

DUAL-TASK PERFORMANCE IN OLDER ADULTS WITH BREAST CANCER WHO

RECEIVED ENDOCRINE THERAPY

ACHIRAYA PAKSA

Graduate School Srinakharinwirot University

2024

ความสามารถในการทำงานสองอย่างในเวลาเดียวกันของผู้สูงอายุที่เป็นมะเร็งเต้านมที่ได้รับการ รักษาด้วยฮอร์โมน



ปริญญานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตร วิทยาศาสตรมหาบัณฑิต สาขาวิชากายภาพบำบัด คณะกายภาพบำบัด มหาวิทยาลัยศรีนครินทรวิโรฒ ปีการศึกษา 2567 ลิขสิทธิ์ของมหาวิทยาลัยศรีนครินทรวิโรฒ

DUAL-TASK PERFORMANCE IN OLDER ADULTS WITH BREAST CANCER WHO RECEIVED ENDOCRINE THERAPY



A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of MASTER OF SCIENCE (Physical Therapy)

Faculty of Physical Therapy, Srinakharinwirot University

2024

Copyright of Srinakharinwirot University

THE THESIS TITLED

DUAL-TASK PERFORMANCE IN OLDER ADULTS WITH BREAST CANCER WHO RECEIVED ENDOCRINE THERAPY

BY

ACHIRAYA PAKSA

HAS BEEN APPROVED BY THE GRADUATE SCHOOL IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE MASTER OF SCIENCE IN PHYSICAL THERAPY AT SRINAKHARINWIROT UNIVERSITY

(Assoc. Prof. Dr. Chatchai Ekpanyaskul, MD.)

-0_

Dean of Graduate School

ORAL DEFENSE COMMITTEE

..... Major-advisor Chair

(Asst. Prof. Dr.Nithinun Chaikeeree)

(Assoc. Prof. Dr.Plaiwan Suttanon)

.....

..... Committee

(Assoc. Prof. Dr.Rumpa Boonsinsukh)

Title	DUAL-TASK PERFORMANCE IN OLDER ADULTS WITH BREAST CANCER
	WHO RECEIVED ENDOCRINE THERAPY
Author	ACHIRAYA PAKSA
Degree	MASTER OF SCIENCE
Academic Year	2024
Thesis Advisor	Assistant Professor Dr. Nithinun Chaikeeree

Dual-task performance simultaneously challenges both dynamic balance and cognitive processing. Endocrine therapy has an adverse effect on cognitive function; and it would be possible that older adults with breast cancer, who received endocrine therapy had problems with dual-task performance. It this essential to examine dual-task performance directly among older adults with breast cancer. The methodology included 30 older adults in each group including those who had breast cancer with endocrine therapy (BCA-Endocrine) and not cancer (Non-CA group) who participated in the study. Their single task performance in balance during walking and cognitive function were measured with the Timed Up and Go test (TUG) and subtraction by three, starting with the range of 70-100. Their dual-task performance was measured using TUG simultaneously with the subtraction task (TUG-Cog). The TUG duration and cognitive task performance under single and dual-task conditions were used to compute the dual-task effect (DTE%) to identify the degree of dual-task effect and ability to balance while walking and on the rate of correct subtraction in a given time (Correct response rate, CRR). The results of the study were as follows: more time spent on the TUG and a decreased number of correct subtractions when performing dual-task were found in both groups. The results from the DTE% analysis were separated into walking balance and subtraction, found that the DTE% in TUG (Mean± SD) in the BCA-Endocrine (85.4± 44) was significantly higher than the Non-CA group (63.2± 32.8) (p=.03). Whereas, DTE% in CRR in the BCA-Endocrine (-50.6± 31.7) and in the Non-CA group (-46.5± 18.2) was not more negative than in the Non-CA (p=.42) In conclusion, older adults with breast cancer who received endocrine therapy had a larger effect of dual-tasking than older adults without cancer. The larger effect was found in balance during walking, but not in the performance in the subtraction task.

Keyword : Dual-task Cognitive function Breast cancer Older adult Endocrine therapy

D

ACKNOWLEDGEMENTS

I would like to express the gratitude to the committee chairman, Associate Professor Dr. Rumpa Boonsinsukh and Associate Professor Dr. Plaiwan Satthanon, for patience and faith in me. I am sure you are the one to lay the basis for my scientific eagerness, and I hope that our fruitful cooperation in the scientific field will continue. And I would also like to my committee members for letting my defense be an enjoyable moment, and for your brilliant comments and suggestions, thanks to you.

I am grateful to my research advisor, Assistant Professor Dr. Nithinun Chaikeeree who has helped me to overcome challenges and given advice on drawing up the dissertation competently.

I would like to acknowledge and give my warmest thanks to my department of Rehabilitation in Chulabhorn hospital for give me a chance to improve myself skill in the way of physical therapist.

I am also sincerely grateful to the Senior citizen center in Nonthaburi to publicize my research to healthy in older adult.

Finally, I wish to acknowledge the Chulabhorn hospital for providing me with scholarship, without which this work could have never begun.

••••••

ACHIRAYA PAKSA

TABLE OF CONTENTS

Page	
ABSTRACT D	
ACKNOWLEDGEMENTSE	
TABLE OF CONTENTSF	
LIST OF TABLES	
LIST OF FIGURESI	
CHAPTER 1 INTRODUCTION1	
Background and rationale1	
Research question4	
Research hypothesis4	
Research objective5	
Advantage of the study5	
Conceptual framework of this study5	
CHAPTER 2 LITERATURE REVIEW6	
2.1 Breast Cancer: general information6	
2.2 Effects of breast cancer on physical and cognitive functions	
2.3 Type of treatment for breast cancer and their side effects	
2.4 Side effect of the endocrine therapy for breast cancer on cognitive decline14	
2.5 Postural control impairments in patients with breast cancer	
2.6 Assessment of cognitive function17	
2.7 Dual-task	
2.8 Factors affecting dual-task performance21	

CHAPTER 3 METHODOLOGY	23
Study design	23
Participants	23
Sample size calculation2	24
Study tools and instrument2	25
Procedure	26
Data analysis	29
CHAPTER4 RESULT AND DISCUSSION	32
Result	32
Discussion	37
Clinical implication	41
CHAPTER 5 SUGGESTION AND CONCLUSION	42
Limitation and Suggestion for Further Study	42
Conclusion	42
REFERENCES	44
APPENDIX	50
VITA	58

LIST OF TABLES

		Page
Table	1 The staging system for breast cancer	8
Table	2 Systemic treatment recommendations	9
Table	3 Possible outcomes of dual-task performance	. 18
Table	4 Example of dual-task paradigms have been used in previous studies	.20
Table	5 Measurement variables, their unit, and scale that was collected for this study	28
Table	6 Demographic and medical information (mean SD or N%)	. 32
Table	7 Performance of participants (Mean± SD)	. 35



LIST OF FIGURES

		Page
Figure	1 Conceptual framework of this study	5
Figure	2 Sample size calculation with G*power program	.25
Figure	3 Study procedure flow-chart	.31
Figure	4 Dual-task effect in TUG duration in BCA-Endocrine and in Non-CA group	.36
Figure	5 Dual-task effect in correct response rate	. 36



CHAPTER 1 INTRODUCTION

Background and rationale

Cancer is one of the most important health problems in many countries. The American Cancer Society's update on female breast cancer incidence rates has risen in most of the past four decades; during the most recent data years (2010-2019), the rate increased by 0.5 percent annually (1) Patients with breast cancer (BC) is the largest group of patients with cancer in women populations(2). Older adults were the most affected by breast cancer as the incidence of breast cancer rises dramatically with age(3). As a previous study reported a large proportion (41%) of all new breast cancer diagnoses was found in women 65 years and older(4). Diagnosis, localized stage, and differentiation for types of breast cancer are important for planning a specific treatment(5). Many types of treatment was provided to patients with breast cancer after primary surgery such as radiotherapy, chemotherapy, and endocrine therapy(4). In the part, mostly older breast cancer was treated with adjuvant chemotherapy. Nowadays, however, endocrine therapy is suggested used more in this population because there are not all older adults with breast cancer derive benefit from chemotherapy(6). Estrogen receptors presented in cancer cells of the breast are involved in the proliferation of cancer cells, thus endocrine therapy was recommended used in patients with hormone receptor-positive subtypes of breast cancer(7). These subtypes of breast cancer are main types of breast cancer found in older women(4).

Tumor cell inducing overexpression of enzyme for estrogen synthesis leading to high levels of estrogen within the tumor niche consequence in estrogenic imbalance and a more proliferation of tumor cells(8). Endocrine therapy has been used to improve symptoms of patients with breast cancer type hormone receptor positive (HR-positive) by reducing estrogen synthesis and the binding of estrogen-to-estrogen receptors in breast cancer cells (9) and estrogen synthesis(9, 10). On the other hand, there are unwanted effects of endocrine therapy on reducing estrogen levels in the body(11). Estrogen is a powerful endocrine molecule affecting the brain's activities and

metabolism. The optimal level of estrogen is essential for normal brain function(12). Many regions of the brain are under influence of the estrogen because of the presented of the estrogen receptor molecules such as hippocampus, prefrontal, cortex and amygdala. These areas of the brain are considered important in cognition, and play a role in performing task requiring executive function, verbal learning, and memory(13). Therefore, decreased estrogen levels in body according to endocrine therapy may contribute to cognitive decline(11). A previous study showed the significant relationship between endocrine therapy in patient who had experience of breast cancer and impairments in various domains of the cognitive function including memory, language and executive function, concentration, understanding, and clarity (11, 14). The effect of endocrine therapy on cognitive function was found one year of receiving this treatment, indicating time concern for cognitive screening in patients with breast cancer especially those who received endocrine therapy(14-16) A more recent study reported that duration of undertook endocrine therapy was risk factor of impaired cognitive function, the longer duration of receiving endocrine therapy, the higher risk for cognitive impairment(17) Among various domains of cognitive function, impairment of executive function seems to be strongly associated with falls are evident in older adult(18).

Falls in older people are a major public health concern, that adversely affect health and lead to minor to major problems such as anxiety, depression, and decreased mobility leading to disability and mortality(19). Many of older adults may experience with fall as a previous study reported that one in three adults over 65 years will fall(20). Fifty eight percent of women with breast cancer undertook endocrine therapy reported a history of fall and half of them experienced recurrent fall within an 18-month period after onset of endocrine therapy(21). Considering fall risk factors in older adults, cancer are a disease affecting body function as a previous study reported the impairment of vestibular and visual processing for postural control in older adults with breast cancer who received chemotherapy and/ or endocrine therapy(22). In addition, a systematic review reported that breast cancer survivors who received mixed type of cancer intervention (i.e., surgery, chemotherapy, and endocrine therapy) experienced with reduced muscle strength, neuropathy induced impaired proprioceptive sensation, impaired functional mobility and balance as they had lower limit of stability, increased center of pressor displacement under displacement of support surface, lower gait speed, and required time to complete timed up and go (TUG) task compared to normal people without cancer. (23). This indicates important of screening postural control performance in older adults with breast cancer. However, insufficient evidence focused on impact of cancer treatment on postural stability under situation that challenge cognitive processing control.

Maintaining postural stability demands cognitive processing capacity for simultaneously performing postural task and another cognitive required task. In everyday life often involve cognitive-motor dual-tasks, e.g. walking while talking, texting on a cell phone, or thinking about one's shopping list (Dual-task walking). (24). The Dual-task walking simultaneously challenges both dynamic balance and cognitive processing(25). Thus, impaired cognitive function affected the effectiveness of the brain to process postural task and cognitive required task simultaneously(26). Higher incident of fall was found in older people with impaired executive function which is a domain of cognitive function compared with the older people without impairment(27), indicating effect of an impaired cognitive function at least one domain can lead to poor in postural control problem in context follow dual-task performance(28, 29).

The most common dual-task paradigm is a protocol designed to assess the ability of a person to perform a cognitive and motor task simultaneously (dual-task)(30) such as performing gait as a motor task using usual pace gait in straight-line or the Timed Up and Go (TUG) with naming animals or counting backward(31). Previous studies dual-task performance in older adult with breast cancer survivor who completed cancer treatment at least 3 months reported that TUG with counting backward are able to predict fall(32). This indicates postural control problem in context of cognitive processing in patients with breast cancer. As mentioned earlier patients with breast cancer who is undertaking endocrine therapy are prone to have a decrease function of estrogen in the brain and may consequently in an impairment of cognitive function (11).

However, a previous study measuring dual-task performance in breast cancer survivors who completed cancer intervention of mixed types of intervention including chemotherapy or chemotherapy follow with endocrine therapy(32). A previous study in older adults with breast cancer reported that those who received chemotherapy and endocrine had different degrees of the decreased cognitive function measured using patients-reported cognitive impairment(33). Thus, it is possible that effect of chemotherapy and endocrine therapy on dual-task performance may not be the same. Therefore, evidence on a dual-task performance in cancer survivor cannot be apply for determining performance in patient with cancer who undertake endocrine therapy. As mentioned above, endocrine therapy has adverse effect cognitive function, thus it would be possible that in older breast cancer with endocrine therapy may have problems with dual-task performance. It this essential to examine dual-task performance directly in patients with cancer, however, there was no evidence to support this hypothesis.

Therefore, this study aims to examine the dual-task performance between older adults who have no and have breast cancer with endocrine therapy. Findings from this research would indicate significance dual-task performance impairment in older adults who is under endocrine therapy for breast cancer and help guide screening for balance problem in this group of population.

Research question

Did the older adults who have breast cancer with endocrine therapy have lower dual-task performance than older adults who have no breast cancer?

Research hypothesis

Older adults who have breast cancer with endocrine therapy have lower dualtask performance compared to older-adult who have no breast cancer.

Research objective

To examine the dual-task performance between older adults who have no and have breast cancer with endocrine therapy.

Advantage of the study

To indicate significance dual-task performance impairment in older adults who were under endocrine therapy for breast cancer and help guide screening for balance problems in this group of population. Research findings will add more knowledge on the importance of screening dual-task performance in patients with cancer especially those who undertaking endocrine therapy for breast cancer.



Conceptual framework of this study

Figure 1 Conceptual framework of this study

TUG = Time up and go test, TUG-Cog= Time up and go with cognitive test, Cog-single= Cognitive single test

CHAPTER 2 LITERATURE REVIEW

This study is related to dual-task assessment in older adults who have breast cancer with endocrine therapy. Literature review topics for this study are included general information, type of treatment for breast cancer and their side effects, Side effect of the endocrine therapy for breast cancer on cognitive decline, Postural control impairments in patients with breast cancer, Assessment of cognitive function, Dual-task performance assessment and Factors affecting dual-task performance.

2.1 Breast Cancer: general information

Incidence of breast cancer

Breast cancer is one of the serious health problems in women population. Cancer cell can develop in many organs of human. Cancer of breast cells is a large group of cancer in women. In United State of America, a total of 2.3 million new cases of patients was reported in 2018. ⁽¹⁾ According to the American Cancer Society, global cancer burden would be 28.4 million cases by 2040, which is approximately forty-seven percent raise compared to 2020 cancer burden. In Thailand, the most cancer type reported in women is breast cancer which is about forty percent of all type of cancer in Thai women. In 2022, the Ministry of Public Health, Thailand reported the incidence of breast cancer in 38,559 cases.⁽²⁾ The increasing age are strongly related to increasing incidence of breast cancer⁽³⁾. Incidence of breast cancer are high in women in older age compared to younger women. ⁽¹⁾ Eighty-two percent of breast cancers are diagnosed among women aged over 50 years old with the median age at diagnosis was at 62 years old⁽⁴⁾. In Thailand breast cancer mostly occurs in women aged 55 years and older⁽²⁾. Meanwhile, Thailand stepping into aging society from 2005 to now and turn to aged society in 2041⁽⁵⁾. Therefore, this cancer become more and more important health issue in older population of Thailand. The possible explanation for the high incident of breast cancer in older women is hormone-receptor-rich and slowly proliferating neoplasms which are the consequence of hormone receptors adaptation in response to the decreased of sex hormone synthesis in older adults⁽⁶⁾.

Sign and symptoms of breast cancer

- Since cancer cell can be developed in various component of breast such as ducts, lobules, fat, connective tissues, lymph nodes and nipples(40), several sings and symptoms can be found in patients.

- The following are common signs and symptoms of breast cancer: a lump or thickening in or near the breast or in the underarm area.

- A change in the size or shape of the breast.

- Nipple discharge or tenderness, or the nipple pulled back (inverted) into the breast.

- Ridges or pitting of the breast, making the skin look like the skin of an orange; and/ or

- Warmth
- Swelling, redness or scaliness of the skin of around areola or nipple.

Medical assessment and diagnosis for breast cancer

The standard practice of assessment and diagnosis for breast lump is composed of three components (The triple assessment) including physical examination, imaging of the breasts, and a biopsy for a lump(40). Physical examination, history taking, medical screening for cancer risk factor, palpation for breast lump are usually first step for cancer examination provided by medical doctor. Three types of imaging medical including mammography, ultrasonography, and breast magnetic resonance imaging (MRI) can be used to diagnose breast cancer and to evaluate the stage and extent of disease. The biopsy is a tissue diagnostic method used to confirm the diagnosis in subtype(41). There are three different types of biopsies including fine needle aspiration (FNA) biopsy, core needle biopsy, and incision and excision biopsy. The combination of the physical examination, imaging, and fine-needle aspiration cytology (FNAC) is used to increase accuracy for cancer diagnosis(40). Physician and oncologist used all results, especially pathologic test to plan for prescribe appropriate treatment for patients with breast cancer.

American joint committee on Cancer (AJCC) categorizes cancer into three stages including noninvasive breast cancer (state 0), early breast cancer (stage I and II), locally advanced breast cancer (stage III) and metastasis (stage IV) breast cancer(42). The cancer stage II and III can be sub-categorized based on primary tumor size, number of affected lymph nodes, and distant metastasis. (Table1)

Breast Cancer Stage		Tumor size	Number of lymph nodes	Metastasis
Noninvasive breast	0	Tis	NO	M-
cancers	2		6	
Early breast cancer		T1 ^a	NO	M-
	IIA	ТО	N1	M-
		T1 ^a	N1	M-
	1	T2	NO	M-
	IIB	T2	N1	M-
	6	Т3	NO	M-
	IIIA	ТО	N2	M-
		T1 ^a	N2	M-
		T2	N2	M-
		Т3	N1	M-
Locally advanced breast	IIIA	Т3	N2	M-
cancer	IIIB	Τ4	NO	M-
		Τ4	N1	M-
		Τ4	N2	M-
	IIIC	AnyT	N2	M-
Metastatic breast cancer	IV	AnyT	AnyN	M+

 Table 1 The staging system for breast cancer

Includes tumors with a microinvasion of 0.1 cm. or less in greatest dimension. M- = no distant metastasis, M+ = distant metastasis, Tis = carcinoma in situ, T1= tumor 2 cm. or less in greatest dimension, T3= tumor more than 5 cm in greatest dimension, T4= tumor of any size with direct extension into the chest wall and/or skin

Breast cancer can be categorized into 5 subtypes (table 2) according to the profiles of hormones' receptor molecule and human epidermal growth factor recepter-2 presented in cancer cell which can be detected using biopsy test with immunohistochemistry lab test and molecular analysis technique (7, 43) Breast cancer with a molecular profile hormone receptor positive (HR-positive) with human epidermal growth factor receptor2 (HER2) negative is categorized into the luminal A-like which are main type of breast cancer found in older women(4). The surrogate subtypes implicate for systemic treatment selection(44) the surrogate subtypes usually used to estimate prognosis and select type of adjuvant chemotherapy and endocrine therapy for patient with breast cancer (45). (Table 2.)

Breast cancer	10	Receptors' profile in cancer	Endocrine/Chemotherapy
subtype		cells	
Luminal A-like	breast	Strong estrogen receptor-positive	Endocrine therapy is the most
cancer		and HER2-negative	critical intervention and is often used
			alone
Luminal B-like	breast	Estrogen receptors positive but	Chemotherapy and adjuvant
cancer		variable degree of estrogen	endocrine therapy
		receptor or progesterone receptor	
		expression	
Luminal B-like	breast	HER2-positive test on biopsy and	Chemotherapy and adjuvant
cancer		estrogen and progesterone	endocrine therapy
		receptors absent	
Non-luminal		HER2 positive	Chemotherapy adjuvant endocrine
			therapy

 Table 2 Systemic treatment recommendations

Breast cancer	Receptors' profile in cancer	Endocrine/Chemotherapy
subtype	cells	
Triple negative	Combination of estrogen receptor	Chemotherapy
	negative, progesterone negative	
	and HER2-negative	

HER2 = human epidermal growth factor receptor-2

2.2 Effects of breast cancer on physical and cognitive functions

Regarding best knowledge from the literature review, there are insufficient articles to provide information on physical and cognitive functions in patients with breast cancer. Generally, persons suspected to have cancer cells will receive a standard examination for cancer diagnosis to provide them with cancer treatment as soon as possible. Much research on breast cancer usually included cancer survivors who were patients who underwent or completed medical treatment for eliminating cancer cells. Most of the studies report physical and cognitive function in pre-post rehabilitation after cancer intervention programs. There are no research articles that directly compare physical and cognitive functions before and after medical intervention. A few research provide knowledge about physical and cognitive functions in subjects diagnosed with cancer are discussed below.

Animal model studies demonstrated cancer-associated muscle dysfunction. Mice with primary mammary tumors have reduced luminal grip strength and declined motor activity (46). Another study on animal models demonstrated and explained that change in limb muscle mass was directly affected by tumor-derived factors, (47). Cytokine molecules from cancer cells induce systemic inflammation in mice and activate muscle protein degradation(48). However, there are no study investigated the direct impact of cancer on human muscle function. Most studies in humans with breast cancer reported muscle weakness, general exhaustion, and other adverse effects of cancer treatment but not the direct impact of the changes molecular profile of cancer cells.

According to the systemic effects of breast cancer can lead to functional limitations in patients who suffer from muscle weakness, fatigue, and pain(49). The

previous study showed breast cancer-related muscle fatigue caused by breast tumor growth(50). Tumors in the breast release growth factors and cytokines into the circulating system. Circulating growth factors and cytokines such as Transforming growth factor beta (TGF- β) and tumor necrosis factor-alpha (TNF- α) are transported into skeletal muscles resulting in defective energetic regulation leading to fatigue in breast cancer patients(49). In addition, activation of nuclear factor-kappa B (NF-KB) signaling pathways accelerates the regulated degradation of muscle proteins and hence causes muscle(51). However, the above studies on mechanisms of the impact of cancer cells on muscle function included only participants with breast cancer undergone cancer treatment(52) or animal model studies(46).

Several studies reported physical and psychological problems in breast cancer from side effects from breast cancer treatment, breast cancer with brain metastasis, and paraneoplastic neurological syndrome(53). Paraneoplastic neurological syndrome decreased performance of upper limb function is a consequence of breast cancer itself. Location of breast closing to lymph node and blood vessel in upper limb and thus affecting upper limb function(54). Symptoms include muscle weakness, difficulty with coordination, sensory changes, and cognitive deficits are reported in patients with breast cancer (53). Manifestation of these symptoms cannot be explained by the underlying cancer-related metastasis, infection, and side effects of treatment since it mostly occurs before the diagnosis of cancer(55). These groups of problems are called paraneoplastic neurological syndrome. It was often found in younger ages (<61 years) and with late-stage disease(56).

For cognitive impairment effects in breast cancer before medical treatment. Depression is reported to characterize the diagnosis of breast cancer with a sense of helplessness, and a lack of motivation to effectively cope with life(57). Cognitive impairments stroke, and encephalopathy occur the first year following the treatment of breast cancer(58) or breast cancer with brain metastatic(53).

There were no studies that compared the effects of breast cancer subtypes on physical function and cognitive function before medical treatment. It may be because the priority for cancer management is to eliminate cancer cells as soon as possible after diagnosis of cancer. Delayed receiving cancer intervention was associated with poorer overall survival(59).

2.3 Type of treatment for breast cancer and their side effects

There are many types of treatment for breast cancer including surgery, radiotherapy, chemotherapy endocrine therapy. Treatment plan is usually regarding to progression of the disease (states of cancer) and subtypes of breast cancer and involves a multidisciplinary approach team such as medical oncologist, medical radiologist, surgical oncology, nurse, pre-and rehabilitation team, and etc(60). Common cancer therapy includes surgery, radiotherapy, chemotherapy, and endocrine therapy. Breast cancer survivors, who having no signs of cancer after finishing treatment(61) may experience with lower balance performance due to reduced muscle strength and loss in proprioception from neuropathy. However, these impairments can be reduced through the recovery phase. (23). On contrary, patients who still received endocrine therapy experience more general fatigue, lower muscle strength than those who completed therapy as the cancer survivor(62). The effect of endocrine therapy on cognitive function was found one year mostly worse of receiving this treatment(15). Therefore, observation of the effect of endocrine therapy on dual-task performance in cancer survivors who completed cancer intervention cannot be implied for patients with breast cancer who is undergoing endocrine

Surgery is the treatment aimed to remove the primary breast tumor and dissection of the lymph nodes. A total mastectomy is a type of surgical treatment that the pectoralis minor muscle is totally removed. A partial mastectomy (i.e., lumpectomy) is a type of mastectomy that a part of pectoralis muscle can be preserved. The dissection of the lymph node is usually operated at ipsilateral axillary lymph nodes including axillary lymph node dissection (ALND) and sentinel lymph node (SLND)(63).

Radiotherapy for breast cancer is a localized cancer treatment aimed for treating invasive disease and reducing pain(64). Radiotherapy is a grama ray that use to kill cancer cells. In breast cancer is usually applied to the whole breast or a portion of

the breast after lumpectomy, to the chest wall after mastectomy, and to the regional lymph nodes. Post lumpectomy (4-6 weeks post-surgical) whole-breast radiation for 5 days/week for 5 weeks is a standard component of breast cancer therapy(63, 64). Dry erythema, hair loss, muscle fatigue, tissue fibrosis, and telangiectasias are common complications of radiotherapy for cancer(64). The effects of radiotherapy on fatigue muscle mostly present only in upper limbs muscle of the affected side(65). However, there are no report regarding side effect of the radiotherapy on cognitive function decline and postural control impairment(66).

Chemotherapy is a treatment for breast cancer which use chemical agents to suppress cell division (67). Generally, chemotherapy is used in combination with other treatment (that is called adjuvant chemotherapy) aimed is to reduce risk of recurrence and mortality(68). Anthracycline and taxane are typical agent used for treating cancer. Cytotoxic drugs such as cyclophosphamide (Cytoxan) and methotrexate (Rheumatrex) are another type of chemotherapy called cytotoxic chemotherapy is also used for cancer therapy(39). Treatment duration of the chemotherapy is request for at least 3 to 12 weeks of multiple cycles of several options of chemical agent. Side effects of chemotherapy are menstrual irregularity, loss of appetite, neuropathy, fatigue, cardiotoxicity, and weight gain or loss(64). Recent evidence for breast cancer reported side effect of chemotherapy on cognitive decline(69, 70), lowers mobility and balance performance (71, 72) and increase risk of fall which detected by TUG-dual-task assessment(32).

Endocrine therapy is a treatment for breast cancer using drug agent to counteracts estrogenic imbalance in patients with breast cancer. Adjuvant endocrine therapy reduces the risk of breast cancer recurrence and mortality(73). Standard endocrine therapy consists of oral antiestrogen medication taken daily for 5 to 10 years(74). It is usually administered to patients at pre or post-surgery, post radiotherapy, or subsequent to chemotherapy (i.e., adjuvant endocrine therapy)(75). However, standalone endocrine therapy (without chemotherapy) usually prescribed for the luminal A-like breast cancer (HR -positive /HER2⁻negative) subtypes(44, 63). There are two

main types of endocrine agents used in endocrine therapy for breast cancer which are estrogen receptor modulator and aromatase inhibitors(63). They involve three mechanisms related to estrogen hormone system including selective modulation of estrogen receptor, competitively inhibits binding of estrogen-to-estrogen receptor, and inhibition conversion of androgens to estrogen. There are several side effects of endocrine therapy for cancer such as blood clots, hot flashes, vaginal dryness, arthralgia, and myalgia(76). and cognitive decline(13). Tamoxifen increases the risk of venous thromboembolism while aromatase inhibitors increase risk of having osteopenia and osteoporosis and are associated with more musculoskeletal symptoms(74).

2.4 Side effect of the endocrine therapy for breast cancer on cognitive decline

The cognitive impairment is found to be related to endocrine therapy. The effects of endocrine therapy on cognitive function decline in breast cancer patients who have postmenopausal status (mean age 68 years old) are found after 1 year of endocrine therapy, especially on verbal memory and executive functioning(15). Bender et al., 2015 reported postmenopausal women with cancer receive chemotherapy plus endocrine therapy (aromatase inhibitor) demonstrated lower working memory and attention performance than postmenopausal women without breast cancer(77). Chen et al.,2017 reported breast cancer patients who received endocrine therapy with tamoxifen drug had lower executive function and working memory than those who did not receive tamoxifen and healthy women(78). In addition, magnetic resonance imaging showed lower functional connectivity of right dorsolateral prefrontal cortex with the right hippocampus in breast cancer who took endocrine therapy drug compared to healthy women(79). Evidence from many studies emphases important side effect of endocrine therapy in breast cancer on cognitive function especially on working memory subdomains of the executive function(11, 80).

Mechanism of side effect of endocrine therapy on cognitive decline. The present of estrogen receptors in those areas of the brain indicates the role of estrogen hormone for brain's function. Estrogen receptor is found in many areas of the brain including hippocampus, prefrontal cortex, and amygdala (13) which are important for performing task requiring executive function, verbal learning, and memory, respectively (13).

There are six domain of the cognitive function including perceptual-motor function, Language, learning and memory, social cognition, complex attention, and executive function(81). The executive function of the brain is important for performing two cognitive-challenged tasks at same time (dual-task)(82). Attention, inhibitory control, working memory, and cognitive flexibility are subdomains of executive function which are essential for stability during walking under complex environment and walking while performing another task(83). Therefore, it would be possible endocrine therapy may have side effect on lowering dual-task performance with decreasing of executive function of the brain.

The effect of endocrine therapy on cognitive function was found one year of receiving this treatment, indicating time concern for cognitive screening in patients with breast cancer especially those who received endocrine therapy(14-16) Standard treatment plan for endocrine therapy is at least 5 years, however, it is insufficient evidence directly compared the effect of different duration of receiving endocrine therapy. A more therapy on cognitive function and duration after completing endocrine therapy. A more recent study reported that duration of undertook endocrine therapy was risk factor of impaired cognitive function, the longer duration of receiving endocrine therapy, the higher risk for cognitive impairment(17).

2.5 Postural control impairments in patients with breast cancer

Postural control system is a complex motor skill derived from the interaction of multiple systems which aimed to control body alignment (postural orientation) and maintain body's center of mass (CoM) within based of support (postural equilibrium)(84). Components of postural control system includes biomechanical constraints, movement strategies, sensory strategies, orientation in space, control of dynamics, and cognitive processing(84). Impairment of any component can lower postural control performance.

Postural control problems such as muscle weakness, poor balance, proprioception, cognitive impairment reported in patients with breast cancer. These problems may lead to an increased risk for falls(21). Muscle fatigue and fibromyalgia are side effect of treatment for patients with breast cancer and cancer survivors who received chemotherapy(85) Breast cancer surgery could lead to weakness of the trunk and upper limb muscles which affect biomechanical constrains and postural control(86). A previous study in patient with breast cancer who received chemotherapy and endocrine therapy reported impairment of vestibular and visual function(22). These problems associated with decrease postural control performance which are risk factors of fall in this group of patients (22). A recent systematic review and meta-analysis of observational studies indicated impairments of system underling postural control such as limits of stability and sensory integration in patients with breast cancer (23). A recent study reported impaired postural response strategies in cancer with chemotherapy, they found the patients have a larger sway amplitude and velocity than healthy persons when they response to external perturbation(87).

Cognitive processing is the brain function that required for controlling postural stability in a complex task such as walking in irregular environment, and simultaneously performing a motor task and a cognitive task (dual-task) The more difficult the postural task, the more cognitive processing is required(88). Individuals who have limited either ability or motor ability may use more of their available cognitive processing to control posture(84). Most of previous studies on side effect of treatment for breast cancer indicated effects of surgery, radiotherapy, and chemotherapy on impairment of system underlying on postural control including dual-task effect. However, there is insufficient evidence to summarize the effect of endocrine therapy postural control, especially on dual-task performance

Previous studies dual-task performance in older adult with breast cancer survivor who completed cancer treatment at least 3 months reported that TUG with counting backward are able to predict fall(32). This indicates postural control problem in context of cognitive processing in patients with breast cancer. As mentioned earlier patients with breast cancer who is undertaking endocrine therapy are prone to have a decrease function of estrogen in the brain and may consequently in an impairment of executive function(11). However, mostly from the previous study in dual-task paradigm was conducted in patients who received chemotherapy with non-endocrine therapy(89).

2.6 Assessment of cognitive function

Several tools can be used to assess global cognitive function and specific cognitive performance(90). The Montreal Cognitive Assessment (MoCA) is one of the most commonly used tools in clinics to screen global cognitive functioning. It includes item for screening function of multiple cognitive domains, including short-term memory, visuospatial skills, executive function, attention, concentration and working memory, language, and orientation. This tool is sensitive and valid to screen mild cognitive impairment with sensitivity ranging from 67 to 100% and specificity ranging from 50 to 95% depending on different study protocols(91, 92). There is Thai version of the Montreal Cognitive Assessment (MoCA-T) which is sensitive (ICC = 0.80) and valid to differentiate older adults having mild cognitive impairment (MCI) and probably having cognitive status at worsen than MCI or having dementia from normal cognitive function(93). The Mini Mental State Examination (MMSE) is one of the most commonly used cognitive screening tools(94). The test can screen function of multiple cognitive domains such as orientation, attention, simple calculation, immediate recall, language, short-term memory, and construct ability. This test is reliable (ICC of 0.95)(95). However, its sensitivity (= 0.50) and specificity (=0.70).(91) to differentiate older adult mild cognitive impairment are lower than the MoCA test (sensitivity >0.80 and specificity>0.80)

2.7 Dual-task

Dual-task is defined as "the concurrent performance of two tasks that can be performed independently, measured separately and have distinct goals" (96). Dual-task is a commonly task found in daily activities such as walking while talking, texting on cell phone, or thinking about one's shopping list (24). Dual-task performance is highly associated with fall history (25). Older adults and patients with neurodegenerative diseases who present deviation of normal gait pattern and/ or decrease cognitive ability under dual-task compared to single task indicating problems with dual-task performance which may lead to falls(24).

The table3 shows nine possible outcomes of dual-task performance test in relative to single-task performance of each task(97). (table 3) There are many factors effect patterns of the change of motor and cognitive performance under dual-task performance relative to single task(98) such as the types and levels of difficulty of tasks, instructions for prioritizing task, and individual characteristics of cognitive and motor abilities, and fear of falling(97).

In older adults, decreasing information processing and executive functioning abilities lead to difficulty in maintaining balance while performing cognitive tasks (99, 100) In cancer patients, Scott at el. in 2019 found executive dysfunction was associated with decreased gait stability during challenging dual-task gait in survivors with sensory symptoms of patients with chemotherapy- induced peripheral neuropathy (CIPN)(101).

		Cognitive performance					
		No Change		Improved	W	/orsened	
Motor	No Change	No	dual-task	Cognitive	М	lotor-related	cognitive
performance		interferen	се	facilitation	in	terference	
	Improved	Motor fac	ilitation	Mutual facilitation	М	lotor-priority tra	ade-off
	Worsened	Cognitive	-related	Cognitive priorit	y M	lutual interferer	nce
		motor inte	erference	trade-off			

Table 3 Possible outcomes of dual-task performance

Dual-task performance assessment

To assess dual-task performance, simultaneously performing motor task and a cognitive task are used in various populations(102). Walking straight on even surface and the Timed Up and Go test (TUG) are frequently used as a motor task of dual-task performance test. The TUG is a reliable assessment with excellent test-retest reliability in

older adults (ICC > 0.98)(28). The TUG-dual-task is valid to determine functional mobility, stability during waking, and identifying older persons who is at risk of falling with 80 percent of sensitivity and 93 percent of specificity(103). The TUG-cognitive is a performance test of TUG with additional cognitive task. The increasement of time to complete TUG-cognitive compared to TUG of 22-25% has been used to indicate impairment on dual-task performance(103). The completion time of TUG-subtraction has 80% sensitivity and 93% specificity for identifying community- dwelling older adults who are prone to falls(103).TUG-cognitive test with serial subtraction are the most reliable (104). Several types of cognitive task used in TUG dual-task performance test such as counting number backward by 3 or 7(105) speaking as many words as possible from a predetermined category (e.g. fruit) for 30 seconds (Verbal fluency task) (106), saying the name of the color and report the color of the text (Inhibitory control)(107). Additionally, to the TUG task, other motor task such straight walking and walking downstair have been used in dual-task performance assessment in older adults. Complexity of motor task affects dual-task performance(105). A straight walking task may have less postural control requirement because of simple of the motor task compared to the TUG which is composed of postural transition and turning. Walking downstairs requires the ability to control deceleration of body mass against gravity which is more challenge than the TUG which less related to gravity. However, going down stair simultaneously with a cognitive task may not saft for older adults who trend to have low performance on executive function as patients with breast cancer.

TUG-cognitive test with serial subtraction test has good psychometric properties with 80% sensitivity and 93% specificity for identifying community- dwelling older adults who are prone to falls(103). This test are reliable for assessing assessment for cognitive motor interference as it can be quantified number of correct answer and time to complete task(104). A previous study in patients with stroke showed that duration for completing TUG-cognitive test with serial subtraction was longest compared to TUG with other cognitive tasks, i.e., auditory working memory, and clock task except phonologic fluency task. It indicated that TUG-cognitive with serial subtraction and

phonologic fluency had similar difficulty(108). This evidence suggested using TUG with serial subtraction or phonologic fluency for TUG-cognitive in patients with stroke. However, there are no evidence in older adults(108). On currently knowledge, TUG dual-task with serial subtraction test is the most appropriate for assessing dual-task performance in older adult regarding reliability, validity, and difficulty of this test.

Article	Participant	Testing procedure	Outcome of interest
Beauchet et al,	Older adult mean	One trial of single task in	Number of enumerated figures in
2007 (7)	aged 84.8 ± 5.2	counting backwards from 50 in	single and dual-task conditions
		ones out loud	Odd ratio to indicate fall risk
		One trial of counting backward	
	• 1	with walking 10 m. as dual-task	
		test	
Beauchet 0,2008	Older adult mean	One trial of walking in 10 m.	Gait speed and level of association
(8)	aged 84.48± 5.3	One trial of counting backward	to <u>recurrent falls (</u> IRR=0.84, 95%CI
	6 910 V	from 50 in ones out loud while	= 0.71 to 0.99
		walking in 10 m.	
Herman, 2010 (9)	community-living	One trial of walking a 25 mlong	
	healthy older adults	(2mwide) for 2 minutes	Swing time variability, high value
	age ranged from 70	Serial subtraction in three from a	associate to recurrent falls
	to 90 years	mental tracking task during	(OR=1.47, 95%CI 1.13 to 1.92)
		walking a 25 mlong (2mwide)	
Shumway-Cook,	Older adult with no	Time up and (TUG) alone	Time duration complete TUG under
2000 (10)	history of fall and	TUG cognitive:	3 conditions Sensitivity= 80%,
	older adult with a	subtraction by 3 from number	specificity=93% in TUG cognitive for
	history of 2 or more	between 20 and 100)	identifying community- dwelling
	falls in previous 6		older <u>adults' risk of fall</u>
	months (mean age	TUG manual: TUG while carrying	
	78 years)	a full cup of water	
Muhaidat J,2014	community-dwelling	Straight walking and visuospatial	Incidence of fall at 6 months follow
(11)	adults with non	clock task/ carrying a cup/	up
	faller	tasking complex streetwalking	
	aged ≥ 65 years	with turns and naming animals/	

Table 4 Example of dual-task paradigms have been used in previous studies

Article	Participant	Testing procedure	Outcome of interest
		counting backwards / avoiding obstacles/ naming animals	
		Timed Up & Go (TUG) and carrying a cup	
		Stair descent and naming animals	

2.8 Factors affecting dual-task performance

There are several factors affect dual-task performance such as age, health condition, and different types of motor and cognitive task(112) thus a study using dual-task paradigm need to concern on factors affecting dual-task performance.

The decline of I body function such as decrease in muscle strength, decrease in mobility lowering dual-task performance⁽¹²⁾. Impairment on cognitive function influence's ability to perform dual-task. Different dual-task performance among three groups of people who have difference cognitive function including older adults with normal cognitive function, mind cognitive impairment, and dementia has been reported⁽¹³⁾. Individual who have chronic disease may have problems with cognitive functions such as Alzheimer's disease, Parkinson' s disease⁽¹⁴⁾, stroke⁽¹⁵⁾, diabetes mellitus⁽¹⁶⁾, and musculoskeletal conditions (e.g. orthopedic impairments, upper or lower extremity fracture in the past 6 months)⁽¹⁷⁾ which may consequence in lowering dual-task performance. Same group of people with similar characteristic could present difference gait and balance parameters such as gait cadence and stride velocity under difference motor-cognitive dual-task conditions⁽¹⁸⁾.

CHAPTER 3 METHODOLOGY

Study design

This study aims to compare the dual-task performance between older adults who have no and have breast cancer with endocrine therapy. An observational analytical design was used to measure TUG-cognitive task performance between two group of participants in this study (BCA-Endocrine and Non-CA). A main researcher (Researcher 1) who was a master's degree student in physical therapy was responsible for collecting the main outcomes of this study (Dual-task performance) and was blinded to the groups of participants. A physical therapist who had experience for 5 years in geriatric patients (Researcher 2) was responsible for screening participants with inclusion and exclusion criteria before beginning of data collection for main outcomes (Researcher 1).

Participants

Two groups of participants participated in this study, including older adults who had no cancer (Non-CA) and those who had breast cancer with endocrine-based therapy (BCA-Endocrine). This study included 30 participants in each group. Inclusion and exclusion criteria for screening eligible participants are listed below. All participants in this study signed a consent form. The study protocol was approved by the Human Research Ethics Committee Chulabhorn Research Institute review board (Approval number:EC001/2567). (Appendix1)

Inclusion criteria

For Non-CA group: aged 60 years and over, able to walk independently with or without an assistive device and able to perform subtraction by three.;

For cancer group: aged 60 years and over, having primary breast cancer in Luminal A-like breast cancer diagnosed by medical doctor, undertaking endocrine therapy (Tamoxifen/ Aromatase inhibitor) at least 1 year⁽¹⁹⁾, having primary treatment by surgery and able to perform subtraction by three.

Exclusion criteria

The tentative participants who meet the inclusion criteria were further screened with the exclusion criteria. Those who met any of the following criteria were excluded from this study:

Having treatment for symptoms associated with metastasis or other primary cancer;

Having history of adjuvant chemotherapy.⁽¹⁹⁾

Having a history of diseases causing organic changes of the brain, neuropsychiatric disorders, or

other acute illness⁽²⁰⁾;

Having neurological, or substance use disorders affecting cognition and exposure to neoadjuvant therapy ⁽²¹⁾,

Having significant musculoskeletal issues in the lower body that would interfere with walking and unstable medical issue or uncontrol disease⁽²²⁾.

Having visual problem and hearing problems that cannot corrected by visual and hearing devices or medication⁽²²⁾.

Probably having cognitive impairment worse than mild cognitive impairment according to the score of Cognitive Assessment Thai version (MoCA-T)⁽²³⁾ score of at 23 points or lower out of a total score of 30 points^(24, 25). In case of having education less than 12 years, additional 1 point was applied for reliability of screening⁽²⁶⁾

Sample size calculation

The minimum number of subjects required for each group is 30 persons. This sample size for study has been estimated based on mean and standard deviation from the data of TUG-Cognitive in breast cancer survivors from a related previous study ⁽²⁷⁾, values of error probability at 0.05, and power beta error at 0.80, using G*power software version 3.1 (Figure 2).



Figure 2 Sample size calculation with G*power program

Study tools and instrument

The study tools and instruments are listed below. Data collection procedure and analysis were explained separately in this chapter's next part.

The Montreal Cognitive Assessment in Thai version (MoCA-T)⁽²³⁾ was used to assess global cognitive status of participants. (Appendix2)

Timed up and go test (TUG) (28)

TUG with cognitive task: 3-serial-subtractions task ⁽²⁹⁾.

The equipment used in this study is listed below:

Chair with a backrest (Approximate seat height of 42 cm.),

Stopwatch,

Measuring tape,

Marking tape

Smartphone with a video recording application

Procedure

Participant screening

Participants for the BCA-Endocrine group were recruited from patients who received intervention at the cancer clinic, Chulabhorn Hospital. Participants for the Non-CA group were recruited from older adults who live in community nearby Chulabhorn Hospital with the inclusion and exclusion criteria mentioned earlier (Researcher 2). Older adults who met the eligible criteria were invited to be the study's participants.

Participants' ability to subtract numbers was screened to ensure the ability to complete the Cog-single test by performing subtraction by 3 starting from 100 with at least 5 numbers correct answers. The initial number used during main outcome test were difference from the screening session to avoid learning effect. Participants were asked to perform the subtraction task in a sitting position (Sitting on a chair with armrest).

Age and education were factors affecting cognitive functions; therefore, this study controlled these confounding factors by matching age and education level between groups of participants. The participants in Non-CA were matched for age and education level with participants in BCA-Endocrine groups (Age- and Education-matched Non-CA group). Two-year-old differences between the age of a participant in Non-CA (Age-matched) compared to BCA-Endocrine were accepted. Education levels were categorized into primary school, secondary school, high school, diploma, undergraduate level, and higher⁽³⁰⁾. Participants' highest education levels were converted to years of education for comparing means between groups. The total years for the highest education level of primary school, secondary school, high school, high school, diploma, bachelor's degree, and master's degree is 6, 9, 12, 16, and 18 years

Demographic and medical information were obtained during an interview and from the medical record form (For the cancer group) and recorded in the data record form. Participants' age, highest level of education and medical history, menopause status, occupational, use of walking aids were asked in both groups and gathered in data collection. Diagnosis of breast cancer about time since taking endocrine therapy, endocrine therapy agents and treatment duration, and history of cancer treatment (Surgery, Chemotherapy, or Radiation) were further collected for the BCA-Endocrine group (Appendix3)

Prior to data collection process, the researcher1 practiced using TUG test, TUG-cognitive test, and reliability test were measured in 10 healthy participants. A high intra-rater reliability with intraclass correlation coefficient of TUG-single ICC(3,1)=.99 and TUG-Cog ICC(3,1)=.99 was as expected⁽²⁹⁾. The researcher2 practiced using MoCA-T in two samples of older adults and the scores from each tool were compared and discussed with a physical therapist who had experience of using this screening tool.

Dual-task performance testing

Participants were asked to perform three test conditions including TUG, and TUG with cognitive (TUG-Cog), and cognitive task when seated (Cog-single) by the researcher1. Demographic of the participants, and medical information was blinded to this researcher. The sequence of the two conditions of the TUG tests were started with TUG and follow by TUG-Cog. Thereafter, the Cog-single were administered and the time to perform were matched to the participants' time completing the TUG-Cog condition. Data collection for all test conditions were conducted at the sample place (A research room at the Chulabhorn hospital) and completed within 1 hour. Prior to data collection, TUG and TUG-Cog were demonstrated and practiced until the participants become familiar with the tasks.

In the TUG condition, participants were asked to sit in a starting position (Sit with back touching the chair arms resting on the chair's arms and walking aid at hand). No physical assistance is given. In the starting position. They were allowed to ware his/ her regular shoes and use a usual walking aid. All participants received the same instruction with the word "Go" (In Thai language) to get up and walk at their comfortable speed to a line on the floor 3 meters away, turn, return to the chair, and sit down again. ⁽³¹⁾ There are different TUG protocols used to determine balance and fall risk screening including walking as fast as possible and comfortable speed⁽²⁸⁾, however, walking at a comfortable speed was used to ensure safety to older participants of this study⁽²⁸⁾. Each

participant was required to perform each task only once during data collection with five minutes of resting between the tasks. Prior to data collection, all tasks were demonstrated and practiced ensuring their understanding in the tasks.

In the TUG-Cog condition, participants are required to perform TUG with the additional of cognitive task. They were instructed to perform both TUG and a cognitive task as their best performance without prioritizing either TUG or cognitive tasks. TUG with number subtraction by 3 starting with a starting number that differs from the cognitive single task condition. After 3 numbers correct answers, participants started to perform TUG, and a stopwatch was used to measure the time to complete the task.

A stopwatch was used to measure the time to complete the TUG and TUG-Cog tasks. Recording time started when the participants' backed off the chair and stopped when the participant's buttock touched the chair, and the trunk was in the strength position. A smartphone video-recorded application was used to record participants' answers while they performed the number subtraction task or ward naming task under single-task or dual-task conditions. The correctness of the cognitive response was determined from the recorded answers of each participant.

In the Cog-single condition, participants were asked to count numbers backward by 3 at the same time of TUG-Cog duration starting from 100 to 70⁽¹⁰⁾ with the following instruction. The number of correct responses was collected by video recorder.

The summary of measurement variables derived from the data collection procedure is showed in the table 5.

Measurement variables	Unit	Measurement scale
Demographic and medical information		
age		Ratio scale
time since taking endocrine therapy		Ratio scale
endocrine therapy agents (tamoxifen,	percent of (N %) tamoxifen and	Nominal scale
Aromates inhibitor)	Aromatase inhibitor in the BCA-	
	Endocrine group	
duration to taking endocrine therapy	Mean (SD)	Interval scale

Table 5 Measurement variables, their unit, and scale that was collected for this study

Measurement variables	Unit	Measurement scale	
history of cancer treatment (surgery,	N% of tamoxifen and Aromatase	Nominal scale	
radiation)	inhibitor in Cancer group		
menopause status	N%	Nominal scale	
number of education years		Ordinal scale	
MoCA score	Mean (SD)	Interval scale	
Main outcomes measurement			
TUG	Second.	Interval scale	
TUG-Cog	Second.	Interval scale	
3-serial-subtractions task	Numbers. /times	Interval scale	

MoCA = The Montreal Cognitive Assessment, TUG= Timed up and go test, TUG-Cog= Timed up and go with cognitive

Data analysis

Participants' demographic and medical information were analyzed using descriptive statistic (means, standard deviation, minimum and maximum data, and percentage). Dual-task performance were determined by the percent dual-task effect (DTE% = [Dual-task – single task)/single task x100]) which represented the influence of the additional cognitive task on performance of the single cognitive task and TUG task⁽³²⁾.

Total time to complete TUG task under each condition of the TUG, i.e., TUG duration and TUG-Cog duration were used to calculate dual-task effect on the motor task (DTE% motor) with below equation. ⁽³³⁾ A greater DTE% in TUG duration implicates greater TUG performance deterioration indicating high degree of dual-task interference⁽²²⁾.

DTE% in TUG duration $= \frac{TUG - Cog (seconds) - TUG (seconds)}{TUG (seconds)} x 100\%$

Prior to the calculation for the DTE% for performance on the 3-serialssubtraction task (DTE% cognitive), the correct response rate (CRR) were calculated with the following equation ⁽³⁴⁾:

$CRR = \frac{number \ of \ correct \ answers}{Time \ (seconds)}$

Times in the CRR equation is time available to perform the 3-serialssubtraction task under cognitive single task and dual-task conditions. The CRR under the cognitive single task and TUG-Cog was calculated and substituted into the DTE% equation:

DTE% in CRR= $\frac{CRR under dual task - CRR under Cog - single}{CRR under Cog - single} x 100\%$

The negative DTE% and the positive DTE% in CRR indicates cognitive performance under dual-task conditions is worse and better, respectively.⁽³⁵⁾

The normality of data was examined by Kolmogorov-Smirnov test. Characteristics and demographic between groups was compared using statistical for two group comparisons. The attention domain score of the MoCA was further analyzed to fine minor difference between groups of participants which might be a possible reason of difference in dual-task interference. Independent t-test was used to evaluate the different DTE% between participants' groups (i.e., Cancer and Non-CA). The Mann-Whitney U test was used in case of data on the DTE% showed non-normal distribution. The alpha level was set at 0.05 to consider a significant difference. Summary of study procedure is showed in Figure3



Figure 3 Study procedure flow-chart

MoCA = The Montreal Cognitive Assessment, TUG= Timed up and go test, TUG-Cog= Timed up and go with cognitive, Cog-single= Cognitive task

CHAPTER4 RESULT AND DISCUSSION

Result

One hundred and seven people were screened and met the inclusion criteria. Twenty older adults in the healthy group and 27 older adults in the cancer group were excluded because of problems with cognitive function ((MoCA-T scores \leq 23 points), resulting in 60 older adults eligible for this study. Thirty participants in each group: older adults who did not have cancer (Non-CA group and had breast cancer with endocrine therapy (BCA-Endocrine group) were willing to sign a consent form to participate in this study. Non-CA Participants' characteristics including age, years of education, hormone therapy agents, MoCA-T scores, history of cancer treatment, and duration of hormone therapy results, are presented in Table 1. Confounding factors of cognitive performance which were age and year of education were not significant differences between groups (p =.888). Regarding medical history, there was a variety in the type of hormones taken by the BCA-Endocrine group. Tamoxifen was found to be the most commonly used hormone therapy drug in this research study (Table 6). There was no significant difference between groups in the MoCA-T scores (p =.156). The BCA-endocrine had lower scores on the attention and the executive domains compared to the Non-CA group with significant differences at p=.007 and p=.021 respectively. However, other domains were not significantly different (p = .1-1.0).

Characteristics	BCA-Endocrine (N=30)	Non-CA (N=30)	<i>p</i> -Value
Age (years)	66.1 ±4.5	66.3 ± 4.6	.888
(Min-Max)	(60.0-77.0)	(60.0-77.0)	
Year of education:	14.3 ± 3.2	14.1±3.4	.785
(Min-Max)	(6.0-18.0)	(6.0-18.0)	

Table 6 Demographic and medical information (mean SD or N%)

Characteristics	BCA-Endocrine (N=30)	Non-CA (N=30)	p-Value
Education level			
Primary school	1 (3)	1(3)	
Secondary school	2 (7)	1(3)	
High school	5 (17)	4(13)	
Diploma	3 (10)	3(10)	
Bachelor's degree	15 (50)	14(47)	
Master's degree	4 (13)	7(24)	
Duration since cancer diagnosis (years)	2.7± 0.6	-	
Type of breast cancer in diagnosis	A Colorador	-	
Luminal A-like	30 (100)		
Primary tumor		-	
pTis	3 (10)		
pT1	16 (53)		
pT2	11 (37)		
pT3	0		
Nodal status			
pN0	16 (53)		
pN1	5 (17)		
pN2	9 (30)		
Cancer treatment:			
Surgery with hormone therapy	8 (27)	-	
Surgery with radiotherapy and hormone	22 (73)		
therapy			
Duration of Hormone therapy (months)	21.4 ± 1.4	-	
Hormone therapy agents:			
Tamoxifen	23 (77)	-	
Aromatase inhibition (AI)	3 (10)		

Characteristics	BCA-Endocrine (N=30)	Non-CA (N=30)	p-Value
Tamoxifen with Al	4 (13)		
MoCA-T (points/30)	25.4 ± 1.7	26.1 ± 1.9	.156
Memory & Attention domain (points/6)	5.03 ± 0.6	5.50 ± 0.6	.007*
Visuospatial/executive (points/5)	3.87 ± 1.2	4.30 ± 0.8	.021*
Naming (points/3)	2.96 ± 0.2	2.96 ± 0.2	1.000
Language (points/3)	2.67 ± 0.5	2.73 ± 0.4	.273
Abstraction (points/2)	1.5 ± 0.5	1.6 ± 0.5	.142
Delayed recall (points/5)	2.87 ± 1.3	3.1 ± 1.2	.442
Orientation (points/6)	5.9 ± 0.2	5.9 ± 0.2	1.000

MoCA-T: Montreal Cognitive Assessment Thai version, Luminal A-like: molecular subtype of breast cancer in hormone receptor-positive and human epidermal growth factor receptor2(HER2) negative, pTis: carcinoma in situ, pT1: tumor 2 cm. or less in greatest dimension, pT3: tumor more than 5 cm in greatest dimension, pNo: No regional lymph node metastases, pN1: Metastases in one to three regional lymph nodes, pN2: Metastases in four or more regional lymph nodes, AI: Aromatase inhibition, Tamoxifen with AI: Tamoxifen with aromatase inhibition.

We first compared participants in dual-task performance testing including TUG, TUG-Cog and Cog single in table 7. TUG-Cog duration time were longer than TUG duration. These findings were found in BCA-Endocrine and Non-CA group. When compared between group, we found that BCA-Endocrine group demonstrated significantly longer TUG and TUG-Cog duration than the Non-CA group (p=0.001). Number of correct answers was not difference between groups for both single and dual-task condition. However, the CRR was lower in BCA-Endocrine group compared to the Non-CA group Both groups showed a decrease in the correct response rate when performing the subtraction task under TUG-Cog condition (CRR TUG-Cog) compared to Cog-single condition (CRR Cog- single). However, overall, group showed a significantly lower number of correct responses than Non-CA group (p < 0.001).

Performance test	(N=30)	Non-CA (N=30)	<i>p</i> -Value
TUG. (sec)	11.0 ± 2.3	9.3 ± 2.2	.001*
TUG-Cog. (sec)	20.0±4.6	15.2±4.7	.000*
Numbers of correct answers			
3 serial-subtraction tasks in TUG-	2.9±2.3	3.7±1.7	.158
Cog	5.9±2.7	7.1±2.9	.084
3 serial-subtraction tasks in Cog-			
single	51/10		
CRR Cog- single	0.3±0.1	0.5±0.2	.000*
CRR TUG-Cog	0.1±0.1	0.2±0.1	.000*

Table 7 Performance of participants (Mean± SD)

TUG: Timed up and go test, TUG-Cog: Timed up and go with cognitive test, CRR: Correct response rate, CRR C0g-single: Correct response rate in Cognitive single test, CRR TUG-Cog: Correct response rate in Timed up and go with cognitive test, * depict a significant between groups at p<.05.

Results on the analysis of the dual-task effect (DTE%), the percent change in dual-task performance showed that the BCA-Endocrine group had significantly greater mean± sd of the DTE% in TUG duration (85.4 ± 44) than the Non-CA group (63.2 ± 32.8) (p =.03) (Figure4). Negative DTE% in CRR rate was found in the BCA-Endocrine group (- 50.6 ± 31.7) and the Non-CA group (- 46.5 ± 18.2) (Figure 5). When compared between groups, the significant difference in the DTE% in CRR was not found (p=.421).



Figure 4 Dual-task effect in TUG duration in BCA-Endocrine and in Non-CA group Data presented as mean and standard deviation for each group. A greater DTE% in TUG duration represents a greater degree of dual-task interference in the TUG performance. * Significant difference between groups at p < .05.</p>

Abbreviations: DTE% = Dual-task effect in percentage, TUG = Timed Up and Go, DTE%TUG = dual-task effect in TUG performance.



Figure 5 Dual-task effect in correct response rate.

Dual-task effect in TUG duration in BCA-Endocrine group and in Non-CA group. Data presented as mean and standard deviation for each group. The negative

DTE% and the positive DTE% in CRR indicates cognitive performance under dual-task conditions is worse and better, respectively.

Abbreviations: DTE% = Dual-task effect in percentage, CRR = correct response rate, DTE%CRR = dual-task effect in correct response rate.

Discussion

Breast cancer patients often receive medical treatment along with rehabilitation through physical therapy for lifesaving and reducing patients suffering from side effects of cancer treatment. Regarding a literature review, hormone therapy has an impact on cognition function⁽³⁶⁾ and a decrease in stability of walking and balance^(37, 38). However, there are no studies regarding dual-task performance in breast cancer with hormone therapy stand-alone ^(37, 39). This study expanded the knowledge on the decline of dual-task performance, an indicator of risk of falling in elderly ⁽⁴⁰⁾, in breast cancer in older adults with endocrine therapy (BCA-Endocrine) was due to the endocrine therapy itself or the aging process. The main results that older adults with breast cancer undergoing endocrine therapy were more susceptible to dual-task interference compared to older adults without cancer. According to the use of the age-matched control group indicated these findings were not due aging process.

Longer TUG duration in the BCA-endocrine that was found in this study indicates lower performance of balance during walking and a high degree of TUG performance deterioration in patients with breast cancer. This result was similar to a previous study that found TUG scores in older adults with various types of cancer were longer than community older adults ⁽⁴¹⁾. Moreover, this result was also in line with the findings of previous studies study of Morishita and colleagues in 2018 ⁽³⁸⁾. They reported that breast cancer survivors have significantly higher TUG duration than healthy subjects ⁽³⁸⁾ and stability decreased during challenging dual-task gait⁽³⁷⁾. The consistency among findings of the present study and those previous studies ^(37, 38, 41) emphasizes problems in balance during walking in patients with cancer.

Results on larger dual-task effect (%DTE) in TUG duration allowed better comparison between the BCA-Endocrine and the Non-CA groups which had different TUG single-task durations. The larger percentage of dual-task effect in TUG duration indicated a larger deterioration in balance during walking dual-task in the participants with breast cancer undergone hormone therapy compared to healthy elderly. The dualtask interference of gait also appears to be age-related, with a more pronounced decrease in performance and a higher dual-task interference seen in older adults than in middle-aged and younger adults⁽¹⁷⁾ In addition education level affects cognitive functions^(30, 42) which turn to affect dual-task performance ⁽⁴³⁾. However, age and education could not be the reasons for the larger dual-task effect in the BCA-Endocrine because of the matching of the age and education level between participants in the BCA-Endocrine and the Non-CA group. Therefore, receiving the endocrine therapy and cancer itself could be a reason for the difference between the group in TUG performance and cognitive performance measured under single-task and dual-task conditions. Regarding literature reviews, the possible reason for a larger dual-task effect in TUG performance in the BCA-Endocrine group may be because endocrine therapy affected cognitive function, especially on the working memory subdomain of executive function and attention ^(44, 45). The attention and executive function of the brain are important for performing two cognitive-challenged tasks at the same time (Dual-task)⁽⁴⁶⁾. In the present study, the BCA-Endocrine and the Non-CA group had no difference in the total score of the MoCA-T indication of similar global cognitive function. However, considering more on the domain score of the MoCA-T we found a significant difference between groups for a score on the attention, memory, and executive domain. The attention domain of the MoCA-T test consists of digit span forward and backward tasks measuring the ability to articulate rehearsal of a set of numbers and a transient working memory, respectively. The backward digit span task requires central executive processing^(26, 47). In addition, serial subtraction performance was lower in the BCA-Endocrine group. This task requires working memory⁽⁴⁸⁾, therefore, it would be possible endocrine therapy may have an effect on lowering dual-task performance through the

decreasing of executive function of the brain. One might argue that cancer itself can affect physical function and lead to larger requirements on control stability thus lowering dual-task performance. Previous studies reported cancer-associated muscle dysfunction. Studies on animal models demonstrated that breast tumor growth releases many cytokines inducing muscle wasting and decreasing the level of physical function in mice⁽⁴⁹⁾. Most of the literature review data typically includes information collected before and after patients have undergone rehabilitation. There are no studies that reported physical performance and cognitive function in research participants prior to breast cancer treatment⁽⁴⁹⁻⁵¹⁾. This is because once patients receive a cancer diagnosis, they are prioritized for immediate medical treatment to preserve their lives, leaving little opportunity for assessments unrelated to the direct treatment of the cancer⁽⁵²⁾. The present study included an assessment of muscle function in patients with cancer. Therefore, we cannot exclude the effect of cancer itself on muscle function and a reason of lowering dual-task performance in patients with breast cancer. However, the impact of breast cancer with endocrine therapy on dual-task performance has strongly supported with results of the present study.

As we found a negative dual-task effect in the correct response rate in the BCA-Endocrine and Non-CA group indicating that subtraction performance under dualtask conditions was decreased when participants performed cognitive tasks simultaneously with the TUG task. Performing a serial subtraction task demands attention and working memory^(48, 53). Therefore, these results can imply that the attention and working memory performance of both groups of participants were affected by dual-task. Although the BCA-Endocrine had lower subtraction performance, the magnitude of the dual-task effect on those cognitive functions was similar between groups. Considering the standard deviation of the dual-task effect (%DTE in cognitive), much variation was found in the BCA-endocrine group meaning the magnitude of the dual-task effect in cognitive function in the BCA-endocrine groups was closer to the Non-CA groups. These results may be because of the difficulty of cognitive task⁽⁵⁴⁾. A previous study found the largest negative effects of the subtraction task on cognitive-motor performance among other cognitive tasks such as the stroop task and phonologic fluency task. ⁽⁵⁵⁾. It is possible that the task was similarly difficult and challenging for both groups of older adults, thus manifesting in a decline in their ability to subtract numbers similarly.

According to the overall results on the dual-task effect, a larger magnitude of dual-task effect in the BCA-Endocrine was found for the TUG performance, but not subtraction performance, indicating inequality magnitude of dual-task interference between motor and cognitive task. These results can be explained by theories related to dual-task interference. There are two main theories including capacity theory⁽⁵⁶⁾ and bottleneck theory⁽⁵⁷⁾. Capacity theory suggests that the nervous system has a limited ability to process information concurrently. When tasked with two simultaneous activities, the processing capacity must be divided. If the processing capacity decreases, it will result in decreased performance in one or both tasks, depending on which task the nervous system prioritizes⁽⁵⁶⁾. On the other hand, bottleneck theory explains that although a large amount of information may enter the nervous system for processing, only a small amount can be processed at a time due to the narrow bottleneck of neural reception⁽⁵⁷⁾. Therefore, if there is a large amount of incoming information awaiting processing, the nervous system prioritizes and processes the information that is more relevant and important first. This prioritization leads to decreased efficiency in performing simultaneous tasks, as the more important task is processed first, causing the second task to be delayed or less efficient. In the present study, participants showed decreased both motor and cognitive performance under dual-task conditions. Therefore, the bottleneck theory may not be the explanation for the inequality magnitude of dual-task interference. Cancer affects cognitive function and additionally, with receiving endocrine therapy, participants in the BCA-Endocrine may have a more limited cognitive capacity for maintaining both motor and cognitive tasks at the same time. Eberling and colleges⁽⁵⁸⁾ reported that tamoxifen-treated breast cancer patients had significantly smaller hippocampi and inferior and dorsal lateral frontal lobes on PET scanning relative to healthy women⁽⁵⁸⁾. In addition, evidence from many studies emphasizes the important side effects of endocrine therapy in breast cancer on cognitive function compared to Non-CA subjects^(44, 45). Therefore, capacity theory seems to be more suitable for explaining the inequality of the larger magnitude of the dual-task effect in this group of participants.

Clinical implication

TUG-dual task performance in an important outcomes measure of balance during walking and the screening for risk of falls. Slower walking while counting backward was associated with fall ⁽⁸⁾. A previous study in older adults who had breast cancer showed validity of the score on TUG with counting backward in predicting falls in the future⁽²⁷⁾. All together previous evidence and the presents study results on the dual-task interference in TUG performance, emphasize the importance of screening for problems and help improve balance during walking, especially for older adults who had breast cancer with endocrine therapy.

Previously assessment and training in the rehabilitation department services for patients with cancer, usually focus on functional balance and mobility, strengthening⁽⁵⁹⁾, but not cognitive performance and dual-task performance. Findings in the present study provides physical therapists with a better understanding balance performance and its relationship with cognitive function additionally with important of the screening of cognitive and dual-task performance in patients with breast cancer with endocrine therapy for planning a more effective fall-preventing exercise in this patient group of patients.

In the cancer rehabilitation center of Chulabhorn Hospital have begun incorporating dual-task performance assessment into our fall risk evaluations for patients receiving hormone therapy for breast cancer. Additionally, we have integrated dual-task exercises into our balance training regimen. We developed a protocol and provided training for our colleagues in the physical therapy department, who have already implemented this protocol for screening and training, as demonstrated in Appendix 4.

CHAPTER 5 SUGGESTION AND CONCLUSION

Limitation and Suggestion for Further Study

We may not be able to clearly state that the decline in dual-task performance in the endocrine therapy group is solely due to the side effects of hormone therapy on muscle function. Patients suspected of having breast cancer typically undergo diagnostic tests directly aimed at detecting cancer and subsequently receive cancer treatment. It is rare for patients not to receive any treatment. Other assessments unrelated to cancer treatment, such as evaluations of physical function or cognitive function, are usually conducted after cancer treatment has been completed and the patient has entered the rehabilitation phase. Therefore, our research cannot randomly collect data from cancer patients who have not undergone treatment to compare with those who have received hormone therapy.

This study was conducted only in participants with normal levels of cognitive function. (Score from MOCA-T >23 points)⁽²⁵⁾. A sub-group analysis follows with cognitive levels to clarify the effect of balance and risk of falling difference is suggested for further study. In addition, older adults with breast cancer undergoing endocrine therapy often experience a decline in executive function. However, in our study, we did not specifically investigate executive function as it relates to dual-task performance; instead, we only assessed global cognitive function and domain score of the MoCA-test in both groups. Therefore, in future studies should assess executive function using specific tests such as the Stroop Color-Word Test, Digit Span Test, and Modified Switching Verbal Fluency Test.

Conclusion

Older adults with breast cancer who received endocrine therapy has lower dualtask performance compared to older adults who have no breast cancer. The significance of dual-task performance impairment in older adults who are under endocrine therapy for breast cancer and help guide screening for balance problems in this group of population. Research findings could add more knowledge on the importance of screening dual-task performance in patients with cancer especially those who undertake endocrine therapy for breast cancer.



REFERENCES

- 1. Kashyap D, Pal D, Sharma R, Garg VK, Goel N, Koundal D, และคณะ. Global increase in breast cancer incidence: Risk factors and preventive measures. Biomed Res Int. 2022;2022:9605439. eng. 2022/04/29.
- 2. institute Nc. Hospital-based cancer registry 2020. Thailand Moph, บรรณาธิการ.: Department of medical service; 2021. 59.
- Benz CC. Impact of aging on the biology of breast cancer. Crit Rev Oncol Hematol. 2008;66(1):65-74. eng. 2007/10/24.
- 4. DeSantis CE, Ma J, Gaudet MM, Newman LA, Miller KD, Goding Sauer A, และคณะ. Breast cancer statistics, 2019. CA Cancer J Clin. 2019;69(6):438-51. eng. 2019/10/03.
- 5. V MPK. Aging soceity and economic in thailand. Department of older persons; 2017.
- Balducci L, Phillips DM. Breast cancer in older women. Am Fam Physician. 1998;58(5):1163-72. eng. 1998/10/27.
- Beauchet O, Dubost V, Allali G, Gonthier R, Hermann FR, Kressig RW. 'Faster counting while walking' as a predictor of falls in older adults. Age Ageing. 2007;36(4):418-23. eng. 2007/03/14.
- 8. Beauchet O, Allali G, Annweiler C, Berrut G, Maarouf N, Herrmann FR, และคณะ. Does change in gait while counting backward predict the occurrence of a first fall in older adults? Gerontology. 2008;54(4):217-23. eng. 2008/04/15.
- Herman T, Mirelman A, Giladi N, Schweiger A, Hausdorff JM. Executive control deficits as a prodrome to falls in healthy older adults: A prospective study linking thinking, walking, and falling. J Gerontol A Biol Sci Med Sci. 2010;65(10):1086-92. eng. 2010/05/21.
- Shumway-Cook A, Brauer S, Woollacott M. Predicting the probability for falls in community-dwelling older adults using the timed up & go test. Phys Ther. 2000;80(9):896-903. eng. 2000/08/29.
- 11. Muhaidat J, Kerr A, Evans JJ, Pilling M, Skelton DA. Validity of simple gait-related dual-

task tests in predicting falls in community-dwelling older adults. Arch Phys Med Rehabil. 2014;95(1):58-64. eng. 2013/09/28.

- Brustio PR, Magistro D, Liubicich ME. Changes in temporal parameters during performance of the step test in older adults. Gait Posture. 2015;41(1):217-21. eng. 2014/12/03.
- 13. Åhman HB, Cedervall Y, Kilander L, Giedraitis V, Berglund L, McKee KJ, และคณะ. Dual-task tests discriminate between dementia, mild cognitive impairment, subjective cognitive impairment, and healthy controls - a cross-sectional cohort study. BMC Geriatr. 2020;20(1):258. eng. 2020/07/31.
- 14. Longhurst JK, Rider JV, Cummings JL, John SE, Poston B, Landers MR. Cognitivemotor dual-task interference in alzheimer's disease, parkinson's disease, and prodromal neurodegeneration: A scoping review. Gait Posture. 2023;105:58-74. eng. 2023/07/25.
- 15. Deblock-Bellamy A, Lamontagne A, McFadyen BJ, Ouellet MC, Blanchette AK. Dualtask abilities during activities representative of daily life in community-dwelling stroke survivors: A pilot study. Front Neurol. 2022;13:855226. eng. 2022/05/21.
- Omana H, Madou E, Montero-Odasso M, Payne M, Viana R, Hunter S. The effect of dual-task testing on balance and gait performance in adults with type 1 or type 2 diabetes mellitus: A systematic review. Curr Diabetes Rev. 2021;17(5):e011020186496. eng. 2020/10/08.
- 17. Brustio PR, Magistro D, Zecca M, Rabaglietti E, Liubicich ME. Age-related decrements in dual-task performance: Comparison of different mobility and cognitive tasks. A cross sectional study. PLoS One. 2017;12(7):e0181698. eng. 2017/07/22.
- 18. de Barros GM, Melo F, Domingos J, Oliveira R, Silva L, Fernandes JB, และคณะ. The effects of different types of dual tasking on balance in healthy older adults. J Pers Med. 2021;11(9). eng. 2021/09/29.
- 19. Schilder CM, Seynaeve C, Beex LV, Boogerd W, Linn SC, Gundy CM, และคณะ. Effects of tamoxifen and exemestane on cognitive functioning of postmenopausal patients with breast cancer: Results from the neuropsychological side study of the

tamoxifen and exemestane adjuvant multinational trial. J Clin Oncol. 2010;28(8):1294-300. eng. 2010/02/10.

- Yamamoto S, Masutani E, Arao H. Self-reported cognitive decline in japanese patients with breast cancer treated with endocrine therapy. Breast Cancer. 2020;27(4):670-82. eng. 2020/03/03.
- Collins B, Mackenzie J, Stewart A, Bielajew C, Verma S. Cognitive effects of hormonal therapy in early stage breast cancer patients: A prospective study. Psychooncology. 2009;18(8):811-21. eng. 2008/12/17.
- 22. Goh HT, Pearce M, Vas A. Task matters: An investigation on the effect of different secondary tasks on dual-task gait in older adults. BMC Geriatr. 2021;21(1):510. eng. 2021/09/27.
- 23. Tangwongchai S, Charernboon T, Phanasathit M, Akkayagorn L, Hemrungrojn S, K P, และคณะ. The validity of thai version of the montreal cognitive assessment (moca-t). 3. 2009. 172.
- 24. Hoops S, Nazem S, Siderowf AD, Duda JE, Xie SX, Stern MB, และคณะ. Validity of the moca and mmse in the detection of mci and dementia in parkinson disease. Neurology. 2009;73(21):1738-45. eng. 2009/11/26.
- 25. Ciesielska N, Sokołowski R, Mazur E, Podhorecka M, Polak-Szabela A, Kędziora-Kornatowska K. Is the montreal cognitive assessment (moca) test better suited than the mini-mental state examination (mmse) in mild cognitive impairment (mci) detection among people aged over 60? Meta-analysis. Psychiatr Pol. 2016;50(5):1039-52. eng

pol. 2016/12/20.

- 26. Julayanont P, Tangwongchai S, Hemrungrojn S, Tunvirachaisakul C, Phanthumchinda K, Hongsawat J, และคณะ. The montreal cognitive assessment-basic: A screening tool for mild cognitive impairment in illiterate and low-educated elderly adults. J Am Geriatr Soc. 2015;63(12):2550-4. eng. 2015/12/10.
- 27. Blackwood J, Rybicki K. Assessment of gait speed and timed up and go measures as predictors of falls in older breast cancer survivors. Integr Cancer Ther.

2021;20:15347354211006462. eng. 2021/04/01.

- 28. Bohannon RW. Reference values for the timed up and go test: A descriptive metaanalysis. Journal of Geriatric Physical Therapy. 2006;29(2).
- 29. Chanakan Rakyoo BH, Rampa Boonsinsukh. Comparison of time spent during timed up and go test with naming or arithmetic calculation in thai elderly. Journal of Physical therapy. 2013;2(35):109-18.
- Lövdén M, Fratiglioni L, Glymour MM, Lindenberger U, Tucker-Drob EM. Education and cognitive functioning across the life span. Psychol Sci Public Interest. 2020;21(1):6-41. eng. 2020/08/11.
- 31. Podsiadlo D, Richardson S. The timed "up & go": A test of basic functional mobility for frail elderly persons. J Am Geriatr Soc. 1991;39(2):142-8. eng. 1991/02/01.
- 32. Kelly VE, Janke AA, Shumway-Cook A. Effects of instructed focus and task difficulty on concurrent walking and cognitive task performance in healthy young adults. Exp Brain Res. 2010;207(1-2):65-73. eng. 2010/10/12.
- 33. Montero-Odasso MM, Sarquis-Adamson Y, Speechley M, Borrie MJ, Hachinski VC, Wells J, และคณะ. Association of dual-task gait with incident dementia in mild cognitive impairment: Results from the gait and brain study. JAMA Neurol. 2017;74(7):857-65. eng. 2017/05/16.
- 34. Yang L, He C, Pang MY. Reliability and validity of dual-task mobility assessments in people with chronic stroke. PLoS One. 2016;11(1):e0147833. eng. 2016/01/26.
- 35. Al-Yahya E, Dawes H, Smith L, Dennis A, Howells K, Cockburn J. Cognitive motor interference while walking: A systematic review and meta-analysis. Neurosci Biobehav Rev. 2011;35(3):715-28. eng. 2010/09/14.
- 36. Chen X. The working memory and dorsolateral prefrontal-hippocampal functional connectivity changes in long-term survival breast cancer patients treated with tamoxifen. Int J Neuropsychopharmacol. 2017;20(5):374-82. eng. 2017/02/09.
- 37. Monfort SM. Exploring the roles of central and peripheral nervous system function in gait stability: Preliminary insights from cancer survivors. Gait Posture. 2019;71:62-8. eng. 2019/04/23.

- 38. Morishita S, Mitobe Y, Tsubaki A, Aoki O, Fu JB, Onishi H, และคณะ. Differences in balance function between cancer survivors and healthy subjects: A pilot study. Integr Cancer Ther. 2018;17(4):1144-9. eng. 2018/07/26.
- 39. Blackwood J. Assessment of gait speed and timed up and go measures as predictors of falls in older breast cancer survivors. Integr Cancer Ther. 2021;20:15347354211006462. eng. 2021/04/01.
- Muir-Hunter SW, Wittwer JE. Dual-task testing to predict falls in community-dwelling older adults: A systematic review. Physiotherapy. 2016;102(1):29-40. eng. 2015/09/24.
- Nikolaus T, Bach M, Oster P, Schlierf G. Prospective value of self-report and performance-based tests of functional status for 18-month outcomes in elderly patients. Aging (Milano). 1996;8(4):271-6. eng. 1996/08/01.
- 42. Bech SR, Kjeldgaard-Man L, Sirbaugh MC, Egholm AF, Mortensen S, Laessoe U. Attentional capacity during dual-task balance performance deteriorates with age before the sixties. Exp Aging Res. 2022;48(1):86-98. eng. 2021/06/08.
- Petrillo K, Javed B, Toosizadeh N. Association between dual-task function and neuropsychological testing in older adults with cognitive impairment. Exp Gerontol. 2023;178:112223. eng. 2023/05/28.
- 44. Haggstrom LR, Vardy JL, Carson EK, Segara D, Lim E, Kiely BE. Effects of endocrine therapy on cognitive function in patients with breast cancer: A comprehensive review. Cancers (Basel). 2022;14(4). eng. 2022/02/26.
- 45. Tenda Y, Miyashita M, Yamada A, Shimizu C, Nakayama K, Honma N, และคณะ. Older patients' experience of living with cognitive impairment related to hormone therapy for breast cancer: A qualitative study. Eur J Oncol Nurs. 2022;57:102115. eng. 2022/03/06.
- 46. Montero-Odasso M, Bergman H, Phillips NA, Wong CH, Sourial N, Chertkow H. Dualtasking and gait in people with mild cognitive impairment. The effect of working memory. BMC Geriatr. 2009;9:41. eng. 2009/09/03.
- 47. Kaneko H, Yoshikawa T, Nomura K, Ito H, Yamauchi H, Ogura M, และคณะ.

Hemodynamic changes in the prefrontal cortex during digit span task: A nearinfrared spectroscopy study. Neuropsychobiology. 2011;63(2):59-65. eng. 2010/12/24.

- Beauchet O, Dubost V, Gonthier R, Kressig RW. Dual-task-related gait changes in transitionally frail older adults: The type of the walking-associated cognitive task matters. Gerontology. 2005;51(1):48-52. eng. 2004/12/14.
- 49. Bohlen J, McLaughlin SL, Hazard-Jenkins H, Infante AM, Montgomery C, Davis M, ແລະ ຄณະ. Dysregulation of metabolic-associated pathways in muscle of breast cancer patients: Preclinical evaluation of interleukin-15 targeting fatigue. Journal of Cachexia, Sarcopenia and Muscle. 2018;9(4):701-14.
- 50. Braithwaite D, Satariano WA, Sternfeld B, Hiatt RA, Ganz PA, Kerlikowske K, และคณะ. Long-term prognostic role of functional limitations among women with breast cancer. J Natl Cancer Inst. 2010;102(19):1468-77. eng. 2010/09/24.
- Wang R, Nakshatri H. Systemic actions of breast cancer facilitate functional limitations. Cancers (Basel). 2020;12(1). eng. 2020/01/17.
- 52. Eaglehouse YL, Georg MW, Shriver CD, Zhu K. Time-to-surgery and overall survival after breast cancer diagnosis in a universal health system. Breast Cancer Res Treat. 2019;178(2):441-50. eng. 2019/08/16.
- 53. Kahya M, Gouskova NA, Lo OY, Zhou J, Cappon D, Finnerty E, และคณะ. Brain activity during dual-task standing in older adults. J Neuroeng Rehabil. 2022;19(1):123. eng. 2022/11/12.
- 54. Woollacott M, Shumway-Cook A. Attention and the control of posture and gait: A review of an emerging area of research. Gait Posture. 2002;16(1):1-14. eng. 2002/07/20.
- 55. Pumpho A, Chaikeeree N, Saengsirisuwan V, Boonsinsukh R. Selection of the better dual-timed up and go cognitive task to be used in patients with stroke characterized by subtraction operation difficulties. Front Neurol. 2020;11:262. eng. 2020/05/12.
- 56. Fraizer EV. Methodological and interpretive issues in posture-cognition dual-tasking in upright stance. Gait Posture. 2008;27(2):271-9. eng. 2007/05/26.

- 57. Kerr B. Cognitive spatial processing and the regulation of posture. J Exp Psychol Hum Percept Perform. 1985;11(5):617-22. eng. 1985/10/01.
- Eberling JL. Estrogen- and tamoxifen-associated effects on brain structure and function. Neuroimage. 2004;21(1):364-71. eng. 2004/01/27.
- 59. Sherrington C, Fairhall NJ, Wallbank GK, Tiedemann A, Michaleff ZA, Howard K, ແລະ ຄณະ. Exercise for preventing falls in older people living in the community. Cochrane Database Syst Rev. 2019;1(1):Cd012424. eng. 2019/02/01.





Appendix1 Human Research Ethics Committee Chulabhorn Research Institute review board (Approval number:EC001/2567)

1	แบบเอกสารที่ ECF-CRA 19
25	ใบอนุมัติโครงการวิจัย
ราชวิทยาลัย จ จุฬาภรณ์	คณะกรรมการจริยธรรมการวิจัยในคน ราชวิทยาลัยจุฬาภรณ์
ชื่อโครงการ (ไทย)	ความสามารถในการทำงานสองอย่างในเวลาเดียวกันของผู้สูงอายุที่เป็น มะเร็งเด้านมที่ได้รับการรักษาด้วยฮอร์โมน
(English)	Dual-task performance in older adults with breast cancer who received endocrine therapy
รทัสโครงการวิจัย	EC 001/2567
ชื่อหัวหน้าโครงการวิจัย	นางสาวอชิรญา ปักษา
สังกัด	โรงพยาบาลจุฬาภรณ์
การรับรอง	คณะกรรมการจริยธรรมการวิจัยในคน ราชวิทยาลัยจุฬาภรณ์ ได้พิจารณาและ มีมติอนุมัติให้กับโครงการวิจัยนี้
วันที่อนุมัต	2 กุมภาพันธ์ 2567
ระยะเวลาที่อนุมัติ	10
วันที่หมดอายุ	1 กุมภาพันธ์ 2568

Burg Vig-(ลงนาม) ..

(ศาสตราจารย์กิดติคุณ นายแพทย์ชัยเวช นุชประยูร) ประธานคณะกรรมการจริยธรรมการวิจัยในคน ราชวิทยาลัยจุฬาภรณ์



Appendix2. The Montreal Cognitive Assessment in Thai version (MoCA-T)

Ref. Tangwongchai, S., Phanasathit, M., Charenboon, T., Akkayagorn, L., Hemrungroin, S., Phanthumchinda, K., et al. (2009). The validity of Thai version of The Montreal cognitive assessment (MoCA-T), dement. Neuropsychol3:172.

This tool asked for permission from ASSOC. PROF. DR. SOLAPHAT HEMRUNGROJN, M.D.



ภาควชา จุฬาองก

ภาควิชาจิตเวขศาสตร์ คณะแททยศาสตร์ จุฬาละกรณ์มหาวิทยาลัย 1873 ถนนพระราม 4 ปทุมวัน กรุงเทพา 10330

15 กุมภาพันธ์ 2567

เรื่อง ตอบกลับการขอให้เครื่อเมื่อวิจัย แบบประเมิน Montreal Cognitive Assessment (MoCA) ฉบับภาษาไทย เรียน นางอริรญา ปักษา

ตามที่ นางอชิรถูา ปักษา นิสิตระดับมหาบัณฑิต สาขาวิชากายภาพบำบัด คณะกายภาพบำบัด มหาวิทยาลัย ครีนครินทรวิโรฒ จะดำเนินการทำโครงการวิจัยเรื่อง "ความสามารถในการทำงานสองอย่างในเวลาเดียวกัน ของผู้สูงอยุที่ เป็นมะเร็งเด้านม ที่ได้รับการรักษาด้วยฮอร์โมน" โดยมี อู้ช่วยศาสตราจารย์ คร.นิชินันท์ จัยคีรี เป็นที่ปรึกษาปริญญานิพนธ์ มี ความประสงค์ขออนุญาตใช้แบบประเมิน Montreal Cognitive Assessment (MoCA) ของ Z.Nasreddine, MD. ซึ่งพัฒนา เป็นฉบับภาษาไทยโดย รองศาสตราจารย์ แพทย์หญิงโสหพัทธ์ เหมรัญชโรจน์ และคณะนั้น

โนการนี้ ภาควิชาจิตเวขศาสตร์ คณะแททยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย และรองศาสตราจารย์ แททย์หญิง โสหพัทธ์ เหมรัญช์โรจน์ ได้พิจารณาแล้ว มีความเห็นว่า สมควรอนุญาตให้ใช้ แบบประเมิน Montreal Cognitive Assessment (MoCA) ฉบับภาษาไทย ในการทำโครงการวิจัยเรื่องดังกล่าว จึงเรียนมาเพื่อทราบ

ขอแสดงความนับถือ

grand 2.

รองศาสตราจารย์ แพทย์หญิงโสหพัทธ์ เหมรัญช์โรจน์ ผู้พัฒนาแบบประเมิน MoCA ฉบับภาษาไทย

สูนย์ฝึกสมอง ฝ่ายจิตเวขศาสตร์ โทร. 02 256 4000 ต่อ 70710, 70711

ที่ ขว. 218 /2567

Appendix3 Data collection form แบบบันทึกข้อมูล โครงการวิจัย

(ชื่อภาษาไทย) ความสามารถในการทำงานสองอย่างในเวลาเดียวกันของผู้สูงอายุที่เป็นมะเร็ง เต้านมที่ได้รับการรักษาด้วยฮอร์โมน

(ชื่อภาษาอังกฤษ) Dual-task performance in older adults with breast cancer who received endocrine therapy

อาสาสมัคร:	รหัสประจำตัวอาส	าสมัคร			อายุ	ปี
ระดับการศึกษา	🗖 ประถมต้น 🗖 เ	ไระถมปลาย 🗖 มั	โธยมต้น	🗖 มัธยมปลาย		
🗖 อนุปริญญา ไ	🗖 ปริญญาตรี 🗖 เ	ไร้ญญาโท 🗖 ปริถ	บูญาเอก			
การวินิจฉัยทางก	าายแพทย์	บ	ปนิดของม	งะเร็งเต้านม		
อาชีพ			+			
Health status						
น้ำหนัก.	กิโลก	ารัม	ส่ว	นสูง	.เซนติเมตร	
โรคประ <i>เ</i>	จำตัว		Π./.			
การรักษ	หามะเร็งร่วมที่ได้รับ.					
Menopa	ause status	Premenopausal		Postmenopausa	al	
ประวัติการรับยา	ต้านฮอร์โมน (endo	ocrine therapy)				
Endocrine there	apy • Tamox	ifen • ,	Aromata	ase inhibitor		
Duration of end	docrine therapy			เดือน		.ปี

ผลการประเมินการทำงานขั้นสูงของสมอง (Cognitive function)

แบบประเมิน	ผลคะแนน
MoCA test	

	0	เด	a v	
ผลการประเมนความสามา	รถการทางานสอ _`	งอยาง ในเวล	าเดยวกน	Dual-task

แบบประเมิน	ผลการประเมิน	หน่วย
TUG single task		Second.
TUG dual-task		Second.
Cognitive single task		Numbers/times
Cognitive task during TUG		Numbers/times
dual test		
The dual-task effect (DTE)		Percent (%)



Appendix 4. Research Exploitation

เอกสารรับรอง การนำผลงานวิจัยไปใช้ประโยชน์อย่างเป็นรูปธรรม

คำขึ้แจง : เอกสารซุดนี้มีวัตถุประสงค์เพื่อประเมินคุณภาพผลงานวิจัยของนิสิตระดับบัณฑิตศึกษา มหาวิทยาลัยศรีนครินทรวิโรฒ ที่สามารถนำไปใช้ประโยชน์อย่างเป็นรูปธรรม

ชื่อ-นามสกุล นางสาวอชิรญา ปักษา

ตำแหน่ง นักกายภาพบำบัด

ชื่อบริษัท/องค์กรโรงพยาบาลจุฬาภรณ์

ได้ใช้ประโยชน์จากปริญญานิพนธ์/สารนิพนธ์ เรื่อง ความสามารถในการทำงานสองอย่างในเวลาเดียวกันของ ผู้สูงอายุที่เป็นมะเร็งเต้านมที่ได้รับการรักษาด้วยฮอร์โมน (Dual task performance in older adults with breast cancer who received endocrine therapy)

ชื่อนิสิต นางสาวอชิรญา ปักษา หลักสูตร วิทยาศาสตร์มหาบัณฑิต กายภาพบำบัด

การนำผลงานไปใช้ประโยชน์อย่างเป็นรูปธรรม :

- ใช้ประโยชน์ในเชิงนโยบายเพื่อใช้ประโยชน์ประกอบการดัดสินใจในการบริหาร หรือกำหนด นโยบาย
 - [🗸] การนำเสนอข้อมูลที่เป็นประโยชน์ต่อหน่วยงาน

ได้มีการทบทวนความรู้ และเผยแพร่ข้อมูลที่ได้จากการรีวิว และเก็บข้อมูลงานวิจัย เรื่องการทำการ ทดสอบ และการรักษา โดยใช้เรื่องการทำงานสองอย่างในเวลาเดียวกัน ให้บุคลากรในหน่วยงานได้ ทราบ รวมทั้ง ได้เพิ่มการ Screening dual task performance ลงในคลินิก Cancer rehabilitation ของผู้ป่วยมะเร็งเด้านม เพื่อเพิ่มความสามารถในการทรงท่า และป้องกันการล้ม ในผู้ป่วยมะเร็งที่ได้รับ การรักษาทางการแพทย์ ตามรูปแนบ ดังต่อไปนี้



รูปภาพการเผยแพร่ความรู้ จากงานวิจัย ในหัวข้อ Dual-task performance in screening and training, และรูปภาพการนำไปใช้จริงกับผู้ป่วย

 การนำผลงานเผยแพร์ในเว็ปไซต์ ระบุเว็บไซต์ เผยแพร์ KM Training Summary สำนักวิชาการ โรงทยาบาลอุหาภรณ์

> Posted in KM Training Summary **Achiraya Paksa** Seen by 1 ... เมษณฑร์ความรู้ความเข้าใจ จากการ 1 ... เมษณฑร์ความรู้ความเข้าใจ จากการ 1 การทำงานสองอย่างในเวลา เกตัววกัน ของผู้ สูงอายุที่เป็นมะเร็งเด้านม และได้รับการ กามาโดยการใช้ของโม

โดย กภ.อชิรญา ปักษา นักกายภาพบำบัด หน่วยกายภาพบำบัด งานเวชศาสตร์พื้นปู และเพทท์ทางเลือก

0 0 0

เผยแพร่ความรู้ความเข้าใจ จากการศึกษาการทำงานสองอย่างในเวลาเดียวกัน ของผู้สูงอายุที่เป็น มะเริ่งเต้านม และให้วับการรักษาโดยฮอร์โมน

.

ผู้นำขึ้นโพสต์

กภ.อซิรญา ปักษา ดำแหน่ง นักกายภาพบำบัด หน่วยกายภาพบำบัด งานเวซศาสตร์พื้นฟูและ แพทย์ทางเลือก โรงพยาบาลจุฬาภรณ์

ลงชื่อ....อนุพันธ์ ต้าน ระงาธิช/

ชื่อผลงาน

(ผู้ช่วยศาสตราจารย์ปฏิบัติการ นายแพทย์อนุพันธุ์ ตันธนาธิป) หัวหน้างานเวชศาสตร์พื้นฟู และแพทย์ทางเลือก โรงพยาบาลจุฬาภรณ์





VITA