4-2011

Safety of Physical Therapy Using Symptomatic Blood Value Guidelines in Children Being Treated for Cancer

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SAFETY OF PHYSICAL THERAPY USING SYMPTOMATIC BLOOD VALUE GUIDELINES IN CHILDREN BEING TREATED FOR CANCER

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April 27, 2011

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Abstract

Background and Purpose: The guidelines set forth by the American Physical Therapy Association (APTA) contraindicate exercise when hemoglobin blood values are <8 g/dL, platelets are <20,000/*m*L, or white blood cells (WBCs) are <5,000/mm^3 accompanied by a fever. The purpose of this study was to determine if APTA hematological guidelines are appropriate for determining activity levels in children undergoing chemotherapy. The guidelines were initially established for patients with acute changes in blood values, but it has been questioned if these guidelines are appropriate for populations with chronically low blood values such as children with cancer.

Methods: A retrospective chart review was done using a consecutive sample of children with cancer being seen for physical therapy (PT) while undergoing chemotherapy. A maximum of four PT sessions per child were included for a total of 201 chart reviews. Subject's hemoglobin, platelet, and WBC values were recorded within 24 hours of a PT session. Interventions and modifications to PT treatment were documented. The patient's chart was reviewed for two days following the PT visit and any critical incidences as defined by the researchers were recorded.

Results: Participants included 33 males and 40 females ranging in age from 3 to 18, with a mean age of 9.5 years. The most common cancer diagnoses were acute lymphoblastic leukemia, Wilms' tumor, and osteosarcoma. A Fisher's exact test showed no significant relationship between low hemoglobin, low platelets, or low WBCs and number of critical incidences (2.56, p = 0.196; 0.198, p = 0.776; 0.501, p = 0.444 respectively). A risk ratio of critical incidences in patients with low blood values versus normal blood values was

found to be 4.3 (CI 0.58 – 32.30) for low hemoglobin, 0.79 (CI 0.29 – 2.20) for low platelets, and 0.64 (CI 0.19 – 2.17) for low WBCs.

Conclusion: Results suggest there was no statistically significant evidence indicating children with chronically low platelets or WBCs were at greater risk for incidences when compared to normal values. In patients with low hemoglobin values there was an increased risk for minor events such as tachycardia. This supports our original hypothesis that a symptom-based approach in determining appropriateness for PT may be utilized in populations experiencing chronically low blood values.

RESEARCH ADVISOR FINAL APPROVAL FORM

The undersigned certify that they have read, and recommended approval of the research project entitled…

SAFETY OF PHYSICAL THERAPY USING SYMPTOMATIC BLOOD VALUE GUIDELINES IN CHILDREN BEING TREATED FOR CANCER

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In partial fulfillment of the requirements for the Doctor of Physical Therapy Program

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Table of Contents

Chapter I

Introduction: Literature Review

When deciding whether or not it is safe to work with a patient, a review of lab values is performed to rule out any critical values that may caution or contraindicate mobilization of a critically ill patient. According to the guidelines put together by the acute care section of the American Physical Therapy Association (APTA) for hematological blood values in particular, these values include: normal white blood cell (WBC) count 4,500-11,000/mm^3 in adult males and females, normal platelet count of 150,000-350,000/*micro*L in adult males and females, and normal hemoglobin (Hgb) 14.4-16.6 g/dL in adult males and 12.2-14.7 g/dL in adult females.[1] Within the article that outlines these normal values it is suggested that therapists do not proceed with exercise if WBC count is less than 5,000/mm^3 and is accompanied by a fever, if Hgb is less than 8 g/dL, or if platelets are less than 20,000/*micro*L.[1]

These guidelines are ambiguous when it comes to pediatric clients. Pediatric values were not specified in any APTA acute care document, however it was noted that they will vary from birth to 15 years old. An online pediatric care resource outlines that normal WBC count in children ranges from 5,500-15,500/mm^3 for those two to five years of age, 5,000- 14,500/mm^3 for those five to eight years, 4,500-13,500/mm^3 for those nine to twelve years of age, and 4,500-13,000/mm^3 in those 13 to 18 years of age.[2] Platelets should range from 150,000-550,000/mm^3, and hemoglobin should be within 11.5 to 15.5 (g/dL).[2] Children's Hospitals and Clinics of Minnesota, the site at which this particular study was conducted, follow these guidelines for WBC count and hemoglobin, with the

exception of 13-16 g/dL as normal hemoglobin for males and 12-16 g/dL as normal for females in the 13-18 year age range. Normal platelets for a child of any age at Children's Hospital of Minnesota range from 250,000-450,000/mm.[3]

Although the guidelines have been in place for many years, evidence for their use is lacking. In fact, no randomized controlled trials were used to establish these normative values. The lab value guidelines given for adults were compiled by a task force of the Acute Care section of the national APTA. They used several acute care textbooks for physical therapists, guides on the interpretation of laboratory tests and critical lab values, and lab value reference books to determine their guidelines.[3] Examining statistics however, may provide further explanation of how these normal values came into existence.

Erstad[4] notes that "normal" lab values are determined by whether the value falls within a normal, bell-shaped curve. He notes that there are people outside of two standard deviations from the mean of a lab value who are still considered healthy individuals. He cautions, along with authors from several other articles, that laboratory values should not be examined in isolation.[1,4,5,6,7] People have died with "normal" lab values, and people have lived perfectly normal lives with "abnormal" lab values. In addition lab values considered "abnormal" may be "normal" for a particular patient. Irion[5] states in his article that therapists should "…use good clinical judgment, communication with other healthcare providers, and monitor[ing] the responses of patients to therapy, rather than follow published guidelines." Thus, there is a consensus among the articles reviewed that laboratory values should not stand alone in determining

whether or not to mobilize a patient, but instead many other factors should also be considered.[5,6,7]

Stiller et al.[6,7] suggests many ways therapists may decide if a patient is safe to be mobilized, including objective and subjective factors. Objective factors include heart rate (HR), blood pressure (BP), rate pressure product (RPP), cardiac status, oxygenation, respiratory pattern, presence of mechanical ventilation, hemoglobin, platelet count, white blood cell count, fever, and blood glucose level. Subjective considerations include the patient's facial expression, emotional state, level of pain, level of anxiety, pallor, rate of perceived exertion (RPE), diaphoresis, and overall physical appearance. Other factors that should be included are whether the patient has any orthopedic precautions, level of cognition, incisions, risk or presence of deep vein thrombosis, nutritional status, as well as the presence of various lines and tubes. These guidelines in conjunction with clinical judgment, reasoning, and experience should help in determining when critically ill patients are appropriate for mobilization.[12,13,15]

There are many physiological reasons behind why we may not mobilize a patient with abnormal blood values. These abnormal blood values are indicative of blood disorders in patients with cancer as the result of chemotherapy and the presence of tumors.[1] Disorders include anemia, leukocytosis, leucopoenia, and thrombocytopenia. Each of these disorders has different implications for therapy when initiating mobilization of the critically ill patient.

Children with cancer, specifically leukemia or lymphoma (two of the most common types), have an increased risk of developing low hemoglobin. This is in part

due to the destruction of red blood cells when these diseases cause the immune system to produce anti-bodies that clump red blood cells together. These clumps of red blood cells are then recognized by the body as foreign and are destroyed.[8] These and other pediatric cancers also often attack the child's bone marrow where red blood cells are made and replace it with fibrotic tissue, or radiation destroys bone marrow stem cells.[8] Chemotherapy drugs also can lower the amount of healthy blood cells, as these drugs are cytotoxic and not specific to only the tumor cells.[8]

Hemoglobin is the predominant oxygen-carrying protein within red blood cells. A low red blood cell count due to a change in the quantity or quality of red blood cells and thus a decrease in the oxygen carrying capacity of the blood is defined as anemia.[8] Therefore, low levels of hemoglobin correspond with a decreased amount of oxygen available to the tissues of the body and often result in anemia.

Exercising a patient with anemia places increased oxygen demands on the body and causes the heart rate to increase. An increase in heart rate can lead to tachycardia, with accompanying fatigue, generalized weakness, loss of stamina, and shortness of breath.[8] Tachycardia can lead to dysrhythmias, which rarely but sometimes can lead to sudden cardiac arrest.[8] One study by Unverferth et al. found an increase in cardiac dysrhythmias recorded on a Holter monitor for patients with cancer who exerted themselves two to six hours following chemotherapy.[9] This study recommended patients undergoing chemotherapy do not exercise within two to six hours following treatment.

One way to determine whether or not a patient has anemia and the severity of anemia is to examine hemoglobin values. Exercise is contraindicated if Hgb is below 8

g/dL. Light exercise is permitted if Hgb ranges from 8-10 g/dL, and Hgb >10 allows for the patient to attempt resistive exercise according to APTA guidelines.[1]

Leukocytosis is the presence of high levels of white blood cells (> 11,000/mm^3), indicating likely presence of infection or fever.[1,5,6] Acute infections and fever often place greater oxygen demands on the body, and therefore, it is important to carefully monitor oxygen saturation levels, respiratory rate, and rate of perceived exertion during therapy.

Leucopenia is the result of an abnormally low WBC count (< 5,000/mm^3), often due to the toxic effect chemotherapy drugs have on these cells. A patient with a low white blood cell count may be at an increased risk for infection and fevers, leading to increased oxygen demands on the body; thus requiring the same precautions as above.[7,8] According to the APTA guidelines, if the WBC count is less than 5,000/mm^3 and accompanied by a fever, exercise is contraindicated. If WBC count is greater than 5,000/mm^3 the patient can participate in light exercise, which can progress to resistive exercise.[1]

Thrombocytopenia is low platelets (< 150,000/*micro*L) in the blood, indicating an increased risk for spontaneous bleeding and decreased ability for the bleeding to clot. Platelets are also made in the bone marrow and can be destroyed by chemotherapy and radiation. Patients with very low platelet counts are at high risk for vascular trauma and bleeding as a result of activity or significant increases in blood pressure.[12,13] Patients with this disorder may present with ecchymosis or purpura spots. According to the APTA guidelines, exercise is contraindicated in patients with a platelet count of less than 20,000/*micro*L. Between 20,000 and 50,000/*micro*L light exercise such as active range

of motion is permitted. If the platelet count is greater than 50,000/*micro*L, resistive exercises can be attempted.[1, 7]

APTA Exercise Guidelines

Hemoglobin: <8: No exercise permitted 8-10: Light exercise permitted >10: Resistive exercises permitted
Platelet Count: <20,000: No exercise 20,000-50,000: Light exercises (no PROM, but light AROM is permitted) >50,000: Resistive exercises permitted
WBC: <5000 with fever: No exercise permitted >5000: Light exercise, progress to resistive exercise permitted

Research and data regarding the risks of exercise and mobility for patients with a cancer diagnosis suffering from the above blood disorders continue to be lacking.[8] Some physicians recommend abstaining from or minimizing amounts of physical exercise due to the increased risk of bleeding and tissue damage in patients with low hemoglobin and platelet blood counts. However, according to Stiller et al.[6] chronically low blood values for a particular patient should be treated differently than an acute change. Chronically low blood values may be seen with some kinds of chronic diseases, such as chronic renal failure.[7] If a patient has been living stably with chronically abnormal lab values it has been the practice of many physicians to allow physical activity in order to prevent the deleterious results of bed rest and inactivity. These deleterious effects include: muscle weakness, decreased muscle endurance, negative nitrogen balance, pneumonia, thrombosis, kidney stones, increased diuresis, orthostatic hypotension, cardiovascular

deconditioning, skin breakdown, depression, fatigue, and decreased quality of life.[10] Therefore, it is important to weigh the possible risks and benefits of exercising a critically ill patient with abnormal blood values. There is a large body of research that has come out in the past two decades which highlights the benefits of exercise for critically ill patients, including our area of interest, patients with cancer.

To date medical professionals continue to debate the possible positive or negative effects exercise has on patients diagnosed with cancer.[14] As mentioned above, it has been theorized that vigorous exercise may be harmful for patients with cancer; however, no literature supports this notion. In a review of literature regarding early exercise therapies for patients with a cancer diagnosis, 16 of out 18 intervention studies and five out of six descriptive studies documented statistically significant results for various quality of life outcome measures. Four meta-analyses and two systemic reviews on the effects of exercise and aerobic capacity, fatigue, and quality of life in patients with cancer were also found.[19] The meta-analyses and systemic reviews on exercise and patients with cancer revealed 12 studies on exercise capacity, 14 on fatigue, and 19 studies regarding the physical quality of life. Nine randomized control trials looked at the effects of exercise training on muscle strength. A large amount of evidence from these studies supports the positive effects of exercise on physiological outcomes during and after cancer treatments.[19] We were unable to find any studies examining the effects of exercise on children with cancer specifically, yet there are many studies of adult cancer populations that show exercise is beneficial, and therefore is likely beneficial in pediatric populations as well.

In accordance with the evidence that shows physical activity to have a positive impact on function, quality of life, and improving psychosocial well-being in patients with cancer undergoing treatment, the studies also revealed that increased physical activity after a cancer diagnosis reduces the risk of cancer reoccurrence and mortality.[19]

The literature has consistently shown that physical exercise following a cancer diagnosis improves quality of life.[16] Many of the physical and functional deficits as a result of cancer and its treatment are impacted by therapeutic interventions including exercise.[16,19] The literature also shows that exercise during and/or following cancer treatments prevents decline and can improve cardio-respiratory function, body composition, immune function, strength and flexibility, body image, self-esteem, and mood. Exercise can also decrease the number and severity of side effects, decreasing duration of hospitalization, and improving the likelihood for completion of chemotherapy treatment. Similar to findings by vanWeert et al.[19] the psychosocial benefits of exercise in patients with cancer include better adjustment to illness, reduction of stress, and decreased rates of depression and anxiety.[20]

Fatigue is one of the most common symptoms experienced after high dose chemotherapy, occurring in 70-90% of patients with cancer.[11,13] Patients describe fatigue as one of the most difficult symptoms to deal with during chemotherapy treatments, even more distressing than pain, nausea, or vomiting. The fatigue experienced is typically thought to be due to cancer related anemia from decreased hemoglobin levels as a result of chemotherpay.[11,13] As previously mentioned, when a patient is experiencing anemia inadequate amounts of oxygen are being delivered to peripheral tissues. This in turn can

lead to breathlessness, tiredness, and extreme fatigue. Other disadvantages of anemia include the need for blood transfusions, diminished energy, lethargy, sexual dysfunction, impaired concentration, impaired memory, and a decline in intellectual ability. This can lead to decrease in a patient's quality of life and reduce the motivation and desire to participate in exercise.[12]

The National Cancer Institute defines mild anemia as hemoglobin levels of 10-11 g/dL. Moderate anemia is defined to be hemoglobin levels between 8-9.9 g/dL, and severe anemia as 6.5-7.9 g/dL.[11] Mild-moderate anemia, although important to note, rarely has a negative impact on a patient's mortality, but has been associated with decreased quality of life and functional status.

As recommended by the APTA,[1] patients with hemoglobin levels between 8-10 g/dL are permitted to participate in light exercise. As physical therapists, this is an ideal time to help improve the quality of life and function of patients receiving chemotherapy and experiencing anemia. Evidence has shown that sedentary patients with breast cancer who have a reduced exercise tolerance report higher degrees of fatigue during chemotherapy treatments when compared to more active, physically fit patients.[13]

Exercise offers the strongest evidence for relieving cancer related fatigue.[2] There have been 11 published reports by four different research groups testing the impact exercise has on fatigue during high dose chemotherapy. Two additional studies have looked at the effects of exercise on patients after treatment has been completed. All 13 studies indicate significantly lower levels of fatigue in patients who exercised compared to sedentary controls.[13] Additional evidence has found physically active patients with

cancer to have lower resting heart rates, lower blood pressure, more energy, increased muscle strength, and improved restful sleep. Many patients undergoing high dose chemotherapy experience feelings of depression, stress, and anxiety.[20] Using exercise as part of rehab can help improve some of the negative psychosocial aspects often accompanying a cancer diagnosis. Although the benefits of exercise in patients with cancer related fatigue have been shown to be consistent across studies, the studies are limited in number of participants, methodology, and often only include women with breast cancer.[13]

The research shows that exercise can improve function, quality of life, and decrease fatigue in individuals with a cancer diagnosis. Exercise has also been found to be safe and improve function in patients with cancer who are critically ill with low blood count values.

Current research regarding decisions on when to mobilize patients in the intensive care unit (ICU) is limited. Mobility interventions for patients in the ICU have not received much attention. Despite the knowledge that exercise is beneficial for decreasing the effects of immobility, and that exercise helps patients return to previous level of functioning, the exact manner and guidelines regarding when to administer rehab treatment or safely administer mobility maneuvers to critically ill patients is not well understood.[6] Research shows improvement in mood, coordination, muscle strength, balance, and work tolerance when critically ill patients receive mobility therapy.[6] Several publications have shown a benefit to early exercise therapies for inpatient populations.[18] Inpatient rehab programs have been shown to benefit exercise capacity, lipid profiles,

weight changes, autonomic function, subsequent hospitalization costs, and cardiovascular morbidity and mortality.[25,19] Inpatients receiving early rehab therapy reported a greater than 50% reduction in depressive symptoms, and also demonstrated better function in activities of daily living (ADLs) after only one month.

Other existing views advise that exercise should only be initiated at the point of complete remission from cancer.[17] Although valuable to acknowledge prevailing advice for patients to rest and avoid intense exercise, this should not outweigh the risks of deconditioning and immobilization. A pilot study by Baker et al.[18] showed that 31 critically ill patients who took part in 69 rehab sessions were mobilized without any deterioration in their health status. Patients were deemed suitable for therapy based on guidelines set by Stiller et al.[6] These guidelines for mobilizing critically ill patients recommend that hemoglobin values be stable and >7g/dL, platelet counts stable and >20,000/*micro*L and white blood cell counts between 4,300-10,800/mm^3. If any blood value is not within these guidelines, appropriateness of mobilization should be discussed with another physical therapist or other medical professionals before deferment.[7,22]

Few research studies measure blood values during exercise interventions for patients with cancer. The research is even more limited when looking at studies that exercised patients with very low blood counts. We did not find any study that exercised patients with hemoglobin, platelets, or white blood cell counts much below recommended guidelines as set by the APTA. A study by Elter et al.[17] looked at the effects of aerobic training on patients with a cancer diagnosis undergoing high dose chemotherapy. The aerobic exercise consisted of three weekly bike ergometer trainings of 15-30 minutes at

sub-maximal intensity. The researchers monitored blood values and set guidelines as for when to discontinue treatment. When patients' platelets were >20,000/*micro*L without any sign of bleeding, they were allowed to proceed with the program but were under special precautions that blood pressure not exceed 170/100. Patients' whose platelets reached <10,000/*micro*L or hemoglobin levels <8g/dL necessitated a blood or platelet transfusion prior to continuation of aerobic training. By the end of the study, all trained subjects performed better on the final test. Sub-maximal endurance capacity also showed significant improvements for the training group during the period of hospitalization. Throughout the study, median platelet count was 27,000/*micro*L with a minimal count of 8,000/*micro*L. Hemoglobin values on average were 9.2g/dL with minimal blood values reaching 7.7g/dL.

Patients participating in aerobic exercise training were found to be more likely to complete the full intended number of chemotherapeutic treatments as compared to untrained patients.[17] The researchers in this study did not use previously set blood value guidelines for the continuation of physical activity. Instead they only judged patients' ability to participate in exercise based on clinical signs of bleeding. None of the patients in the study with platelet counts <10,000/*micro*L or hemoglobin values <8g/dL suffered bleeding or adverse reactions to exercise. Patients with severe active infection were not allowed to participate in exercise training. This study illustrated the positive effects exercise has on patients with cancer undergoing high dose chemotherapy. It also showed that for patients with cytopenia, aerobic exercise was safe and did not cause increase in bleeding.[17]

Dimeo et al.[21] looked at the effects of an interval training program on patients with cancer receiving high dose chemotherapy. Sixteen patients participated in a rehab program for six weeks and another 16 patients served as controls. Exercise treatments were held for 15-30 minutes at an intensity of approximately 80% of heart rate maximum. Physical function, cardiac function, and hemoglobin concentrations were measured at the time of discharge from the hospital and then again seven weeks later after the training intervention. At baseline, hemoglobin levels were 10±1.4g/dL for the training group and 10±1.2g/dL for the control group. After seven weeks, hemoglobin concentration was significantly higher in the training group, 13±1.0g/dL versus 12±1.4g/dL for the control group. There were no cardiac, infectious, or bleeding complications seen throughout the training program. To reduce the risk of bleeding or infections in the training group, patients in this study were not allowed to start training until their platelet counts were >20,000/*micro*L and leukocyte levels $>1.5x10^9/mm^3$. No adverse reactions were noted for any of the patients in the training group. Anemia was not a contraindication for inclusion in the training program. The researchers felt it was important to allow patients with anemia to participate in training due to the positive effects exercise has been shown to have on improving physical performance and hemoglobin levels in patients with cancer. Many patients with cancer suffer from anemia so defining this condition as a contraindication for the exercise program would exclude many patients from rehab at a time when they might benefit from it most.[21] The exercise program was shown to partially improve anemia in patients. All patients in the study had

stem cell transplantation, and the effect the aerobic training program would have had on the patients without stem cell transplantation remains unknown.

A study by Dimeo et al.[14] looked at the effects of aerobic exercise on patients with cancer. The treatment group took part in daily aerobic exercise programs consisting of biking with a bed ergometer for one minute at an intensity level of at least 50% of cardiac reserve. This was repeated 15 times with one minute breaks between exercise bouts for a total of 30 minutes each day. Patients with a fever >37.5 degrees Celsius or platelets $<10x10^9$/L were instructed to discontinue training until their fevers went away. Individuals who continued to have severe infections or multiple complications were not allowed to resume training. Patients were transfused when hemoglobin blood counts were <8g/dL or when platelets were $<20X10^9$/L. This study found the training group to have shorter duration of neutropenia 6.6±1.5 days versus the control group 7.6±1.6 days. The training group also required less platelet transfusions and was found to have shorter duration of thrombopenia (platelets $<50x10^9$/L) 10.9±3 days versus the control group 12.4±3.7 days. There were no complications in the patients who participated in rehab immediately after completing high dose chemotherapy. The aerobic exercise improved physical performance and reduced fatigue in patients. The researchers concluded that the severe loss of function often observed after high dose chemotherapy can be partially prevented with rehab exercises.

Stiller et al.[22] also looked at the effects of mobilizing critically ill patients with low blood values. Patients' baseline hemoglobin concentration had a mean value of 9.1±1.0g/dL and a range of 7-15.8g/dL. Baseline platelet values had a mean value of

301,000/*micro*L with a range of 42,000-742,000/*micro*L. White blood cell counts ranged from 4,400-20,100/mm^3 with a mean baseline value of 10,500/mm^3. In two of 69 sessions for mobilization, patients reported feeling dizzy but did not require any direct medical intervention, nor did it limit the treatment session. No change in the severity or frequency of cardiac arrhythmias was noted during mobilizations.[22] In three of 69 occasions, a deterioration in patients' condition required intervention. All three occasions were due to a fall in SpO_2. Although there was a low incidence of problems during the treatment mobilizations a comprehensive screening process was used to select appropriate patients for mobilization. The guidelines set by Stiller et al.[13] were used as parameters for mobilization. These included hemoglobin values stable and >7g/dL, platelet counts stable and >20,000/*micro*L and white blood cell counts between 4,300-10,800/mm^3. The low incidence of adverse reactions in this study suggests that guidelines by Stiller et al.[13] and utilizing clinical judgment to assist in deciding appropriateness of critically ill patients for mobilization is safe.

In another study, 20 patients with cancer undergoing bone marrow transplantation participated in a rehab program. The program consisted of treadmill walking according to an interval training protocol for six weeks. Each treatment session was approximately 30 minutes at an intensity 80% of heart rate maximum.[23] Inclusion criteria for the study included sustained platelet counts >20,000/*micro*L, absolute neutrophil count of $1x10^9$, and stable clinical condition. Throughout the six week training program, physical performance improved and no cardiac, infectious, or bleeding adverse reactions occurred. All patients reached a cardiovascular performance level that equates that of carrying out

all basic activities of daily living. Other studies have reported impaired physical functioning by patients participating in training programs after receiving bone marrow transplantation. No such evidence of this was found in this study, and instead, Dimeo et al.[23] observed patients gaining self-confidence, improved physical functioning, and improved mood, resulting in higher levels of independence and improved quality of life.

No evidence currently exists on the safety of exercise for pediatric patients with chronically low blood values due to cancer treatment. However, given the evidence that exercise may be appropriate for these patients, we decided to examine the safety of physical therapy treatment to see if any critical incidents occur when children with low blood values exercise versus children with normal lab values. Specifically, we looked at hemoglobin, white blood cell count, and platelet count in relation to critical events for a population of children receiving physical therapy at one site where the current practice is to set exercise parameters based on the symptom assessments of the attending physical therapists and not on the blood values guidelines. This situation gives us the unique ability to look at the safety of exercise in patients who may have chronically low blood values but are clinically stable.

Chapter II

Methods

For this study a retrospective chart review was performed. The subjects were a sample of 73 consecutive children diagnosed with a non-CNS cancer. The children ranged in age from 3 to 18 years and had received physical therapy while undergoing chemotherapy treatment at Children's Hospitals and Clinics of Minnesota. Subjects who

met the inclusion criteria and did not meet the exclusion criteria were selected consecutively by the lead researcher from the Children's Hospitals and Clinics of Minnesota pediatric oncology database. The inclusion criteria for subjects included a current diagnosis of a non-CNS cancer, a chemotherapy treatment time greater than or equal to two months (to ensure likelihood of chronic low blood values), were between 3 and 18 years of age, and had at least two sessions of physical therapy from Children Hospitals and Clinics of Minnesota. Subjects were excluded if they did not meet the inclusion criteria, had a previously diagnosed cardiac disorder, or if they had undergone a recent surgical resection.

For each subject, up to four physical therapy (PT) visits were identified in the electronic medical record and examined until 201 chart reviews were completed. Only physical therapy visits within 24 hours of a complete blood count were reviewed. The patient's hemoglobin, platelets, and white blood cell values were recorded once a qualifying (within 24 hours of a CBC) PT visit was identified, along with the type of interventions performed, the patient's subjective symptoms, and any modifications made by the therapist during treatment. The electronic medical record was then examined for two days following the PT visit for any critical incidents that may have occurred. The areas of the chart reviewed included hematology/oncology notes, nursing notes, and emergency department notes. Critical incidents were defined as: syncope, cardiac arrhythmia, low blood pressure, oxygen saturation <90%, shortness of breath, bradycardia, tachycardia (based on age-adjusted normal values), falls, pain, impaired skin integrity, fever, and negative patient subjective complaints. (See Appendix A)

Chapter III

Analysis/Results

Once the data was gathered, a Chi-square analysis was used to look for a correlation between critical incidents and chronically low hemoglobin, platelets, and white blood cells. For cases where Chi-square cells were <5, a Fisher exact test of significance was used. Risk ratio was also calculated in order to determine the relative risk of a critical incident following physical therapy intervention when subjects' blood values were low as compared to subjects with normal blood values.

The retrospective chart review included 201 physical therapy treatment sessions for a total of 73 patients. No more than four physical therapy sessions per child were analyzed with a mean number of 2.8 visits per child. The mean age was 9.5 years old and ranged from 3-18 years. The three most common cancer diagnoses were leukemia (60%), solid tumors (32%), and lymphoma (8%). Forty-five percent of the subjects were male and 55% were female. Approximately 14% of the subjects had had either a red blood cell or platelet transfusion in the past week. Fifteen percent of the patients were being seen for inpatient physical therapy, whereas 85.5% were seen in an outpatient setting.

The mean blood values for hemoglobin, platelets, and white blood cells taken within 24 hours of a patient's physical therapy treatment session were found (Table 1). The mean hemoglobin for this patient population was found to be 10.5 g/dL. The mean platelet value was 226.6 $x10^3$/*micro*L, and the mean white blood cell value was 3.5 $x10^3/mm^3$. According to the age adjusted blood count reference values from Children's

Hospitals and Clinics of Minnesota, the percentages of subjects whose values were normal versus abnormal were calculated (Table 1).

Table 1.
Mean blood values for the examined pediatric oncology population and percentages of normal and abnormal blood lab values (n=201)

	Hemoglobin (g/dL)	Platelets ($x10^3$/*micro*L)	White Blood Cells ($x10^3/mm^3$)
Mean	10.5+/-1.7	226.6+/-129.8	3.5+/-5.4
Normal	24.9%	37.3%	14.9%
Abnormal	74.6% 50.3% >10 39.9% 8-10 9.8% <8	62.7% 91.3% >50,000 3.1% 20,000-50,000 5.5% <20,000	85.1%

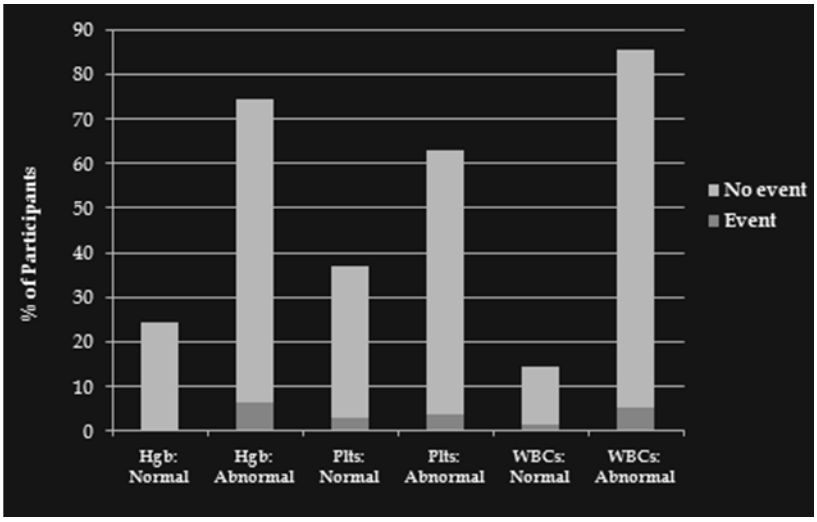
Abnormal hemoglobin and platelet values were divided further according to APTA guidelines for exercise. Ten percent of the patients had hemoglobin values of <8 and 5.5% of the subjects had platelet values <20,000 indicating no exercise permitted. It is important to note the low percentages of patients with normal blood values and the very high percentages of patients with abnormal blood values in this pediatric oncology population. More than two thirds of the pediatric oncology population receiving physical therapy at Children's Hospitals and Clinics of Minnesota had abnormal blood values. Very few patients had such low blood values that no exercise would have been recommended by the APTA guidelines.

Of the 201 patient charts reviewed, there were a total of thirteen critical incidents that occurred within two days following a physical therapy treatment session.

Approximately 6.5% of the patient population actually had a critical incident, as defined by the research study. The thirteen events included seven events of tachycardia, three subjective complaints of pain, two fevers, and one fall that occurred during the physical therapy session. There were no episodes of arrhythmia, syncope, hypotension, oxygen de-saturation less than 90%, shortness of breath, major bleeds, or skin integrity issues. Having a critical incident was very rare, and those that did occur were not severe enough to institute major medical attention. Seventy-six percent had no documented adverse symptoms during their physical therapy session. The remaining 24% had complaints of fatigue, pain, nausea, and/or shortness of breath. Physical therapy was modified accordingly in 5.5% of patient cases. These symptoms were not defined as critical incidents.

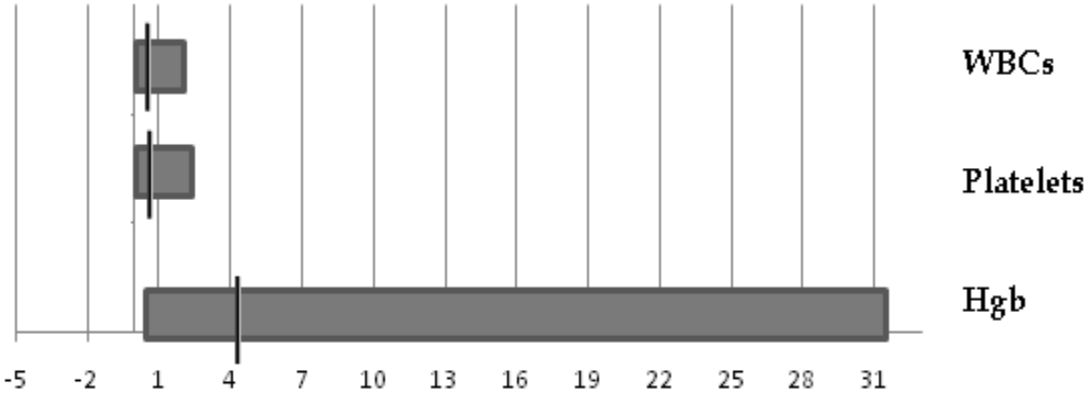
There was very little difference in the percentages of patients experiencing critical events when blood values were normal as compared to abnormal blood values (Figure 1). For example, 3% of patients with normal platelet values had a critical event, whereas 4% of patients with abnormal platelet values had an event. There was only a 6% difference in critical events between subjects with normal hemoglobin values and abnormal values. A Fisher's exact test showed no significant relationship between low hemoglobin, low platelets, or low white blood cells and the number of critical incidents. Chi-Square was 2.56 ($p= 0.196$), 0.198 ($p=0.776$), and 0.501 ($p=0.444$) for low hemoglobin, low platelets, and low white blood cells, respectively.

Figure 1.
Distribution of Critical Events in Patients with Normal versus Abnormal Blood Values



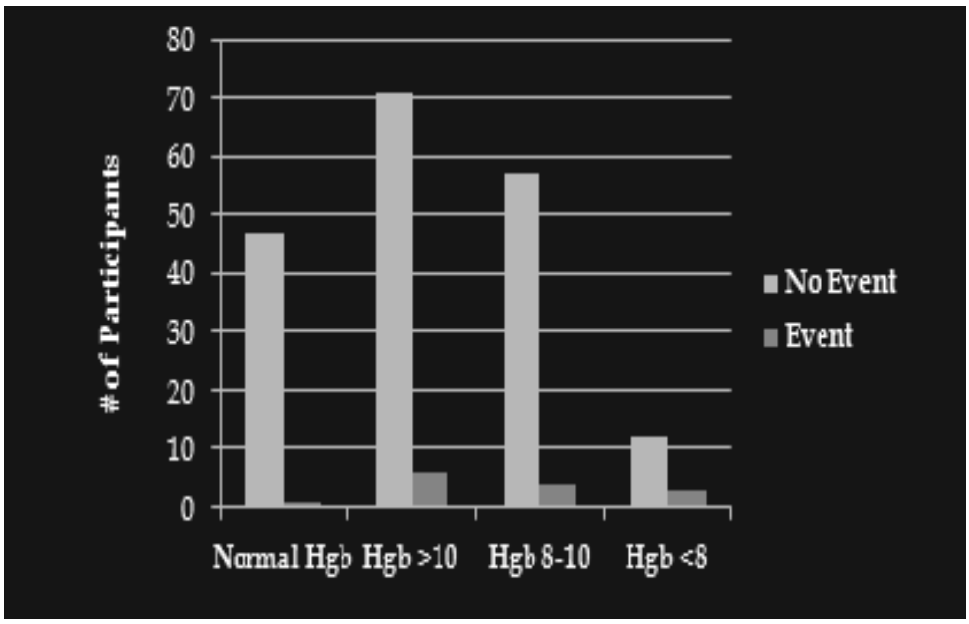
The risk ratio for low hemoglobin was 4.3 (CI= 0.58-32.20) (Figure 2). For low platelets the risk ratio was 0.79 (CI= 0.29-2.20). The risk ratio for low white blood cell count was 0.64 (CI= 0.19-2.17). All confidence intervals include one, and therefore demonstrate there may not be an increased risk of critical event when blood values are low versus normal blood values (Figure 2).

Figure 2.
Risk Ratios of Critical Incidents in Patients with Low Blood Values versus Normal Blood Values with Respective Confidence Intervals



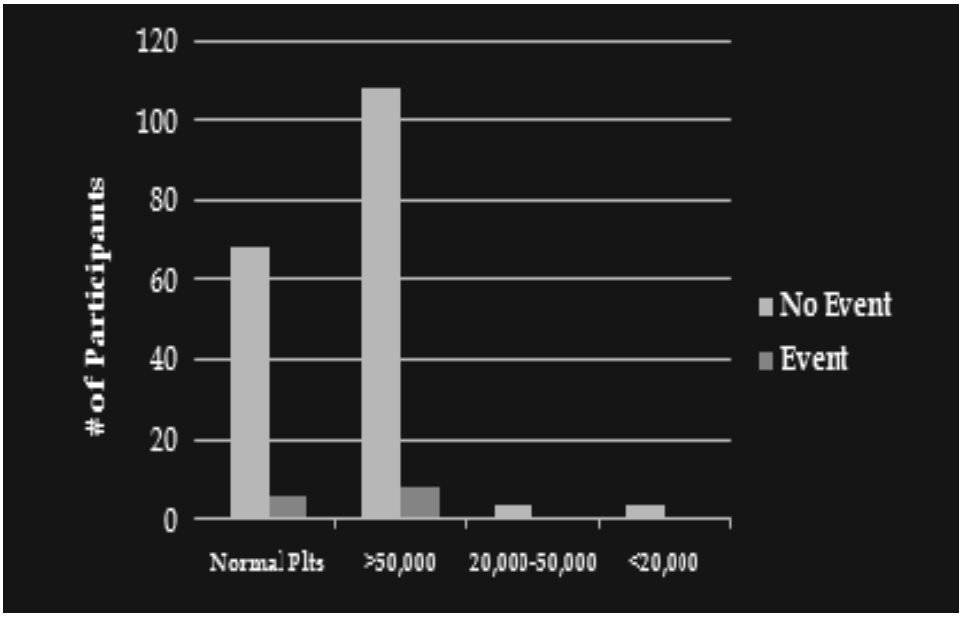
The distribution of critical incidents for normal and abnormal hemoglobin values was also analyzed (Figure 3). For patients whose hemoglobin values were within normal age adjusted ranges, 2% had a critical event. For patients with an abnormal hemoglobin value yet >10, 8% of subjects had a critical event. For hemoglobin values 8-10, 6.5% had a critical event. For hemoglobin <8, indicating no exercise permitted, 20% had a critical event. No significant differences were found in the way confidence intervals were distributed for platelets (X^2=5.795, p= 0.122). A power analysis indicated insufficient power to be confident that no relationship exists between critical incidents and low hemoglobin.

Figure 3.
Distribution of Critical Events for Normal and Abnormal



The distribution of critical events for normal and abnormal platelet values found that 8% of patients whose platelets were normal had a critical event (Figure 4). For patients with abnormal platelets, yet >50,000, 7% had a critical event. For values 20,000-50,000, zero out of the four participants had a critical event. For patients with platelets <20,000, indicating no exercise permitted, zero of the seven had a critical event. No significant differences were found in the way confidence intervals were distributed for platelets (X^2=0.974, p= 0.808) (Figure 4).

Figure 4.
Distribution of Critical Events for Normal and Abnormal Platelet



For patients with low platelet blood values, it is recommended that physical therapy avoid activities such as stretching due to the decreased ability of the patient's blood to clot. When patients' platelet values were abnormally low, there was no significant difference found in the distribution of critical incidents in patients with

stretching versus no stretching (X^2=0.769, p= 0.476) (Table 2). Four percent of patients with abnormal platelets and were stretched had a critical event, whereas 8% of patients without stretching during physical therapy had a critical event. Another common concern is for patients with low hemoglobin values performing endurance exercises. It is recommended that physical therapy avoid endurance exercises when patients' hemoglobin values are abnormally low due to increased risk of fatigue, tachycardia, and the increased oxygen demands placed on the body's tissues. There was no significant difference found in the distribution of critical incidents in patients with abnormally low hemoglobin when endurance exercises were done versus no endurance exercises (X^2=0.066, p= 1.00) (Table 3). Eight percent of patients with abnormal hemoglobin values who performed endurance exercises had a critical event, whereas 9% of patients without endurance exercises during physical therapy had a critical event.

Table 2.
Patients with abnormal platelet values. Distribution of critical events when stretching versus no stretching was done

	No Critical Event	Critical Event
No Stretching	70	6
Stretching	48	2

Table 3.
Patients with abnormal hemoglobin values. Distribution of critical events when endurance exercises versus no endurance exercises were done during PT.

	No Critical Event	Critical Event
No Endurance Ex.	90	9
Endurance Ex.	47	4

The correlation between certain sub-groups of patients and critical incidents was also analyzed. There were no relationships found between critical incidents and type of cancer (X^2=1.87, p=0.39) or age (X^2=0.104, p=0.75) of the patient. The correlation between the types of physical therapy exercise performed was also analyzed for relationship with critical events. There were no statistically significant relationships ($p<0.05$) found between critical incidents and interventions tested. Interventions included strength training with resistance (X^2=0.686, p=0.404), strength training with jumping (X^2=2.093, p=0.247), gait training (X^2=0.329, p=0.593), endurance (X^2=0.124, p=1.0), balance (X^2=0.163, p=0.777), and stretching (X^2=0.492, p=0.576).

Chapter IV

Discussion

Chi-Square analyses indicated no significant correlation between critical incidents and chronically low hemoglobin, low platelets, or low white blood cells. High percentages of patients in the pediatric oncology population have chronically low blood values. According to Stiller et al.[6] chronically low blood values for a particular patient should be treated differently than an acute change. If a patient has been living stably with chronically abnormal lab values it has been the practice of many physicians to allow physical activity in order to prevent the deleterious results of bed rest and inactivity. These deleterious effects include: muscle weakness, decreased muscle endurance, negative nitrogen balance, pneumonia, thrombosis, kidney stones, increased diuresis, orthostatic hypotension, cardiovascular deconditioning, skin breakdown, depression, fatigue, and decreased quality of life.[10] Therefore it is important to weigh the possible

risks and benefits of exercising a patient with abnormal blood values. In the current study, physical therapy was found to be very safe when using symptom based guidelines for activity in children being treated for cancer with a very low percentage of critical events.

Of the thirteen critical incidents that did occur, all events were minor with approximately 50% having symptoms of tachycardia. Tachycardia happens to be a common symptom of low hemoglobin, and its occurrence is somewhat expected and does not merit discontinuing physical therapy. No major events such as heart arrhythmias, syncope, hypotension, or major bleeds occurred in any of the patients receiving physical therapy treatment.

There was also no increased risk of critical events in children with low platelets or low white blood cells when compared to normal blood values with risk ratios 0.79 and 0.64 respectively. An increased risk ratio of 4.3 was noted for critical incidents in subjects with low hemoglobin as compared to normal hemoglobin values. Despite an increased risk ratio, a confidence interval of 0.58-32.30 indicates patients had a decreased risk of event, no additional risk, or an increased risk of critical event. We cannot be confident that the risk ratio for hemoglobin is significant. A power analysis for hemoglobin indicated insufficient number of subjects to be confident in the finding of no relationship.

A study by Dimeo et al.[14] found similar results when looking at the effects of aerobic exercise on adult patients with cancer. The treatment group took part in daily aerobic exercise programs consisting of biking with a bed ergometer for one minute at an

intensity level of at least 50% of cardiac reserve. This was repeated fifteen times with one minute breaks between exercise bouts for a total of 30 minutes each day. There were no complications in the condition of patients who participated in rehab immediately after completing high dose chemotherapy. The aerobic exercise improved physical performance and reduced fatigue in patients. The researchers concluded that the severe loss of function often observed after high dose chemotherapy can be partially prevented with rehab exercises.

Stiller et al.[22] looked at the effects of mobilizing ill patients with low blood values. Patients' baseline mean hemoglobin values were 9.1 g/dL and ranged from 7-15.8g/dL. Baseline platelet values had a mean value of 301,000/*micro*L and ranged from 42,000-742,000/*micro*L. During 2 of 69 mobilization sessions, patients reported feeling dizzy but did not require any direct medical intervention. In 3 of 69 occasions, a deterioration in patients' condition required intervention. All three occasions were due to a fall in SpO_2. There was no change in the severity or frequency of cardiac arrhythmias noted during mobilizations.

In an additional study by Dimeo et al.[23] patients with cancer undergoing bone marrow transplantation participated in a rehab program. The program consisted of treadmill walking according to an interval training protocol for six weeks. Throughout the six week training program, physical performance improved and no cardiac, infectious, or bleeding adverse reactions occurred. No such evidence of impaired physical functioning was found. Instead, patients gained self-confidence, improved physical

functioning, and had less depressive moods resulting in higher levels of independence and improved quality of life.

In the current study, there was also no significant relationship between critical incidents and specific sub-populations of patients such as type of cancer, age, or type of physical therapy exercise. When patients' platelet values were abnormally low, there was no significant difference found in the distribution of critical incidents in patients with stretching versus no stretching. There was no significant difference found in the distribution of critical incidents in patients with abnormally low hemoglobin when endurance exercises were done versus no endurance exercises.

These results of the current study suggest the use of a symptom-based approach in determining appropriateness for physical therapy may be utilized in pediatric populations experiencing chronically low blood values. An additional screening process for determining patients appropriate for physical therapy has been proposed by Stiller et. al.[13] The guidelines recommend that hemoglobin values be stable and >7g/dL, platelet counts stable and >20,000/*micro*L and white blood cell counts between 4,300-10,800/mm^3. If any blood value is not within these guidelines, appropriateness of mobilization should be discussed with another physical therapist or medical professional before deferment. Therapists may be able to decide if a patient is safe for physical therapy based on additional objective and/or subjective factors. Objective factors include heart rate, blood pressure, cardiac status, oxygenation, respiratory pattern, or blood glucose levels. Subjective symptoms such as the patient's facial expression, emotional state, pain, anxiety, pallor, rate of perceived exertion, and/or diaphoresis may be used for

determining patients' appropriateness for physical activity. These guidelines in conjunction with clinical judgment, experience, and current APTA hematological guidelines may be utilized in populations experiencing chronically low blood values.

Limitations of this study include the small sample size. Of the 201 total charts reviewed, there were only 13 critical incidents identified. Having so few critical incidents makes it difficult to find statistically significant correlations. Only 9.8% of the patients receiving physical therapy had hemoglobin values <8 and only 5.5% of patients had platelets <20,000. Conducting a larger study with more participants may result in more subjects with extreme low blood values allowing researchers to investigate the relationship between physical therapy and critical incidents. Also, if we are suggesting a symptom-based approach to determining level of activity during physical therapy, it would be interesting to note the types of modifications physical therapists made to treatment sessions when patients' blood values were low. Although efforts were made to record any changes to physical therapy treatment sessions, all modifications may not have been fully documented limiting our ability to know what specific changes actually minimized the occurrence of critical events. In addition, it is possible we may not have had access to all emergency medical files from outside hospitals. Although one can expect a phone call would be made from the outside hospital and placed in the child's medical record, we cannot be completely confident we were able to record all critical incidents.

Chapter V

Conclusion

The results of this study support our original hypothesis. There was no difference in the amount of critical incidents occurring within two days after physical therapy in pediatric oncology patients with chronically low blood values versus normal blood values. Physical therapy was found to be safe for children experiencing chronically low blood values from chemotherapy treatment when the therapist used symptoms as a guideline for treatment parameters. Additionally, when analyzed, there were no sub-populations of patients found to be at an increased risk of critical events. The evidence suggests a symptom-based approach in determining appropriateness for physical therapy may be utilized in populations experiencing chronically low blood values. Future studies with larger samples sizes are needed to ascertain whether these findings are consistent and statistically significant.

Appendix A

Patient ID: PT Treatment Date:
Age: Gender: M / F
Type of cancer: Time in Oncology Treatment: (months)
Transfusions in last week: _____RBC _____Platelets
Physical Therapy seen as: _____ Inpatient _____ Outpatient

Lab Values Date and Time: _____
Hemoglobin: _____
Platelets: _____
WBC Count:_____

Physical Therapy Interventions:
_____ Strength Training, if yes → Resistance given Yes / No circle type: weights, bands, manual
_____ Gait Training Pilates, jumping, closed chain
_____ Endurance Exercise, if yes → Running Yes / No
_____ Balance Training
_____ Stretching, if yes → Joint Mobilization Yes / No
_____ Other:

PT recorded modified due to symptoms: ____ Yes ____ No
Symptoms noted by PT:
_____ Paleness _____Fatigue _____ Headache
_____ Shortness of breath _____ Increased HR _____ Lethargy
_____ Bruising _____Bleeding of gums reported
_____ Parent reporting change in behavior
_____ Other: _____
_____ Other: _____

Date and Time of Physical Therapy:	**Critical Incidences during PT**	**Critical Incidences w/in 2 hours after PT**	**Critical Incidences 1 day after PT**	**Critical Incidences 2 days after PT**
Syncope	Yes / No	Yes / No	Yes / No	Yes / No
Cardiac arrhythmia	Yes / No	Yes / No	Yes / No	Yes / No
Low blood pressure	Yes / No BP:	Yes / No BP:	Yes / No BP:	Yes / No BP:
SpO_2 <90%	Yes / No	Yes / No	Yes / No	Yes / No
Shortness of Breath	Yes / No	Yes / No	Yes / No	Yes / No
Heart Rate **at rest**: Bradycardia Tachycardia (use age app. Values)	Normal Brady / Tachy	Normal Brady / Tachy	Normal Brady / Tachy	Normal Brady / Tachy
Falls	Yes / No	Yes / No	Yes / No	Yes / No
	Description of fall:	Description of fall:	Description of fall:	Description of fall:
Pain Rating 0-10				
Skin integrity (ecchymosis, breakdown, erythema)				
Fever	Yes / No Temp:	Yes / No Temp:	Yes / No Temp:	Yes / No Temp:
Pt. Subjective complaints				

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