Prehabilitation Telemedicine in Neoadjuvant Surgical Oncology Patients During the Novel COVID-19 Coronavirus Pandemic

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Running Head:
Pandemic Prehabilitation
MINI-ABSTRACT

In the setting of the novel COVID-19 pandemic, prehabilitation may support cancer patients who are receiving neoadjuvant therapy prior to anticipated surgery. Recommended “social distancing” among these immunocompromised patients may decrease their physical activity and increase the risk of cardiopulmonary deconditioning and sarcopenia, in addition to the psychosocial stress of a cancer diagnosis, predicted future surgery, and community withdrawal. The resultant cascade of physiologic and psychosocial deterioration can result in increased surgical risk. A multimodal, home-based, virtual prehabilitation program that could be delivered through telemedicine has the potential to counteract these effects.
Prehabilitation involves health optimizing interventions aimed at enhancing patients’ ability to tolerate an upcoming stressor. Surgical prehabilitation is typically multimodal and has been shown to enhance health and treatment outcomes. In the setting of the novel COVID-19 pandemic, prehabilitation may counteract the unintended sequelae of “social distancing” that may result in decreased cardiopulmonary fitness arising from increased sedentary behavior, theoretically leading to increased morbidity and mortality, particularly in patients with advanced age or medical frailty. Notably, among a subgroup of Italian fatalities, approximately 20% of patients infected with COVID-19 had active cancer. In addition, guidance related to nutrition and maintenance of psychologic health is impacted due to reduced availability of in-person visits with oncologic providers. Prior to the COVID-19 pandemic, our group was conducting a registered phase II clinical trial (NCT0386587) on the feasibility and benefits of prehabilitation during neoadjuvant therapy prior to surgical resection in patients with pancreatic ductal adenocarcinoma. Since pausing the trial, we turned our attention to supporting patients through telemedicine platforms. Here, we report our adaptive response to pandemic-related prehabilitation barriers using a virtual platform.

Neoadjuvant Therapy During the Pandemic

In addition to the aforementioned cardiopulmonary deconditioning that may occur with social distancing, other complicating factors that have arisen in the setting of COVID-19 include changes to neoadjuvant protocols that are extended to keep patients out of the hospital for their own safety and to preserve valuable hospital resources. Changes to neoadjuvant therapy implemented at our institution include, but are not limited to, increased number of cycles of neoadjuvant chemotherapy over an extended duration and increased referrals for neoadjuvant therapy rather than upfront surgery in cases of upfront resectable tumors. By delaying “elective” operations and increasing the neoadjuvant treatment period, patients may encounter additional physiologic deterioration as a result of prolonged cytotoxic therapy.

Neoadjuvant therapy is known to be associated with a reduction in physical activity and increase in sarcopenia. Sarcopenia itself may result in decreased overall survival. Specifically, among patients with gastrointestinal cancers, the risk of malnutrition due to the disease process and side-effects of treatment poses a real danger. In a pandemic, however, malnutrition may be compounded by reduced access to healthful foods, which can further complicate patients’ nutritional status.

A Telemedicine Home-Based Prehabilitation Program

In response to the COVID-19 pandemic, we have developed a home-based prehabilitation program following evaluation of our preliminary trial results. The program we describe here may be considered for patients who are undergoing neoadjuvant therapy while awaiting surgery during the current pandemic. The proposed multimodal intervention, consisting of a standardized fitness program, nutrition...
supplementation, smoking cessation, and mindfulness practice, could be extrapolated for all oncologic patients awaiting eventual surgical intervention following the COVID-19 pandemic.

Our multidisciplinary team at the Massachusetts General Hospital (MGH) consists of physicians in the oncologic disciplines and physical medicine and rehabilitation. In addition, the team includes providers specializing in physical therapy and cancer nutrition.

**Exercise Intervention**

Patients receiving neoadjuvant treatment prior to surgery are screened by a physician to determine if it is safe and feasible to participate in home-based training. Safety considerations are based on established exercise-oncology guidelines. If a patient is deemed appropriate for referral to the prehabilitation program, patients complete a virtual baseline assessment for placement into a fitness tier (basic, intermediate, or advanced) that informs the exercise prescription (Figure 1). Evidence on the validity and reliability of virtual fitness testing is limited. However, under COVID-19 circumstances where patients would not otherwise receive care, we have employed the well-validated and simple 30-second Sit-to-Stand (30StS) test for home-based self-assessment to triage patients into the fitness tiers. The established tiers in Figure 1 were constructed from preliminary data from our clinical trial that demonstrated variance in patient fitness capacity based on these cut-offs. Participants in each tier are encouraged to complete 3 sessions per week for as long as the social distancing restrictions apply.

Using the 30StS scores, the patient is provided a “whole body” exercise prescription developed by a licensed cancer exercise specialist. This whole body approach is critical in the setting of inactivity and during neoadjuvant therapy to mitigate the effects of muscle wasting on core muscle groups. Each exercise tier is comprised of a 10-minute cardiovascular warm-up, followed by 20 minutes of cardiovascular endurance training, and ending with 30 minutes of resistance and flexibility exercises. Clinicians should use their judgement, based on patient symptoms, comorbidities, and home-settings, to modify aspects of this suggested regimen for individual patients. Cardiovascular endurance exercises are modified according to patients’ needs and living situation, and outdoor exercise (e.g., walking) is encouraged for added psychological benefit, provided social distancing criteria are met. Target intensity of exercise is based on the American College of Sports Medicine (ACSM) recommendations for cancer survivors. The ACSM guidelines recommend cancer patients exercise to 60-85% HR reserve for cardiovascular endurance exercises and a HR of 60-70% per repetition for resistance exercises. The exercise prescriptions are intended to require minimal or no fitness equipment, but can be included if available to the patient without attending a public/shared fitness facility.

Resistance training includes body weight, resistance band, or free-weights exercises that target the large upper and lower body muscle groups, as well as core stability (Supplemental Table 1). In the absence of free-weights, different objects in the home may be used if they can be safely held and provide the requisite training stimulus (e.g. full water bottles, cans, or cloth bags with sufficiently heavy contents). Flexibility exercises such as stretching target major muscle groups activated during the exercise. If available,
participants are encouraged to use their physical activity trackers and associated health apps. Smartphones are nearly ubiquitous and often have built-in technology that can track steps and/or heart rate, as well as support apps to log the details of exercise bouts.

**Nutrition Intervention**

In addition to a nutritious diet, it is important for patients to account for glycemic control and enhance protein intake. Glycemic control is important in mitigating infections while increased protein intake provides the building blocks during muscle conditioning. Prehabilitation research suggests that whey and/or plant-based protein supplementation may be helpful, and assuming there are no contraindications, we suggest that patients consume a daily supplemental protein intake of 30g in addition to their normal dietary intake. While daily consumption is optimal, our trial data demonstrated that daily compliance may have been an issue based on preliminary reports. Therefore, a more realistic goal to be sustained over months is to consume this supplement 4 times per week rather than daily. The specific supplement of use can be determined on an individual basis by the treating physician or licensed dietitian/nutritionist to meet the unique needs of each patient and to promote compliance.

**Smoking Cessation**

Substance abuse can undermine conditioning, tolerance of therapy, and prehabilitation at a time of increased anxiety and heightened stress. Social distancing can be either a positive or negative influence in the attempt to help patients quit smoking in the setting of a newly diagnosed illness. One can anticipate that a pandemic may result in reduced access to and income for cigarette purchasing, and it is likely that some patients may increase their smoking while others may aim to decrease it or even be amenable to cessation altogether. Therefore, virtual oversight of the use of tobacco products (and also alcohol as well as other substances) with individualized health advice (e.g., smoking cessation or alcohol reduction) from the treating physician at each telemedicine oncology visit is paramount at this time. Smoking cessation is imperative for optimal surgical outcomes. Therefore, appropriate advice and medical intervention (including medications that can be e-prescribed and symptoms monitored virtually) may be helpful.

**Mindfulness**

Increased stress is common in cancer patients under usual circumstances. However, in this global pandemic, patients now have the added uncertainty of how their cancer and overall health will fare and whether delays in care may result in detrimental outcomes. Encouraging stress reduction interventions is best practices in general, and may provide an added benefit during this particularly challenging time. There are many types of interventions such as meditation, guided imagery, yoga, etc. Many mindfulness platforms exist free-of-charge online and can be tailored to individual patient preferences.

**Risks to Participants**

As noted, physicians should provide initial evaluations and appropriate follow up for all oncology patients throughout the pandemic. Although many studies have documented that exercise in cancer survivors, even those undergoing neoadjuvant therapy, is safe, caution is still warranted, particularly given the reduction in
direct supervision. Before commencing exercise sessions, patients should be instructed to be mindful of any significant changes in symptoms (e.g. excessive shortness of breath) or the presence of new symptoms (e.g. chest pain), to determine if patients should engage in exercise on a given day. Common side-effects include muscular fatigue and soreness, as well as transient increases in treatment-related symptoms. Rarer risks include the possibility of injury due to unknown bone metastases or acute cardiac events in conjunction with cytotoxic therapy. Intensity and acute changes in symptoms should be closely monitored and reported.

In conclusion, a structured multimodal virtual prehabilitation program for cancer patients during the COVID-19 pandemic may help promote optimal outcomes during neoadjuvant therapy and better prepare them for future surgery. The unique availability of time and social distancing provides a distinct opportunity to improve patients’ health by optimizing cardiopulmonary reserve, skeletal muscle mass, nutritional status, and mental well-being. A virtual prehabilitation intervention would focus on modifiable predictors of outcomes and empower patients to regain control of their cancer.
ACKNOWLEDGEMENTS

NMS was supported by the NIH T32 Research Training in Aging grant 5T32AG023480-14. The NIH had no involvement in study design; collection, analysis or interpretation of data; writing of the report; or decision to submit the article for publication.
REFERENCES


Figure 1. Example of a Multimodal Prehabilitation Program for Oncology Patients Undergoing Neoadjuvant Therapy
**30 second Sit-to-Stand Test**

**Technique:**
Place a sturdy chair against a wall to utilize during the test. The patient begins seated in the middle of the chair, back straight with feet placed on the floor. The patient’s arms are crossed and held against their chest. At the sound of the timer, the patient is to rise to a full stand and then return back to the initial seated position.

The patient is to complete as many full stands as possible within a 30-sec time limit. The patient is required to be fully seated between each stand. Incorrectly executed stands are not counted.

<table>
<thead>
<tr>
<th>Results</th>
<th>Tier 1: Beginner</th>
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| 1-11 stands | **Resistance Exercises:**  
| Tier 2: Intermediate |  
| 12-24 stands |  
| Tier 3: Advanced |  
| 25 and above |  

<table>
<thead>
<tr>
<th>Tier 1: Beginner</th>
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| 10 min Warmup  
| 20 min Cardiovascular  
| Walking  
| 30 min Resistance  
| 2 to 3 sets of 12 repetitions  
| No weights, body resistance only  
| Resistance Exercises:*  
| Abdominal Bracing  
| Supine Retraction  
| Seated Knee Raises  
| Side Leg Lift  
| Standing Hamstring Curl  
| Triceps Kickbacks  
| Wall Pushup  

<table>
<thead>
<tr>
<th>Tier 2: Intermediate</th>
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| 10 min Warmup  
| 20 min Cardiovascular  
| brisk Walking  
| Elliptical or Stationary Bike  
| 30 min Resistance  
| 3 sets of 12 repetitions  
| 5 pound weights or equivalent  
| Resistance Exercises:*  
| Bridge  
| Chest Press  
| Hip Abduction to Adduction  
| Lying Triceps Extension  
| Modified Plank  
| Row  
| Sit to Stands  

<table>
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<tr>
<th>Tier 3: Advanced</th>
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</table>
| 10 min Warmup  
| 20 min Cardiovascular  
| Jogging  
| Elliptical or Stationary Bike  
| 30 min Resistance  
| 3 sets of 12 repetitions  
| 5 to 10 pound weights or equivalent  
| Resistance Exercises:*  
| Lying Triceps Extension  
| Plank  
| Push Up  
| Reverse Lunge  
| Row  
| Single Leg Bridge  
| Squats  

**Nutrition Supplements**

There are many commercial products for whey and plant-based protein supplements. Shakes, protein bars and other products may contain high levels of sugar, which may adversely affect glycemic control. Protein powders can be added to a variety of regular foods that a patient consumes.

**Smoking Cessation Medications**

| Varenicline (Chantix/E)  
| Day 1 – 3: 0.5 mg tablet once daily  
| Day 4 – 5: 0.5 mg tablet twice daily  
| Day 6 – 12: 1 mg tablet twice daily | nicotine patches (Nicoderm)  
| > 10 cigarettes per day  
| 21 mg patch once daily x 6 weeks followed by  
| 14 mg patch once daily x 2 weeks followed by  
| 7 mg patch daily x 2 weeks  

| Bupropion (Zyban/E)  
| Day 1 – 3: 150 mg tablet once daily  
| Day 4 – Week 12: 150 mg tablet twice daily |  
| ≤ 10 cigarettes per day  
| 14 mg patch once daily x 6 weeks followed by  
| 7 mg patch daily x 2 weeks  

**Stress Reduction Strategies**

There are many different strategies available and compliance is often based on patient preference. Free electronic apps are available for meditation, guided imagery, and other mindfulness interventions.

* Complete descriptions of each intervention can be found in Supplemental Table 1.

**Note**: The information contained in this figure is designed to be an example of a multi-modal rehabilitation program in an immunocompromised nononcology patient population. In clinical care, whether through virtual or in-person visits, rehabilitation interventions should be individualized and based on the patient’s current health status and upcoming surgery or other treatments. Safety is always a priority, and there is no substitute for accurate clinical judgement.
### Supplemental Table 1. Descriptions of Prehabilitation Exercises

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Abdominal Bracing</td>
<td>Begin either seated or lying flat. Place your hands on your abdomen. First inhale, then as you exhale, flex your abdomen so that it pushes your hands away with your muscles. Hold for 5 seconds. Release and repeat.</td>
</tr>
<tr>
<td>Bridge</td>
<td>Start by lying on your back with the knees bent and feet flat on the floor. Push from your heels as you lift your hips towards the ceiling, raising your back off of the floor until shoulder level. Slowly lower your hips back to resting position. Repeat.</td>
</tr>
<tr>
<td>Chest Press</td>
<td>If utilizing body weight or free-weights, begin by lying flat upon the floor. Start by abducting your shoulders by 90 degrees and positioning your elbows in an upright position, with your forearms at a 90 degree position to your upper arms against the floor. Hold one weight in each hand. Exhale and press your arms forward, extending your arm fully until there is only a small bend in the elbow. Inhale and bend the elbows back to a neutral position against the ground. Repeat. If using a resistance band, you may rather position yourself sitting upright in a chair. The middle of the band should be placed behind the chair with each end of the hand held firmly in each hand. Perform the same motions as described above.</td>
</tr>
<tr>
<td>Hip Abduction to Adduction</td>
<td>Begin by standing either behind a chair or facing a wall. Utilize either the chair or wall for support. Begin the exercise by extending your right leg laterally, out to the side, as far as is comfortable. Slowly bring the leg back towards center and continue extending it across your body. This is one repetition. Repeat both outward and inward motions for a full set before switching legs.</td>
</tr>
<tr>
<td>Lying Triceps Extension</td>
<td>Start by lying flat against the floor. If using weights, place one in each hand. Begin with the arms extended forward from your shoulders and with your elbows bent towards your head at 90 degrees. As you inhale, bend your elbow further so that your hands +/- weights come behind your ears. Then, as you exhale, extend your arms fully until there is only a small bend in the elbow. During this motion, it is imperative to keep your shoulders still, will all ranging coming from the elbow. Repeat.</td>
</tr>
<tr>
<td>Modified Plank</td>
<td>Begin by lying flat on your stomach with your elbows directly under your shoulders and your forearms flat on the ground. As you exhale, lift only you abdomen, leaving your knees on the ground. Distribute your weight between your elbows and knees. Keep your back straight and core muscles flexed while holding this position for 30 seconds.</td>
</tr>
<tr>
<td>Plank</td>
<td>Lie flat on your stomach. Place your forearms directly under your shoulders so that they lie flat on the ground. Exhale and lift your torso and legs off the ground. Distribute your weight between your feet and forearms. Keep your back straight and core muscles flexed while holding this position for 30 seconds.</td>
</tr>
<tr>
<td>Exercise</td>
<td>Description</td>
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<tr>
<td>Push Up</td>
<td>Begin in a plank-like position that is modified so that your arms are extended fully so that only your hands and toes are touching the floor. Place your arms directly underneath your shoulders. Your weight should be evenly distributed onto your hands and toes. While keeping your back straight, bend at the elbows as far as you can, but not past 90 degrees. This should lower your chest towards the ground. As you exhale, extend your arms back to the starting position.</td>
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<tr>
<td>Reverse Lunge</td>
<td>Begin by standing with your feet shoulder-width apart. Step one foot backwards while bending at both the front and back knees so that they are each at 90 degree angles. Ensure that the knee of your front leg does not bend past the toes. Exhale and push through your front foot to return to a standing position. Repeat this motion on one leg for the set, then switch legs. Weights may be held in each hand if desired.</td>
</tr>
<tr>
<td>Row</td>
<td>In a standing position, lean forward towards the floor while keeping your back straight and flexing at the hips. If you choose to use a resistance band, place the middle of the band underneath your feet and grasp the ends. Begin with your arms extended forward, then pull your elbows backwards as you exhale. Keep your elbows next to your body as you pull, bringing your shoulder blades together. As you inhale, extend your arms back to the neutral position.</td>
</tr>
<tr>
<td>Scapular Retraction</td>
<td>Start in a seated position with your elbows bent and arms facing forward. As you exhale, squeeze your shoulder blades together. Hold this position for 3 seconds. Slowly return to the neutral position. You may hold a resistance band between your hands for increased resistance.</td>
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<tr>
<td>Seated Knee Raises</td>
<td>Begin in a seated position with the feet shoulder-width apart. Slowly lift your right knee up to a height approximately at your navel. Then slowly lower your foot back to the ground. Repeat this exercise with one leg for one set and then switch.</td>
</tr>
<tr>
<td>Side Leg Lift</td>
<td>Begin by standing either behind a chair or facing a wall for support. Slowly lift your right leg out to the side while keeping your upper body completely still. Return your leg to neutral. Repeat for a set before switching legs.</td>
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<tr>
<td>Single Leg Bridge</td>
<td>Start by lying against the floor with your knees bent so that your feet are flat. Extend one leg outwards so that it is completely straight. Lift this leg off of the ground and hold the leg in place. With your bent leg, slowly push your heel into the ground so that your hips up lift off of the ground towards the ceiling. Slowly lower your hips to the ground. Repeat.</td>
</tr>
<tr>
<td>Sit to Stands</td>
<td>Begin seated in a chair with your feet shoulder-width apart. Place your arms across your chest. Utilize your core and leg muscles to push from your heels to stand upright. Slowly lower yourself back to a seated position. Repeat.</td>
</tr>
<tr>
<td>Squats</td>
<td>Start in a standing position with your feet shoulder-width apart and your arms across your chest. As you inhale, bend at the knees to lower your body into a seated position. Your hips should push backwards with this motion. Do not allow your knees to come forward past your toes. As you exhale, push through your heels to return to a neutral standing position. Repeat. Weights may be used if desired.</td>
</tr>
<tr>
<td>Standing Hamstring Curl</td>
<td>Begin standing behind a chair, holding the back of the chair for stability. Bend your right knee so that your foot raises off the ground until your knee is at 90 degrees. Lower your leg to neutral. Repeat for one set before switching legs.</td>
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<tr>
<td>Triceps Kickbacks</td>
<td>It is best to use light weights or water bottles for this exercise. Begin seated in a chair. Lean forward, bending at the hips. Hold a weight in each hand and bend your elbows upwards to 90 degrees, while keeping your elbows next to</td>
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<tr>
<td><strong>Wall Pushup</strong></td>
<td>Stand facing a wall with your feet approximately 6 inches away. Keeping your feet in one position, lean forward so that your hands are placed shoulder-width apart against the wall. Slowly bend at the elbows, bringing your body closer to the wall. As you exhale, push your body away from the wall, back to the starting position. Repeat.</td>
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