper and lower limbs with at least 2 sets, depending on individual tolerance and performance. Home exercise program including stretching, aerobic and resistance training, and breathing exercises will be prescribed to patients with guided videos. Advice on smoking cessation and positive psychology support will be given to patients during the prehabilitation program.

Nutritional care pathway for prehabilitation (Fig 2)

Patients with MST score >=2 will be referred to dietitian at Shatin Hospital for nutritional prehabilitation. Two sessions of nutrition therapies will be offered to each eligible patient. The first session will be completed at 4-week before the operation, and the second session will be given to the patient at 1-week before the operation. Assessments by dietitians include nutritional status assessment, anthropometric measurement, body composition analysis (muscle mass, percentage body fat), phase angle, and dietary intakes will be collected in each intervention. During the first and second intervention, energy level of 25-30kcal/kg/BW and protein level of 1-1.5g/kg/BW will be prescribed. During the second intervention, immunonutrition support, using a nutrition supplement containing arginine, nucleotides and omega-3 fish oil will be prescribed 5-7 days prior to surgery to metabolically prepare the body cells for surgical stress. Patients with poor renal function, poor sugar control, and severely impaired liver function will be excluded for nutritional prehabilitation.

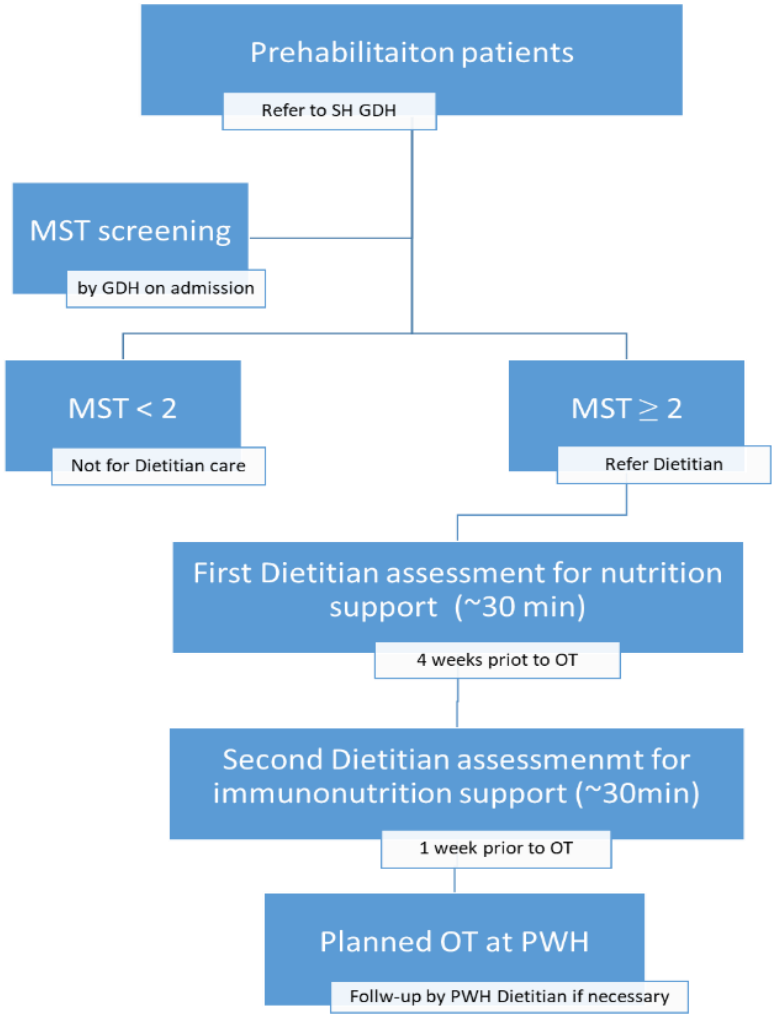

Fig 1. Nutritional care pathway for prehabilitation patients

Inclusion and exclusion criteria

We have procedure-specific and patient-specific criteria for inclusion. For procedure-specific criteria, we include major hepatectomy (resection of 3 or more Couimaud's segments), pancreaticoduodenectomy, esophagectomy and radical cystectomy. For patient-specific criteria, we include adult patients age 50 or older, undergoing elective major procedures from the following surgical specialties (hepatobiliary and pancreatic, upper gastrointestinal, colorectal and urological), together with one of the following:

1. American Society of Anaesthesiologists physical status (ASA-PS) score >=3
2. Pre-frail to moderately frail patients with a Clinical Frailty Scale[18] 3-6 at time of assessment at prehabilitation clinic
3. 6-minute walk test distance < 400 metres
4. Duke Activity Status Index[19] < 34
5. Malnutritional Screening Tool[20] score >=2

All patients are required to have an estimated 5 weeks or more of surgical waiting time to ensure the listed surgery date is compatible with an optimal prehabilitation time of 3 weeks or more[17].

The exclusion criteria are:

1. Patients with unstable angina or unstable cardiac syndrome (New York Heart Association Class IV, critical left main coronary disease, hospitalization for arrhythmias, congestive heart failure or acute coronary syndrome before assessment at prehabilitiation clinic)
2. Patients with left ventricular outflow obstruction (severe aortic stenosis, hypertrophic cardiomyopathy)
3. Chronic obstructive pulmonary disease GOLD stage IV
4. Abdominal aortic aneurysm >8.0cm or suspected dissecting or leaking aortic aneurysm
5. Cognitive deficits unable to comply with study procedures, physical limitations that would prelude rehabilitation and inability to regularly attend prehabilitation sessions.

Data collection

Frailty measures (CFS, 30 seconds sit-stand test, hand grip strength, time-up-and-go test) and functional capacity measures (6MWT distance, calculated peak oxygen uptake, DASI score) will be collected at prehabilitation clinic and upon first and last prehabilitation session. We will also evaluate the dose-response effect of the number of prehabilitation sessions attended. The cause for any premature termination of prehabilitation, for example, change in surgical plan or date, patient non-compliance, or logistic difficulties will also be analysed. Quality of life measurement using EQ-5D and emotional resilience screen using DASS-21 will be done at the first and last prehabilitation session. Nutritional status based on measurement of weight, BMI, muscle mass and percentage body fat will be recorded at the first and last prehabilitation session.

The following demographic data will be collected at baseline including age, gender, body weight, body mass index, ASA-PS, details of surgical procedures, length of hospital and ICU stay, pulmonary complications, discharge destination (home, hospital or nursing aged-care facility) and 30-day mortality from patient's medical record.

Table 1 Assessments overview

Assessment	**Baseline**	**First prehab session**	**Last prehab session**	**POMI**
Enrolment				
Eligibility screen	X			
Demographic data	X			
Comorbidity data	X			
Primary outcomes				
6MWT	X	X	X	
Secondary outcomes				
DASI	X			
Clinical Frailty Scale	X			

Other frailty measures (Hand grip strength, 30s sit-stand test)		X	X	
DASS-21		X	X	
Nutritional status (muscle mass, % fat, BMI, weight)		X	X	
3-day food record		X	X	
Length of hospital and ICU stay				X
Pulmonary complications				X
30-day mortality				X
DAH_{30}				X

Outcome measures

Primary outcomes

The primary outcome is the changes in the 6MWT distance and the calculated peak oxygen uptake ($VO2_{peak}$) between baseline and upon completion of prehabilitation program. A dose-response effect on 6MWT distance and calculated $VO2_{peak}$ with regards to the number of prehabilitation sessions attended will be investigated. The 6MWT evaluates the ability of an individual to maintain a moderate level of physical endurance. Moderate to strong correlations have been found between the 6MWT and $VO2_{peak}$ obtained with other modes of exercise testing. Participants are instructed to walk back and forth a 30m stretch of hallway for 6min at a pace that would make them tired by the end of the walk. A change in 6MWT distance of 20m was considered meaningful as this is the estimated measurement error in community-dwelling elderly[26].
We will also assess the feasibility of the program by examining the recruitment, attrition and adherence of patients to the prehabilitation sessions. The reasons for drop-out from prehabilitation will be recorded.

Secondary outcomes

Secondary outcome measures include patient reported outcomes before and after the prehabilitation program. These include the followings:

<u>Emotional resilience</u>

The Chinese (Hong Kong) version of the Depression Anxiety Stress Scale (DASS-21) will be used as a measure of psychological stress[25]. It is widely used in the measurement of depression, anxiety and stress. This self-reported questionnaire has three subscales corresponding to depression, anxiety and stress. Each of the three subscales includes 7 items. Patients are asked to rate each item on a 4-point scale (0 to 3) based on their experience during the past week. The scores on DASS-21 are multiplied by 2 to calculate the final subscale scores, producing a maximum of 42 points in each subscale. The higher the score, the greater the severity of depression, anxiety and stress. DASS-21 will be measured at baseline and upon completion of prehabilitation.

Nutritional outcomes

Nutritional status before and after prehabilitation will be measured using body weight, BMI, muscle mass and percentage body fat. Dietary assessment will be performed using 3-day food record. Patients will be asked to record all foods and beverages consumed over a period of 3 days. The dietary intake adequacy relative to the expected individual requirement, the energy intake, and the amount of protein intake measured from the 3-day food record will be compared before and after prehabilitation.

Clinical outcomes

The length of hospital stay, in-hospital pulmonary complications, 30-day mortality and discharge destination (home, hospital or nursing aged-care facility) will be recorded. Pulmonary complications are defined using the NSQIP Definitions of Postoperative Complications (pneumonia, unplanned intubations, pulmonary embolism, failure to wean from the ventilator for more than 48 hours postoperatively)

Others

Other secondary outcome measures include the changes in hand-grip strength, time-up-and-go test and 30 second sit-stand test before and after prehabilitation.

Sample size and statistical analysis

According to a randomized controlled trial published 2014 that addressed the effect of prehabilitation in patients undergoing colorectal resection for cancer[27], the patients in prehabilitation group had their 6MWT distance significantly improved by 25.2m (SD 50.2) compared to baseline after 4 weeks exercise training, while those in control group declined by 16.4m (SD 46.0). Using a sample size calculator, a sample size of 46 will achieve 80% power to reject the null hypothesis with an effect size of 0.86 and a significant level of 0.05 using a 2-sided two-sample equal variance t-test.

Data will be analyzed using SPSS 26.0 software (SPSS, Inc, Chicago, IL, USA). Continuous variables will be presented as mean +/- standard deviation or median +/- interquartile range if not normally distributed. The Shapiro-Wilk test will be used to check data for normality. Categorical data will be shown as numbers and percentages. Comparison of continuous data will be performed with Student's *t* test with normal distribution and by Mann-Whitney U test for non-normally distributed data. Chi-square test will be used to compare groups with categorical variables. P value less than 0.05 is considered significant.

Ethics

Patients attended the prehabilitation clinic from August 2019 to November 2021 were included in this retrospective study. Data will be kept confidential in secure offices of the Department of Anesthesia and Intensive Care, Prince of Wales Hospital. Ethics approval will be obtained from the Joint CUHK-NTEC Research Ethics Committee. The study will adhere to local laws and the Declaration of Helsinki.

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