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Culturally-Adapted Translation, Psychometric and Predictive Validation
of the Reported Edmonton Frail Scale-Thai version (REFS-Thai)

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Abstract

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Abstract

Background: Frailty, a geriatric syndrome, results in increasing vulnerability, disability, and adverse health outcomes in older adults. In order to provide better care, early detection is the best approach to manage frailty. However, gaps exist in identifying frailty as instruments to measure the construct are not widely available. This is particularly true in the Thai language, where there are no published studies that investigate frail orthopedic patients in Thailand. To promote healthy aging and enhance equity of care, early identification of frailty with a reliable and cross-culturally sensitive instrument is necessary for reaching the goal in this population. This

dissertation is composed of a series of research studies that focus on cross-cultural frailty in order to enhance equity and quality of care in an older Thai population.

Objectives: The first paper aims to identify and evaluate frailty instruments used with hospitalized older orthopedic patients. The second paper aims to: 1) translate and culturally-adapt the Reported Edmonton Frail Scale (REFS) for use in hospitalized older adults in Thailand, and 2) evaluate the psychometric properties of the translated instrument, the REFS-Thai. The third paper aims to test the ability of the REFS-Thai to predict hospital outcomes compared with standard preoperative assessment measures, the American Society of Anesthesiologists physical status classification (ASA) and the Elixhauser Comorbidity Measure (EMC) in older Thai adults who were scheduled for a major orthopedic surgery.

Research design: The data for the manuscripts of the dissertation were drawn from two main methodological approaches: a scoping review (the first study) and two observational studies—a cross-sectional (the second study) and a prospective cohort study (the third study).

Subjects: Hospitalized older adults who were scheduled for elective surgeries (N = 341)

Measures: In the observational studies, we used the REFS-Thai version, Mini-Cog Thai version, and the 4 “A” test- Thai version (4AT). The preoperative health status was assessed by the American Society of Anesthesiologists physical status classification (ASA), and the Elixhauser Comorbidity Measure (EMC) were extracted from medical records. For psychometric validity, the Cronbach’s alpha and inter-rater reliability were analyzed. Firth logistic regression and Robust Poisson regression were applied to evaluate the association between frailty and outcomes. Predictive ability was examined using cross-validation comparing the area under the receiver operating characteristic curve (AUC) and the mean squared errors (MSE).

Results: The scoping review identified 14 reliable frailty instruments currently used in orthopedic patients. Of all of these instruments, the REFS appeared to be the most practical as it measured multiple dimensions of frailty, had few requirements for training, and could be administered in hospitals with limited-resources. For the cross-sectional study, the findings revealed that the REFS-Thai was a reliable tool to assess clinical frailty and had a content validity index of 0.97 and Cronbach's alpha of 0.73. Inter-rater reliability was good, the linear weighted Kappa was 0.87 ($p < 0.001$). The instrument was completed, on average, in less than 6 minutes. For the prospective cohort study, frailty as evaluated by the REFS-Thai, showed significant association with an increased risk of postoperative complications (odds ratio [OR] = 2.38, $p = 0.049$), postoperative delirium (POD) (OR = 3.52, $p = 0.034$), and prolonged-length of stay (relative risk [RR] = 1.42, $p = 0.043$). Using the REFS-Thai shows good performance in predicting postoperative complication (AUC = 0.81, 95% confidence interval [CI] = 0.74-0.88) and POD (AUC = 0.81, 95% CI = 0.72-0.90).

Conclusions: Comprehensive screening of frailty that is culturally appropriate has the potential to improve person-centered preoperative care. The REFS-Thai—a brief and valid instrument—may be a practical tool for the multidimensional evaluation of frailty in Thailand. Providing a frailty instrument that can be used in multiple settings results in enhancing equity for the screen of frailty.

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Chapter 1. Introduction

The management of geriatric syndromes, delaying dependency and promoting healthy aging are global concerns (WHO, 2015). Frailty is a common, serious and potentially modifiable geriatric syndrome associated with increased vulnerability to adverse health events due to age-related changes (Chen, Mao, & Leng, 2014; Fried et al., 2001). In hospitalized patient populations, older adults with frailty are at increased risk of institutionalization, morbidity, postoperative complications, and mortality (Cesari & Vellas, 2015; Dent, Kowal, & Hoogendijk, 2016; Theou et al., 2018). Therefore, it is logical to believe that as the aging population increases globally, escalating care burden of frail older adults might significantly affect either direct or indirect health-care costs. Importantly, no pharmacological treatment exists to reverse frailty; therefore, prevention and early identification is informative for effective and efficient care planning. In order to prevent poor outcomes, early detection of frailty is beneficial in clinical care for risk stratification, treatment decision-making, and surgical planning in the older population.

Precisely identifying those who are frail presents significant challenges. However, screening for frailty in hospital, termed clinical frailty, has limitations because there is a need for an instrument to be both precise to screen for frailty and effective for use in clinical settings. Several conceptual models of frailty exist and various instruments have been developed to identify its' characteristics (Buta et al., 2016; Chen et al., 2014; Dent et al., 2016; Fried et al., 2001; Sutton et al., 2016). A significant limitation to-date is that there has been no reliable evidence of a gold standard or universal instrument for frailty (Buta et al., 2016; Dent et al., 2016; Theou et al., 2018). Existing frailty instruments are varied, ranging from simple to complex assessment, which depends on the number and type of items and/or the complexity of the instrument (Buta et al., 2016; Dent et al., 2016; Sutton et al., 2016). However, most of the

clinical frailty instruments require specific equipment, training, and extensive time to administer (Buta et al., 2016; Dent et al., 2016; Sutton et al., 2016). Thus, selecting an appropriate frailty instrument to use might be problematic in limited-resource settings. Another significant limitation is that separating clinical frailty from disability or comorbidity is challenging in some populations (Fried, Ferrucci, Darer, Williamson, & Anderson, 2004; Sieber, 2017). Current evidence underlines that age-related musculoskeletal (MSK) conditions—osteoarthritis (OA), osteoporosis, rheumatoid arthritis (RA)—may initiate the cycle of frailty and interfere with the precision of its’ interpretation in hospitalized older adults (Dawson & Dennison, 2016; Gielen et al., 2012; Zlobina, Krivtsunov, Bogat, & Prashchayeu, 2015). The predominant characteristics of MSK conditions, physical limitation of daily activity, joint stiffness, severe pain or chronic fatigue, and sarcopenia, may compound frailty and lead to frailty misclassification (Afilalo, 2016; Chen et al., 2014; Cooper et al., 2012; Fried et al., 2004). For clinical frailty in MSK conditions, adverse health outcomes are commonly reported (Bellamy et al., 2017; Buta et al., 2016; Cooper et al., 2012; Kistler, Nicholas, Kates, & Friedman, 2015; Kua, Ramason, Rajamoney, & Chong, 2016). Thus, evaluation and accurate detection of clinical frailty with an appropriate instrument, particularly hospitalized populations with MSK conditions, is still a formidable challenge.

Screening for frailty is important, yet some limitations exist, including in settings in countries such as Thailand. Language barriers or unavailability of translated and culturally-appropriate frailty instruments can be an issue in many geographical areas (Buta et al., 2016; Dent et al., 2016; Theou et al., 2018). More specifically in Thailand, a few challenges currently exist that might further impede the evaluation of frailty. First and foremost, it is not clear how to identify frailty in older adults with MSK conditions in the Thai context. To date, there are no

published studies, either of frailty in hospitalized individuals in Thailand or testing frailty instruments in Thai language. Using culturally-adapted instruments not only establishes meaningful results of the same perspective of health in other cultures or languages, but also enables one to investigate the differences between cross-cultural populations (Braun, Gruneberg, & Thiel, 2018; Hambleton, 2005). Thus, a culturally-adapted frailty screening instrument is crucial for promoting older Thai orthopedic patients' health. Another challenge is to apply a practical screening frailty instrument into the routine preoperative care in limited-resource settings (Cesari & Vellas, 2015; Wildiers, 2013). Comparing many clinical frailty instruments, a brief instrument such as the Reported Edmonton Frail Scale (REFS) shows strong validity and reliability in screening frailty and is a good predictor of postoperative complications. This instrument takes less than 10 minutes to screen an older adult for frailty, regardless of specific geriatric training (Hilmer et al., 2009; Kua et al., 2016). The REFS may be a better choice compared to other frailty instruments in effectively evaluating frailty in limited-resource settings. Further, effective clinical screening for frailty serves the fifth priority area in the World Health Organization (WHO) 2020-2030 focus of improving screening measurement for delaying care dependency and enhancing the quality of care to aging populations (WHO, 2015) within the Thai population.

CONTENT OF THE DISSERTATION

This dissertation consists of a series of three studies. The purpose of the first study is to identify and evaluate frailty instruments used with hospitalized older orthopedic patients through the conduct of a scoping review. The purpose of the second study is to 1) translate and culturally-adapt the REFS for use in hospitalized older adults in Thailand, and 2) evaluate the psychometric properties of the REFS-Thai. The purpose of the third study is to test the ability of the REFS-

Thai to predict hospital outcomes compared with two standard preoperative assessment measures [the American Society of Anesthesiologists physical status classification (ASA) and the Elixhauser Comorbidity Measure (EMC)] in older Thai patients undergoing major orthopedic surgeries.

Frailty is associated with adverse health outcomes in older adults. The best approach to manage frailty is early detection of those who are at risk of frailty. This dissertation might be the first study that provides evidence concerning clinical frailty and its consequences in Thai older adults. The findings will facilitate the integration of a reliable cross-cultural frailty instrument—REFS-Thai—in regularly preoperative assessment and planning patient-centered care to enhance equity and quality of care in this population.

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Chapter 2. Frailty Measures in Older Orthopedic Patients: A Scoping Review

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Abstract

Background: Frailty has emerged as a valid concept with prognostic implications for older adults undergoing surgical procedures. Despite orthopedic surgery being common in older adults, the strengths and limitations of different approaches to measure frailty are rarely discussed in this population. A thorough review of instruments used to appraise frailty in older patients undergoing orthopedic procedures is needed to fill this gap.

Objectives: To identify and compare frailty instruments used with hospitalized older orthopedic patients.

Design: A scoping review guided by the Arksey and O'Malley framework.

Data sources: PubMed, CINAHL, PsycINFO, Scopus, and EMBASE databases were searched to identify studies published from July 2006-July 2018 regarding frailty instruments in older orthopedic patients.

Review method: 1) Identified the research question; 2) Identified relevant studies; 3) Selected the studies; 4) Charted the data; and 5) Assembled, summarized and reported the results.

Results: The initial search resulted in 764 articles. Initial screening of titles and abstracts excluded 180 articles. Further refinement using full text excluded an additional 160 articles. A final set of 21 articles was used to identify 14 unique frailty instruments. Ninety percent (n=19) of the articles were from Western countries. Fried's phenotype (3 studies) and the modified Frailty Index (6 studies) were commonly used approaches to measure frailty. Physical function was frequently modified to measure frailty particularly in patients with hip fractures. Most frailty instruments were administered by trained physicians (13 instruments) and nurses (1 instrument). Frailty screening was commonly administered at hospital admission and used to prognosticate postoperative complications (19 studies), length of stay (15 studies), mortality rate (13 studies),

discharge disposition (12 studies), physical and cognitive function (10 studies), readmission (9 studies), adverse events (7 studies), and re-operation (5 studies). Average time to complete frailty instruments ranged from 1-10 minutes. Reported psychometrics had acceptable reliability and validity.

Conclusion: There are reliable frailty measures that are used in the inpatient orthopedic setting; although evidence is still lacking for a frailty instrument that is the gold standard. More research is needed to identify the best-performing measure. Evaluation of frailty in orthopedic patients with physical limitations is a challenging task. Promoting healthy aging through measuring frailty is important for an aging society. When selecting a frailty instrument one needs to consider the clinical context, resources required, and instrument quality.

Keywords: *Frailty, Older adults, Orthopedic surgery, Patient care, Scoping review, Quality of care*

What is already known about the topic?

- Frailty is a common geriatric syndrome associated with poorer health outcomes in older surgical patients.
- Strengths and limitations of different approaches to measure frailty in orthopedic patients are rarely discussed in the literature.
- Frailty assessment tailored to older orthopedic patients might be instrumental in improving quality of care.

What this paper adds

- We described 14 frailty instruments frequently used in clinical orthopedic settings. Fried's frailty phenotype and the modified Frailty Index were the most commonly used approaches to frailty.
- The clinical manifestations of musculoskeletal (MSK) conditions in orthopedic patients may bias frailty classification, rendering the need for a more nuanced approach to frailty measurement in this population.
- Although most frailty instruments were reliable to measure frailty, gaps exist in non-accessible frailty instruments across all populations.
- Current evidence is insufficient to prioritize one frailty instrument over others for screening older, orthopedic patients; therefore, clinical context, resources, and pragmatic considerations should guide decisions for frailty instrument selection.

1. INTRODUCTION

As life expectancy has increased globally, promotion of healthy aging, maintenance of functional ability and support of well-being in older adults has become a global priority (WHO, 2015). Musculoskeletal (MSK) conditions are common, and they are likely to have an important negative impact on older adults' functional ability and lead to escalation of the burden of disease in an aging society (Briggs et al., 2016; Briggs and Dreinhofer, 2017). To slow down or reverse functional decline, surgical treatment may be required. Orthopedic surgeries for conditions like hip, knee, and spine degeneration have increased, with a parallel rise in postoperative complications and mortality seen in older populations (Gleason et al., 2017; McIsaac et al., 2018; Rothrock et al., 2018; Segal et al., 2018; Wilson et al., 2018). Frailty is a geriatric syndrome that has emerged and been identified as an important concept that captures older adults' vulnerability to have adverse health events (Fried et al., 2004, 2001). Although the prevalence of frailty is

fairly low in MSK conditions [approximately 4.9-10.7%;(Choi et al., 2015; Nguyen et al., 2015)], it has been associated with degenerative MSK (Milte and Crotty, 2014; Zlobina et al., 2015). Frailty is also linked to an increase in adverse surgical outcomes with postoperative complications (Ondeck et al., 2018; Theou et al., 2018). Frail older adults with MSK conditions are at higher risk of mortality, fall-related injury, disability, and hospital readmission (Bellamy et al., 2017; Charest-Morin et al., 2018; Ondeck et al., 2018; Shin et al., 2016; Walters et al., 2016). Notably, there is no proven pharmacological treatment to reverse frailty. Prevention and early screening of frailty can improve clinical care for risk stratification, treatment decision-making, and surgical planning. Hence, selecting efficient frailty screening instruments is prerequisite to delay dependency, promote health and support well-being of older orthopedic populations.

In the hospital, despite the importance of screening for frailty in orthopedic populations, there are two main challenges of selecting an instrument to measure clinical frailty. The first challenge is to identify which instruments provide accurate frailty identification in orthopedic patients. The musculoskeletal aging phenotype comprising osteoporosis, osteoarthritis (OA), and sarcopenia may affect the accuracy of a frailty evaluation (Dasgupta et al., 2009; Kistler et al., 2015; Krishnan et al., 2014; Kua et al., 2016). The predominant clinical characteristics of orthopedic patients, particularly physical limitations, weakness or immobility due to pain, and neuromuscular impairment, may cause the misinterpretation of someone being frail (Beudart et al., 2015; Chen et al., 2014; Collino et al., 2013). Orthopedic patients who are frail may present either as highly sensitive or insensitive to frailty measures. The second challenge in assessing frailty is how to apply a frailty instrument in the clinical setting. Although various instruments have been developed, frailty instruments are unavailable in many geographical areas and languages (Buta et al., 2016). Overcoming language barriers and cultural issues to assess frailty

is important for better care. Further, applying common frailty instruments may not fit with all hospital settings; for instance, resource limitations, clinical context, instrument quality and cultural sensitivity (Buta et al., 2016; Theou et al., 2018). Clinical circumstances arise in selecting a frailty instrument in hospitals such as what equipment to use, how much time is needed to use the instrument, and the instrument's quality and cultural sensitivity. Therefore, selecting optimal frailty instruments for use in hospital orthopedic settings is critical to inform care. This review will cover the above-mentioned gaps and will provide information about frailty instruments to be used by clinical specialists and healthcare teams in the orthopedic population.

2. METHODS

2.1. Aim

To identify and compare frailty instruments used with hospitalized older orthopedic patients.

2.2. Design

The Arksey and O'Malley framework (Arksey and O'Malley, 2005) was used as a guide for this review. The framework has 5 steps: 1) identifying the research question; 2) identifying relevant studies; 3) study selection; 4) charting the data; and 5) assembling, summarizing and reporting the results.

2.3. Methods and search strategy

2.3.1 Stage 1: Identifying the research question

The first stage included a preliminary exploration of the literature aimed at identification of knowledge gaps on frailty in hospitalized orthopedic patients. Research questions for this review

were: 1) What frailty instruments are currently in use in inpatient orthopedic settings; 2) Which instruments are reliable and practical to measure frailty in an inpatient orthopedic setting?

2.3.2. Stage 2: Identifying relevant studies/Search strategy

The literature search was performed by two co-authors (IR & OZ) in consultation with a health science librarian. The search was conducted in the main health databases—PubMed, CINAHL, PsycINFO, Scopus, and EMBASE. The combination of Medical Subject Headings (MESH) and keywords were modified for each database to optimize search strategies. The search included publications from July 1, 2006 to July 31, 2018. Keywords used were orthopedic surgery, musculoskeletal diseases, screening or assessment or instrument or tool or scale or measure or indicator, frailty or geriatric syndrome. The search strategies were presented in Appendix B. Last, the coauthors (OZ & IR) and a third doctorally-prepared researcher (SA) independently verified search terms and discussed initial results to confirm the strategies performed.

2.3.3. Stage 3: Study selection

Peer-reviewed original research articles retrieved from the databases were considered eligible for further review. Conference proceedings, preprints, policy or hospital reports, and other papers such as grey literature were not included.

2.3.3.1 Eligibility criteria

The inclusion criteria were: 1) article included frailty instrument(s); 2) the instrument was completed by hospitalized adults; 3) average age of study participants was 65 years or older; 4) setting was hospital orthopedic settings (units, wards, or surgical department including orthopedics); and 5) article was published in English between July 2006 - July 2018. The

exclusion criteria were: 1) articles that were unrelated to frailty; 2) articles of frailty in community settings; and 3) articles that mentioned frail patients without measuring frailty.

2.3.3.2. Selection of studies for inclusion

Following the initial search, two co-authors (IR and OZ) independently reviewed the titles and abstracts to determine eligibility. Next, they independently reviewed full-text articles and identified potential articles for inclusion. Any disagreement among the initial reviewers (IR and OZ) was arbitrated by a third person (SA). The third person reviewed the articles in which there was disagreement about inclusion between IR and OZ, discussed and made a decision to include or exclude. The workflow was summarized using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline (Moher et al., 2010) (Figure 2.1).

2.3.4. Stage 4: Charting the data

The combination of Microsoft Excel 2016 and EndNote X7 were used to remove duplicates and build a summary table focusing on: the country the study was conducted in, study design, name of frailty instrument, number and type of items, administration instructions and time to complete the instrument, scoring, population, health outcomes, instrument requirement, and quality of the instrument. A subset of 5 studies was selected for a pilot for data extraction.

2.3.5. Stage 5: Assembling, summarizing, and reporting the results

The identified studies were summarized and relevant data was abstracted (Table 2.1, Supplement 2.1). Following Arksey and O'Malley (2005), no quality appraisal of the included studies was conducted. Reliability, responsiveness and validity of each frailty instrument was evaluated based on the standard measurement properties of health questionnaires (Terwee et al., 2007).

3. RESULTS

3.1. Characteristic of publications

The search initially identified a total of 764 articles (Figure 2.1). After duplicate article removal and abstract screening, 180 articles were included for final review, with 95 percent agreement between two reviewers. After additional selection 21 articles were retained and evaluated for this review. Studies included in the final sample primarily included older adults undergoing orthopedic surgery (Table 2.1). Data was collected in the United States (n =13), Canada (n = 3), United Kingdom (n = 3); Korea (n = 1) and Singapore (n = 1). Nineteen percent of the studies used retrospective designs (n = 4). The average age of participants was 81 (range 65-92 years old). Study participants had multiple comorbidities and underwent orthopedic surgical procedures. We identified 14 unique frailty instruments. Translation and cross-cultural validation was mentioned for 6 instruments (42%) (Table 2.2).

3.2. Frailty instruments used in an orthopedic setting

Different frailty concepts led to differences in its operational definition, structural domains, scales and scorings across the studies. Fourteen frailty instruments were identified (Table 2.1): the Edmonton Frailty Scale (EFS); modified Frailty Index (mFI)/ Simplified Frailty Index; Fried's Phenotype criteria (FP criteria); Frailty Index (FI); Modified Fried Index; Modified Fried's Criteria (MFC); Reported Edmonton Frailty Scale (REFS); Hip-Multidimensional Frailty Score (Hip-MFS); Maastricht Frailty Screening Tool for Hospitalized Patients (MFST-HP); 5-item mFI; Clinical Frailty Scale (CFS); FRAIL Scale (Fatigue, Resistance, Ambulation, Illnesses, and Loss of Weight); and PRISMA-7; Groningen Frailty Index (GFI). Across all instruments, the number of frailty domains varied from three to more than 10 domains. The number of items ranged from 5 (e.g., FP criteria) to 51 items (e.g., Frailty

Index). Self-report combined with other assessment methods (42%, n = 6) were mostly applied. Only one tool- the CFS used clinical descriptors, pictographs of activity, and functional assessment for frailty screening. Five frailty instruments (35%) in the identified studies were modified from the originally published instruments (Table 2.2).

Deficit accumulation (n = 6) and phenotype-informed (n = 3) were the main approaches to determine frailty. Physical function, fatigue, weight loss, cognitive function, limitation of activities, and comorbidity were common criteria across instruments (n= 14). Two instruments, the FP criteria (Kistler et al., 2015) and MFC (Kua et al., 2016), were used to measure frailty in hip fracture patients and modified physical function/walking performance measures in order to allow self-report (Table 2.1). Most instruments used a binary cut-off point (frail/non-frail), but the FI had more than one cut-off to quantify frailty severity. Frailty was commonly measured pre-operatively. Frailty assessments were used to predict short and long-term outcomes such as postoperative complications (19 studies), length of stay (LOS [15 studies]), mortality rate (13 studies), discharge disposition (12 studies), physical or cognitive function (10 studies), readmission (9 studies), any adverse events (7 studies), and re-operation (5 studies).

3.3. Data sources, equipment and training

Assessing frailty required different resources. The majority of frailty instruments required specific training for use (n = 9, 64%), while many used other standard assessment information (n = 5, 35%), or used additional equipment (n = 4, 28%). The mFI, FI, MFST-HP, and 5-items mFI required information from medical records only. The Hip-MFS relied on many sources including standard assessment information, physical performance, laboratory testing, mid-arm circumference, and specific training in order to evaluate frailty. The PF criteria required training, physical performance testing, and specific equipment (a hand grip strength dynamometer). The

Modified Fried Index and MFC also needed specific training and dynamometer. In contrast, only four frailty instruments (REFS, Frail Scale, PRISMA-7, and GFI) obviated the need for specific equipment and training to measure clinical frailty.

3.4. Measurement occasion and time.

All frailty instruments were utilized for preoperative assessment on hospital admission, but no instruction on appropriate or optimal time to measure frailty was provided. Of these, in two instruments, the authors selected a time point to measure frailty: the MFST-HP was used to assess frailty at 48-hours post hospital admission, while the FRAIL Scale was used to evaluate frail status on the first day of hospital admission.

The range of time spent to complete the frailty measures was between 1-10 minutes (n = 6). Fifty-seven percent (n = 8) of frailty instruments did not report the time required to complete the instrument. Employing the REFS, the patients needed approximately 7 to 10 minutes to complete it. However, the MFC, MFST-HP, and Modified Fried Index were completed within less than 6 minutes. The CFS was reported to be completed in one minute.

3.5. Human resources

Evaluating frailty, the MFST-HP was used by registered nurses (RNs), without additional training. The other frailty instruments used trained research staff, such as physicians, to administer the frailty instruments (n = 13). All of the frailty instruments assessed frailty status of the patients, yet none of these studies mentioned other people such as proxy, caregivers, or family members who might be involved in evaluation. It was noted that staff requested assistance with using frailty instruments that included data from other sources and/or trained personnel.

3.6. Quality of instruments

No information was provided in any of the articles on content validity testing. One article that included the MFST-HP reported construct validity testing (Warnier et al., 2016). Eighty percent (n = 11) of the articles reported criterion validity; the American Society of Anesthesiologists (ASA) and Charlson Comorbidity Index (CCI), standard instruments, were frequently selected to confirm validity testing (Bellamy et al., 2017; Choi et al., 2017; Cooper et al., 2016; Kua et al., 2016; Runner et al., 2017; Shin et al., 2016; Vu et al., 2017). Three instruments (the EFS, PRISMA-7, and GFI) tested criterion validity with other frailty instruments (Walters et al., 2016). The FP, FI, and MFST-HP were verified for reliability. The MFST-HP demonstrated excellent reliability, both intra-rater and inter-rater (ICC (intra-rater) = 0.93, ICC (inter-rater) = 0.95) (Warnier et al., 2016) (Supplement 2.1). Poor reliability, weighted Kappa less than 0.6, was reported in FP criteria and FI (K = 0.53 (95%CI 0.44-0.61), 0.42 (95%CI 0.36-0.49), respectively) (Cooper et al., 2016). The REFS and MFC mentioned reliability from original studies, but not in the orthopedic population (Kua et al., 2016). Regarding responsiveness of the identified frailty instruments, 35% (n = 5) of frailty instruments reported responsiveness evaluation, which were the EFS (Dasgupta et al., 2009), mFI (Ondeck et al., 2018), Modified Fried's Index and CFS (McIsaac et al., 2018) which demonstrated intermediate quality. Notably, the FI showed good quality (Krishnan et al., 2014) in predicting most of the adverse clinical outcomes.

4. DISCUSSION

This scoping review aimed to identify and evaluate frailty instruments used in hospitalized older adults in orthopedic settings. We identified and reviewed 14 frailty instruments, which were found to be reliable for identifying frailty. The Frailty Index and Fried

phenotype were the most commonly used instruments. Modified Frailty Instrument, particularly physical function assessment was frequently used in hip fracture patients.

Across all studies where outcome was measured, regardless of instrument used, frailty results in increased postoperative complications, prolonged LOS, discharge disposition, adverse events, reoperation, readmission, and mortality rate. In orthopedic settings, more evidence is needed to identify the best performing frailty. The current review may be the first published study to identify frailty instruments used in orthopedic patients.

Based on our review, there are three potential concerns in selecting a frailty instrument for identifying frailty in orthopedic patients. First, understanding the clinical context such as the clinical orthopedic characteristics is important in the measurement of frailty. Although our findings revealed few commonalities across frailty instruments, adjustment of frailty instruments may be necessary to identify frailty in orthopedic clinical populations. The review revealed that some authors modified existing frailty instruments including tailoring scores, changing cut-off points, and adapting components from the original version. The FP criteria were altered and the name was changed to measure frailty: MFC and Modified Fried Index. These findings show similarity to a meta-analysis analyzing current frailty instruments which indicated that there were 262 different versions of the FP criteria which were used in clinical settings (Theou et al., 2015). Clinical characteristics of orthopedic patients such as poor physical function, muscle loss/weakness, and posture imbalances may impede interpretation of a frailty assessment. A few frailty instruments have been created for specific MSK conditions like the Hip-MFS for hip fractures (Choi et al., 2017). The FP criteria (Kistler et al., 2015) and MFC (Kua et al., 2016) modified the physical function components with the aim to precisely measure frailty in older adults with physical limitations. Our findings emphasize that identifying frailty in an orthopedic

population could be complicated due to the overlap between physical limitations and frailty which impacts frailty interpretation (Dasgupta et al., 2009; Fried et al., 2004; Kistler et al., 2015; Krishnan et al., 2014; Kua et al., 2016).

Second, it is important to identify the resources needed to use a frailty instrument such as equipment requirements and human resources. Additionally, it is important to factor in the amount of time to complete the measure. Equipment costs for measuring frailty should be considered when selecting an instrument for use in limited-resource hospitals and clinics. The FP criteria, Modified Fried Index, and MFC required objective measurement via a dynamometer for evaluation of one component of frailty. The Hip-MFS used surrogate markers and specific laboratory values, in evaluating frailty. The more human resource requirements and equipment used for measuring frailty, the less practical regular evaluation of frailty becomes. In hospitals with staff limitations, using instruments that do not require additional training may be most appealing such as the REFS, FRAIL Scale, PRISMA-7, and GFI.

In this review, all the frailty instruments identified directly assessed frailty status of the patients. None of the studies mentioned other people—proxy, caregivers, or family members who might be involved in an evaluation. Integrating family members and caregivers evaluation of their loved ones frailty may provide additional information.

Our findings revealed a range of completion time for frailty screening (1-10 minutes). Increasing the time of frailty assessment may depend on factors including the number of items, the clinical experience, the specific MSK limitations, and the complexity of the assessment. The majority of frailty instruments required clinical experiences of the users; thus, novice clinicians spent more time than the experts in administering an instrument. Notably, functional limitation due to MSK conditions may increase the time to complete a frailty evaluation, especially one that

involves a physical performance. Some frailty instruments required more information than standard assessments and might be impractical in some settings. Although screening frailty is necessary, frailty instruments that require high-cost equipment and specialized-training may be problematic for limited resource areas and busy hospitals. This is important to consider as a recent report notes that to promote health outcomes and control costs, hospitals should be concerned about fostering early detection and screening for frailty (Grimes et al., 2018; WHO, 2015).

Third, focusing on the quality of instruments is significant in accurately detecting frailty. In our review, frailty instruments detected both pre-frail and frail status in older adults with MSK conditions. However, poor inter-rater reliability was also discovered in popular frailty instruments: FP criteria and FI (Cooper et al., 2016). The poor inter-rater reliability indicated different judgment of frailty in orthopedic patients. These findings may support previous literature findings that musculoskeletal aging phenotype or clinical symptoms interfere the accuracy of frailty evaluation (Dasgupta et al., 2009; Kistler et al., 2015; Krishnan et al., 2014; Kua et al., 2016) and confirm overlap of frailty and disability found in previous studies (Fried et al., 2004, 2001). In an aging society, MSK conditions are a significant health problem, so frailty identification is needed to promote health and equity. Our findings show consistency with a recent systematic review about frailty instruments in acute care which emphasized that frailty instruments are not accessible in all geographic locations and languages (Buta et al., 2016; Dent et al., 2016; Theou et al., 2018). As the majority of these instruments integrated self-report in measuring frailty, clear communication is of concern in older adults (Fick and Lundebjerg, 2017). Promoting effective frailty screening in different settings will provide health care equity resulting in enhancing quality of life to all.

5. LIMITATIONS OF THE REVIEW

This review was limited in several ways. First, it only considered studies that were reported in English. Second, based on the search terms and selection criteria used, some relevant studies might have been missed such as emergency orthopedic surgery, surgery for bone tumor / sarcoma and hospitalized adults less than 65 years. However, we are confident that the current findings provide useful evidence on frailty instruments used for orthopedic patients.

6. CONCLUSIONS

Early detection of frailty in the preoperative period is essential to prevent negative outcomes and provide better care in hospitalized older adults undergoing orthopedic surgery. Current frailty instruments may be useful in inpatient orthopedic settings, although evidence is lacking for the best frailty measure to use in this environment. Considerations when selecting a frailty instrument to use in orthopedic patients include clinical context, resources requirement, instrument's quality and cultural sensitivity to minimize the gaps of care and provide quality of care for all older adults. Applying frailty screening in regular preoperative care or integrating family involvement to monitor frailty trajectories may delay dependency and enhance health outcomes in this population. Future research that explores the feasibility and acceptability of using frailty instruments in more hospital settings is crucial for providing equity and quality of care for all older adults.

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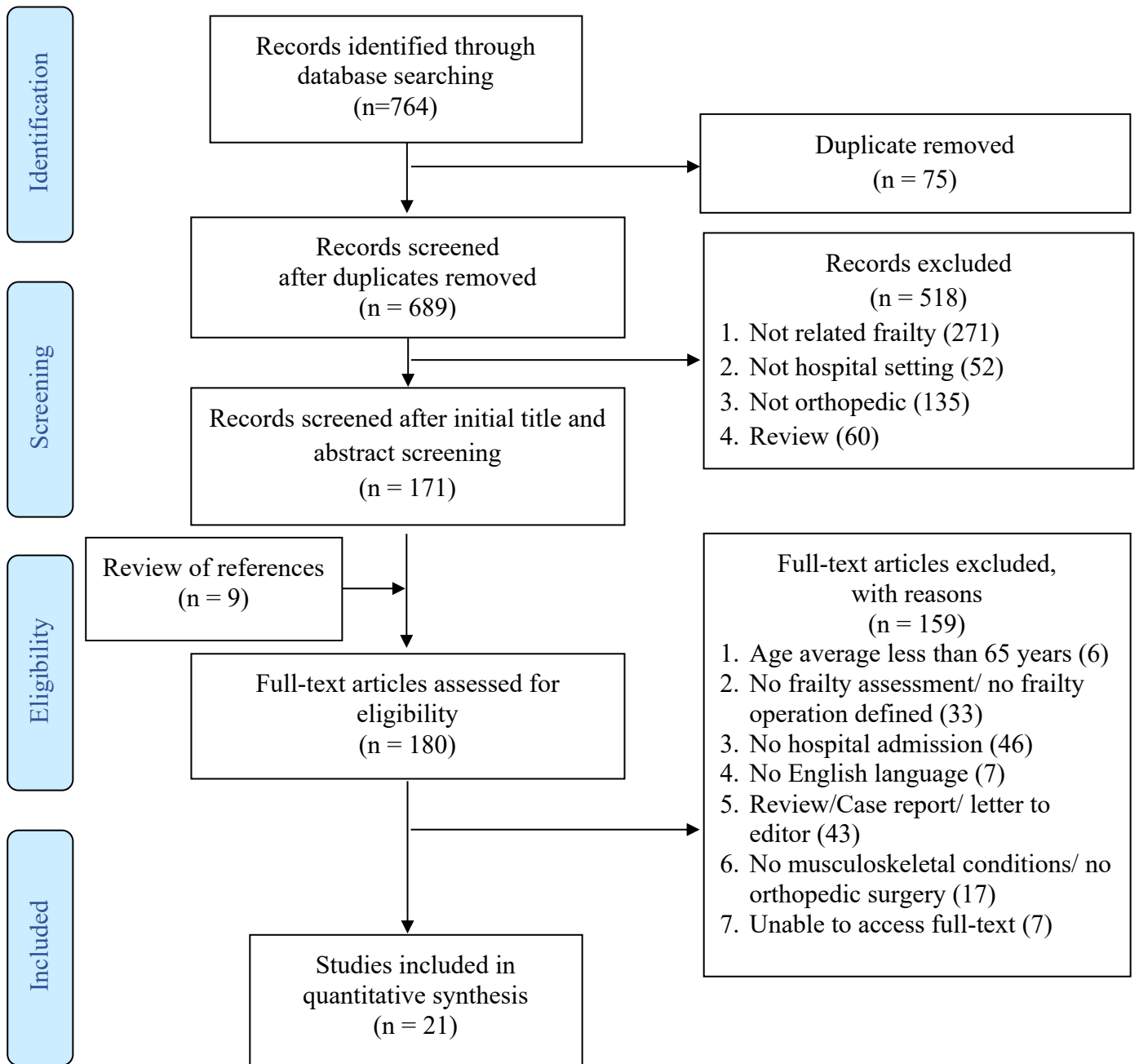


Figure 2.1 PRISMA flow diagram

Table 2.1 Summary of characteristics of frailty instruments commonly used in orthopedic patients

Frailty Instrument	Domains	Population/ References	Outcome of interest
EFS	9 domains (9 items): cognitive impairment, dependence on daily activity living, recent burden illness, self-perceived health, depression, weight loss, medication issues, incontinence, inadequate social support, and mobility difficulty.	A single non-cardiac surgery (mean age 77) / (Dasgupta et al.,2009)	-Postoperative complications, the length of hospital stay (LOS), and ability to be discharged home in older adults undergoing elective non-cardiac surgery
EFS		Vertebral fracture (mean age 80) / (Walters, Chan, Goh, Ong, & Sahota, 2016)	Functional ability, cognitive function, prevalence of frailty in fragility fracture of hip and vertebral fracture.
mFI	11 domains (11 items) from the Canadian Study of Health and Aging Frailty Index (CSHA-FI) matched to items from the American College of Surgeons National	Primary TKA & THA (mean age 66)/ (Shin, 2016)	-Clevein-Dindo classification gr. IV -Hospital-acquired conditions -Any complications -Mortality

Frailty Instrument	Domains	Population/ References	Outcome of interest
	Surgical Improvement Program (NSQIP): change in everyday activity, problems with getting dressed, history of diabetes mellitus, lung problems, respiratory problems, congestive heart failure, myocardial infarction, cardiac problem, cerebrovascular problem, history of stroke, and decrease peripheral pulses.		
mFI		THA (mean age 82)/ (Ondeck et al., 2018)	<ul style="list-style-type: none"> -Occurrence of adverse events -Death -Severe and minor adverse events -Extend hospital stay.
mFI		Orthopedic surgery (mean age 79.5)/ (Vu, Runner, Reisman, & Schenker, 2017)	<ul style="list-style-type: none"> - 30-days Mortality -Postoperative complication -30-days reoperation

Frailty Instrument	Domains	Population/ References	Outcome of interest
			-Readmission -Adverse discharge -LOS
mFI		THA (mean age 71.2)/ (Bellamy, 2017)	-Readmission -Any complications -Reoperation -Adverse discharge -Mortality -Specific complications after THA regardless of age
mFI		primary TKA (mean age 70.75)/ (Runner, 2017)	-Postoperative complications -Reoperation -Readmission

Frailty Instrument	Domains	Population/ References	Outcome of interest
mFI		Non-complex lumbar spine surgery (median age 72)/ (Charest-Morin et al., 2018)	<ul style="list-style-type: none"> -Occurrence of any perioperative adverse events -Postoperative complication -LOS -Postoperative discharge to a facility -In-hospital mortality.
FP criteria	5 domains (5 items) and adapted some domains by using self-reported due to patient conditions: Shrinking (self-reported), exhaustion (self-reported), slowness (self-reported), weakness (grip strength), and physical activity (Minnesota leisure time questionnaire)	Hip fracture (mean aged 86) / (Kistler et al., 2015)	<ul style="list-style-type: none"> -Postoperative complications during hospital admission -LOS -Specific complications such as pneumonia, cardiac complications, surgical site infection, deep vein thrombosis and/or pulmonary embolism, bleeding, renal insufficiency or failure, and delirium

Frailty Instrument	Domains	Population/ References	Outcome of interest
FP criteria	5 domains (5 items) as CHS and Women’s Health and Aging Study (WHAS): Slow gait (3m-walk), weakness (grip strength), low activity (energy expenditure), involuntary weight loss, and exhaustion	Orthopedic surgery (mean age 77)/ (Cooper et al., 2016)	-Relationship between FP criteria and FI with baseline demographic and functional measure -Postoperative complications -LOS -Discharge to Post-Acute Institutional Care (PAC) -Readmission within 300 days
FP criteria		Lumbar spine stenosis (mean age 71)/ (Kim et al., 2018)	-Back-specific function outcome -Quality of life
FI	Multiple domains (51 deficit domains) based on deficits identified at the time of assessment	Hip fracture (mean age 81)/ (Krishnan et al., 2014)	-LOS -Overall hospital outcomes at 30 days after admission.

Frailty Instrument	Domains	Population/ References	Outcome of interest
FI	Multiples domains (42 deficits domains)	Orthopedic surgery (mean age 77)/ (Cooper, 2016)	-Postoperative medical and surgical complications -LOS (\geq 5days) -Discharge to PAC -Readmission within 300 days
MFC	Modified 5 domains from FP criteria (5items): Exhaustion, weight loss, weakness, modified slowness (asking about the last 2 weeks walking ability), and physical activity level	Hip fracture (mean age 79.1) / (Kua, 2016)	-Postoperative complication during hospital admission: delirium, pneumonia, constipation, cardiac problems, pulmonary embolism, deep vein thrombosis, stroke, gastrointestinal bleeding, new pressure sore, urinary tract infection, and retention urine. -The 6 months functional parameter of the hip, and mortality rate.

Frailty Instrument	Domains	Population/ References	Outcome of interest
Modified Fried Index	Modified 5 domains from CHS (5 items): weight loss (>101 lbs unintentionally in prior year), grip strength (lowest 20% by gender and body mass index), exhaustion (self-report), slowness (asking about 15 feet walking ability speed by gender and height), and low activity (kilocalories per week male< 383, female<270).	Surgical patients included orthopedic (mean age 73)/ (McIsaac et al., 2018)	<ul style="list-style-type: none"> -All causes mortality -New disability 90 days after surgery -LOS -Total cost in hospital -Discharge disposition -Any complications and adverse events
REFS	9 domains (13 items): General health status, nutrition, self-reported performance, functional independence, cognition, social support, medication use, mood, and continence	Hip fracture (mean age 79.1)/ (Kua, 2016)	<ul style="list-style-type: none"> -Postoperative complication during hospital admission: delirium, pneumonia, constipation, cardiac problems, pulmonary embolism, deep vein thrombosis, stroke, gastrointestinal bleeding, new pressure sore, urinary tract infection, and retention urine.

Frailty Instrument	Domains	Population/ References	Outcome of interest
			-The 6 months functional parameter of the hip, and mortality rate
Hip-MFS	8 domains (8items): Serum albumin level, mid-arm circumference, Charlson comorbidity index, walking dependency, cognitive function, risk of fallings, nutrition status, and sex	Hip fracture (mean age 80.4)/ (Choi, 2017)	<ul style="list-style-type: none"> -At 6 months all causes mortality -Postoperative complications -LOS -Prolonged total hospital stay institutionalization -1-year-all cause of mortality
MFST-HP	3 domains (15 items): physical (9 items), psychological (4 items), and social (2 items).	Hospitalized older adults including orthopedic (mean age 76.7)/ (Warnier, 2016)	<ul style="list-style-type: none"> -Intra and inter-rater reliability -Feasibility -Construct validity
5-items mFI	5 Domains (5-items):	Patients undergoing distal radius fracture procedure	-Postoperative complication after receiving orthopedic surgery in Distal Radius fracture

Frailty Instrument	Domains	Population/ References	Outcome of interest
	History of Diabetes Mellitus, Congestive Heart Failure (new diagnosis or exacerbation of chronic congestive heart failure within 30 days of surgery), hypertension requiring medication, history of chronic pulmonary disease or pneumonia, and non-independent functional status (partially or completely dependent in activities of daily living within the last 30 days prior to surgery).	(mean age 65)/ (Wilson, Holzgrefe, Staley, Schenker, & Meals, 2018)	-Readmission -Reoperation -LOS
5-items mFI		Patients undergoing Kyphoplasty vertebral augmentation (mean age 73.98)/ (Segal et al., 2018)	-30-days postoperative complication -Reoperation -Readmission -LOS

Frailty Instrument	Domains	Population/ References	Outcome of interest
CFS	4 domains (N/A items): mobility, energy, physical activity, and function	Surgical patients included orthopedic (mean age 73)/ (McIsaac et al., 2018)	<ul style="list-style-type: none"> -All causes mortality -New disability 90 days after surgery -LOS -Total cost in hospital -Discharge disposition -Any complications and adverse events.
FRAIL scale	5 Domains (5 items): Fatigue, resistance, aerobic capacity, illness, and weight loss.	Spine surgery (median age 71)/ (Rothrock et al., 2018)	-Postoperative physical functional and cognition recovery in 3 months.
FRAIL scale		Orthopedic trauma surgery(mean age 82.3)/ (Gleason et al., 2017)	<ul style="list-style-type: none"> -Postoperative complication -Unplanned ICU admission -LOS -Discharge disposition -30-days readmission -30-days mortality.

Frailty Instrument	Domains	Population/ References	Outcome of interest
PRISMA-7	7 Domains (7 items): age > 85 years, male gender, health problems that limits activities, needs for support by others, health problems that require staying home or someone takes care of, use of walker or wheelchair.	Vertebral fracture (mean age 80)/ (Walters et al., 2016)	-Functional ability -Cognitive function -Prevalence of frailty in fragility fracture of hip and vertebral fracture.
GFI	4 Domains (15 items): Physical, cognition, social, and psychological.	Vertebral fracture (mean age 80)/ (Walters et al., 2016)	-Functional ability -Cognitive function -Prevalence of frailty in fragility fracture of hip and vertebral fracture.

Abbreviations: EFS= Edmonton Frail Scale; mFI= Modified/Simplified Frailty Index; FP criteria: Fried's Frailty Phenotype criteria; FI= Frailty Index; MFC= Modified Fried's Criteria; REFS= Reported Edmonton Frail Scale; Hip-MFS= Hip-Multidimensional Frailty Score; MFST-HP= Maastrich Frailty Screening Tool for Hospitalized Patients; 5-items mFI = 5 items modified Frailty Index; CFS = Clinical Frailty Scale; FRAIL scale = Fatigue, Resistance Ambulation, Illness, and Loss of Weight scale; PRISMA-7 = GFI= Groningen Frailty Indicator, THA= Total hip arthroplasty; TKA= Total knee arthroplasty.

Table 2.2 Comparison and evaluation of frailty instruments commonly used in orthopedic settings.

Measurement	EFS	mFI	PF criteria	FI	Modified Fried Index	MFC	REFS	Hip-MFS	MFST-HP	5-items mFI	CFS	FRAIL Scale	PRISMA-7	GFI
Country of study	US/ UK	CA/ US	US/ KR	US/ UK	CA	SG	SG	KR	US	US	CA	US	UK	UK
Retrospective study design		√						√		√		√		
Administration: - Observation - Self-reported only - Self-reported + performance - Self-reported + other standard assessments											√		√	√
	√	√	√	√	√	√	√	√	√	√		√	√	√
Frailty Domains	10	11	5	10 ⁺	5	5	9	8	3	5	4	5	7	4
Number of items	10	11	5	51, 42	5	5	9	8	15	5	N/A	5	7	15
Cut-off point of frailty	≥ 7	≥ 0.25	≥ 3	Varies	≥ 3	≥ 3	≥ 8	≥ 8	High score,	≥ 2	≥ 5	≥ 3	≥ 2	≥ 4

Measurement	EFS	mFI	PF criteria	FI	Modified Fried Index	MFC	REFS	Hip-MFS	MFST-HP	5-items mFI	CFS	FRAIL Scale	PRISMA-7	GFI
Comparison									more frail					
Modified from original measurement		√			√	√	√			√				
Requirement of measurement:														
- Other assessment information	X	√	X	√	X	X	X	√	√	√	X	X	X	X
- Specific equipment	X	X	√	X	√	√	X	√	X	X	X	X	X	X
- Specific training	√	√	√	√	√	√	X	√	X	√	√	X	X	X
Time preference for measuring frailty	Pre-op	Pre-op	Pre-op	Pre-op	Pre-op	Pre-op	Pre-op	Pre-op	48 hrs. post admission	Pre-op	Pre-op	1 st day of admission	Pre-op	Pre-op
Human resources involved	Researcher	Researcher	Researcher/training	Researcher	Researcher	Researcher	Researcher	Researcher	Nurse	Researcher	Researcher	Researcher	Researcher	Researcher

Measurement Comparison	EFS	mFI	PF criteria	FI	Modified Fried Index	MFC	REFS	Hip-MFS	MFST-HP	5-items mFI	CFS	FRAIL Scale	PRISMA-7	GFI
Reliability	X	X	X	√	X	X	X	X	√	X	X	X	X	X
Responsiveness	X	√	X	√	√	X	X	√	X	X	√	X	X	X
Time to complete (mins)	N/A	N/A	N/A	<10	< 6	3-5	7-10	N/A	< 3	N/A	< 1	N/A	N/A	N/A
Cross-culture validation study	√	N/A	N/A	√	N/A	N/A	N/A	N/A	N/A	N/A	√	√	√	√

Abbreviation: Canada (CA), The United States of America (US), South Korea (KR), Singapore (SG), United Kingdom (UK).

N/A= No information, (√) = report, (X) = no report. EFS= Edmonton Frail Scale; mFI= Modified/Simplified Frailty Index; FP criteria: Fried's Phenotype Criteria; FI= Frailty Index; MFC= Modified Fried's Criteria; REFS= Reported Edmonton Frail Scale; Hip-MFS= Hip-Multidimensional Frailty Score; MFST-HP= Maastrich Frailty Screening Tool for Hospitalized Patients; CFS = Clinical Frailty Scale; GFI= Groningen Frailty.

Supplement 2.1. Evaluation of the Frailty Instruments

Measures/ Studies	Content validity	Internal consistency	Criterion validity	Construct validity	Reproducibility		Responsiveness	Modified component of original instruments
					Agreement	Reliability		
EFS (Dasgupta et al.,2009)	0	0	+ Detsky criteria	0	0	0	(-) (the AUC of EFS = 0.69, 95%CI 0.58- 0.79).	0
EFS (Walters, Chan, Goh, Ong, & Sahota, 2016)	+ (referred original instrument)	0	+ compared with other frailty instruments.	0	0	0	0	0
mFI (Shin et al., 2016)	0	0	+ (obesity class III; ASA)	0	0	0	0	0
mFI (Bellamy et al.,2017)	0	0	+ (ASA)	0	0	0	0	0

Measures/ Studies	Content validity	Internal consistency	Criterion validity	Construct validity	Reproducibility		Responsiveness	Modified component of original instruments
					Agreement	Reliability		
mFI (Runner et al., 2017)	0	0	+	0	0	0	0	0
mFI (Vu, Runner, Reisman, & Schenker, 2017)	0	0	+	0	0	0	0	0
mFI (Charest- Morin et al., 2018)	0	0	0	0	0	0	0	0
mFI	0	0	+	0	0	0	(-)	0

Measures/ Studies	Content validity	Internal consistency	Criterion validity	Construct validity	Reproducibility		Responsiveness	Modified component of original instruments
					Agreement	Reliability		
(Ondeck et al., 2018)			Elixhauser Comorbidity Measure (ECM), Charlson Comorbidity Index (CCI)				The AUC value analysis of mFI for any adverse events= 0.586 (0.581-0.592); Death = 0.641 (0.624-0.659); Severe adverse events = 0.615 (0.608-0.622); Minor adverse events= 0.559 (0.533-0.565); Extend LOS =0.612 (0.606=0.617).	

Measures/ Studies	Content validity	Internal consistency	Criterion validity	Construct validity	Reproducibility		Responsiveness	Modified component of original instruments
					Agreement	Reliability		
FP criteria (Kistler et al., 2015)	0	0	+ Montreal Cognitive Assessment, Charlson Comorbidity score	0	0	0	0	+ Modified original to a new instrument “Geriatric Hip Fracture Frailty Assessment”.
FP criteria (Cooper et al., 2016)	0	0	+ (FI)	0	+	(-) using 3 categories of frail: weight kappa =0.42, 95%CI= 0.36- 0.49, while using 2 categories of prefrail and robust, weight	0	0

Measures/ Studies	Content validity	Internal consistency	Criterion validity	Construct validity	Reproducibility		Responsiveness	Modified component of original instruments
					Agreement	Reliability		
						kappa =0.53, 95%CI= 0.44- 0.61)		
FP criteria (Kim et al., 2018)	+	0	0	0	0	0	0	0
FI (Krishnan et al., 2014)	0	0	0	0	0	0	+	0
							(Area under curve: AUC for FI =0.82; 95%CI= 0.75-0.89 to predict failure to return home by 30 days in hip fracture)	
FI (Cooper et al., 2016)	0	0	+	0	+	(-)	0	0
			(FP criteria)			(using 3 categories of frail: weight		

Measures/ Studies	Content validity	Internal consistency	Criterion validity	Construct validity	Reproducibility		Responsiveness	Modified component of original instruments
					Agreement	Reliability		
						kappa =0.42, 95%CI=0.36- 0.49, while using 2 categories of prefrail and robust, weight kappa =0.53, 95%CI= 0.44- 0.61)		
MFC (Kua et al., 2016)	0	0	+	0	0	0	0	0
Modified Fried Index (McIsaac et al., 2018)	0	0	+	0	+	0	(-) AUC curve for predicting death or new disability of Modified Frailty Index = 0.68).	+ (Modified)

Measures/ Studies	Content validity	Internal consistency	Criterion validity	Construct validity	Reproducibility		Responsiveness	Modified component of original instruments
					Agreement	Reliability		
			Schedule (WHODAS)					
REFS (Kua et al., 2016)	0	0	+	?	0	?	0	0
			(MFC)	(referred to others)		(referred to others)		
Hip-MFS (Choi et al., 2017)	0	0	+	0	0	0	(+) AUC for prediction 6-months mortality =0.78, 95%CI= 0.78-0.79 better than age, ASA, NHFS	0
			(Conventional risk factors: age, ASA, NHFS)					
MFST-HP (Warnier et al., 2016)	0	0	0	+	+	+	0	0
				(factors analysis showed 6 components		(ICC for intra- rater=0.93, 95%CI= 0.86- 0.97; ICC for		

Measures/ Studies	Content validity	Internal consistency	Criterion validity	Construct validity	Reproducibility		Responsiveness	Modified component of original instruments
					Agreement	Reliability		
				with an Eigenvalue >1)		inter-rater = 0.95, 95%CI = 0.90-0.97; weighted kappa ≥ 0.6		
5-items mFI (Wilson, Holzgreffe, Staley, Schenker, & Meals, 2018)	0	0	+ mFI 11 items Claven –Dindo grade IV complication	0	0	0	0	+ (modified from mFI 11 items)
5-items mFI (Segal et al., 2018)	0	0	+ Clavien-Dindo complication	0	0	0	0	+ (modified from mFI 11 items)

Measures/ Studies	Content validity	Internal consistency	Criterion validity	Construct validity	Reproducibility		Responsiveness	Modified component of original instruments
					Agreement	Reliability		
CFS (McIsaac et al., 2018)	0	0	0	0	0	0	(-) AUC = 0.67 in predicting death and new disability.	0
FRAIL scale (Rothrock et al., 2018)	0	0	+	0	0	0	0	0
FRAIL scale (Gleason et al., 2017)	0	0	+	0	0	0	0	0

Measures/ Studies	Content validity	Internal consistency	Criterion validity	Construct validity	Reproducibility		Responsiveness	Modified component of original instruments
					Agreement	Reliability		
PRISMA-7 (Walters et al., 2016)	0	0	+	0	0	0	0	0
GFI (Walters et al., 2016)	0	0	+	0	0	0	0	0

Abbreviation: EFS= Edmonton Frail Scale; mFI= Modified/Simplified Frailty Index; FP criteria: Fried’s Phenotype Criteria; FI= Frailty Index; MFC= Modified Fried’s Criteria; REFS= Reported Edmonton Frail Scale; Hip-MFS= Hip-Multidimensional Frailty Score; MFST-HP= Maastrich Frailty Screening Tool for Hospitalized Patients; CFS = Clinical Frailty Scale; GFI= Groningen Frailty Indicator, THA= Total hip arthroplasty; TKA= Total knee arthroplasty. **Interpretation:** (+) = have information, (0) = no information, (?) = unclear information. **Agreement** focuses on an absolute measurement error: (+) = MIC < SDC OR MIC outside the LOA, (-) = MIC ≥ SDC OR MIC equals of inside the LOA, 0 = no information. **Reliability** focuses on the relative measurement error: (+) = ICC or weight Kappa ≥ 0.7, (-) = ICC or weight Kappa < 0.7, 0 = no information found. **Responsiveness** aims to an AUC of at least 0.70 to be adequate: (+) = AUC > 0.70, (-) = AUC < 0.7, 0 = no information.

Supplement 2.2 Search Terms

orthopedic surgery OR (orthopedic AND surgery) OR musculoskeletal diseases

AND

screening OR assessment OR instrument* OR tool* OR scale* OR measure* OR indicator* OR index*

AND

frail OR frailty* OR geriatric syndrome

AND

(aged[MeSH])

AND

(aged, 80 and over[MeSH] OR aged[MeSH])

Then, used specific date of publication: July 1st, 2006 to July, 31st 2018.

Chapter 3. Culturally-Adapted Translation and Psychometric Validation of the Reported
Edmonton Frail Scale-Thai version (REFS-Thai)

Target journal: Nursing and Health Sciences

Abstract word count: 174 out of 180

Manuscript word count (without references): 3,988 of 4,000

Tables: 5 out of 5

References: 32 out of 40

Abstract

Frailty leads to increased vulnerability, disability, and adverse health outcomes in older adults. Early detection is the best approach to manage frailty. However, frailty instruments are not widely available, especially in Thai. The purpose of this cross-sectional study was to culturally-adapt, translate, and validate psychometric properties of the Reported Edmonton Frail Scale-Thai version (REFS-Thai) in Thai hospitalized older adults. Validity testing was completed by three experts and cognitive interviews with 10 participants. Reliability (n=31) and internal consistency (n=100) was examined. Participants completed questionnaires, which included demographic and health information and the REFS-Thai. Results revealed that the REFS-Thai was a reliable instrument. The content validity index was 0.97. Cronbach's alpha was 0.73. The inter-rater reliability was good; the linear weights Kappa was 0.87 ($p < 0.001$). On average, REFS-Thai was completed in less than 7 minutes. The results suggest that the REFS-Thai may be a practical tool for frailty evaluation and could guide inpatient care in a middle-income country.

Keywords Cultural-adapted instrument, Frailty, Hospitalized older adults, Psychometric properties, Reported Edmonton Frail Scale, Thai language

1 INTRODUCTION

Frailty is a clinical symptom associated with age-related decline (Fielding, 2015; Sieber, 2017) that has been called “a new geriatric giant” (Morley, 2016, p. 59). It is known that frailty drastically influences health in older adults, leading to raised vulnerability, adverse health outcomes, long-term care needs, and higher mortality rates (Buigues, Juarros-Folgado, Fernandez-Garrido, Navarro-Martinez, & Cauli, 2015; Buta et al., 2016; Theou et al., 2018; Zaslavsky et al., 2013). Frailty dramatically impacts direct and indirect healthcare costs (Cesari & Vellas, 2015; Sieber, 2017). Although the consequences of frailty have been extensively investigated, identifying and assessing frailty in clinical care has been challenging. Early detection of frailty by health care professional is pertinent as it might delay dependency and prevent poor health outcomes in older adults. Thus, it is essential to assess for frailty so as to strengthen clinical-decision making and model appropriate care planning (Sieber, 2017).

Many tools have been used for frailty assessment in older adults; however, gaps still exist in evaluating clinical frailty. One barrier is there have been only few clinical frailty instruments translated into other than English (Braun, Gruneberg, & Thiel, 2018; Buigues et al., 2015; Buta et al., 2016; Jung et al., 2016). Another barrier is that most clinical frailty instruments require specific equipment, training, and longer assessment times (Buta et al., 2016; Dent, Kowal, & Hoogendijk, 2016; Sutton et al., 2016). Thus, identifying a reliable and rapid comprehensive assessment may be a key to choosing a frailty instrument for integration in usual clinical care. Due to the lack of a universal frailty standard assessment, selecting a frailty instrument to measure frailty status may also be limited to some settings and countries (Buta et al., 2016; Cesari & Vellas, 2015; Sutton et al., 2016). Evaluating frailty in various geographical areas with culturally-adapted instruments is important to capture the meaning of frailty within and across

cultures (Beaton, Bombardier, Guillemin, & Ferraz, 2000; Sousa & Rojjanasrirat, 2011). Thus, using culturally-adapted instruments establishes meaning of differing perspectives of frailty and enables one to benchmark frailty across a population (Beaton et al., 2000; Hambleton, 2005).

Remarkably, in Thailand, there is no published study regarding either a Thai-translated frailty instrument or a study investigating hospitalized frail older adults. To overcome this gap and to promote equity, and improve quality of care, performing a translation and validation of such a frailty instrument may be practical for monitoring health outcomes, making clinical decisions, and enabling appropriate frailty management in Thai older adults. Therefore, the aims of this study were to: 1) translate and culturally-adapt the frailty instrument—the Reported Edmonton Frail Scale (REFS) into the Thai language; and 2) evaluate the psychometric properties of the REFS-Thai instrument in hospitalized older adults.

1.1 Literature review

Fostering healthy aging and enhancing care quality are significant challenges in an aging society. Therefore, promoting early detection and delaying dependency has become of interest in geriatric care (Briggs & Dreinhofer, 2017). Geriatric syndromes such as frailty must be addressed to enhance care quality. Since the cause of frailty is not well understood, different concepts of frailty are proposed. Currently, the concept of “frailty” has been widely accepted as a condition of age-related decline, which is an important factor in increasing vulnerability to stress, leading to decreasing physiological reserves, and diminishing homeostasis across multiple organ systems (Fried, Ferrucci, Darer, Williamson, & Anderson, 2004; Fried et al., 2001; Xue, 2011). This recognized definition of the concept of frailty is most consistent with Fried’s frailty phenotype model (Fried et al., 2001). In clinical settings, frailty is a common, serious and potentially modifiable geriatric syndrome associated with increased vulnerability to adverse

health events due to age-related changes (Fried et al., 2004, 2001). Major adverse outcomes of frailty are disability, functional impairment, incidence of hospitalization, and death (Cooper et al., 2012; Perez-Zepeda, Cesari, & Garcia-Pena, 2016; Zaslavsky et al., 2013). Therefore, it is logical to believe that as aging population increases globally, the escalating care burden of frail older adults might affect either direct or indirect health-care costs. In order to prevent poor outcomes and promote health, it is important to identify frailty early.

Several definitions of frailty have been proposed which has resulted in a variety of instruments to evaluate frailty status. However, the lack of consensus for one definition of frailty has also resulted in debate regarding the optimal or gold standard instrument to evaluate frailty (Buta et al., 2016; Dent et al., 2016; Cesari & Vellas, 2015; Sutton et al., 2016). A second limitation is that frailty evaluation in clinical settings has been somewhat restricted (Buta et al., 2016; Theou et al., 2018). The majority of frailty instruments require specific equipment or training, laboratory tests, or are time-consuming to complete (Cesari & Vellas, 2015; Dent et al., 2016; Zaslavsky et al., 2013). Most of the clinical frailty measurements may not encompass a multidimensional assessment of frailty such as the cognition, social support, and emotion domains (Buta et al., 2016; Dent et al., 2016). Lastly, a significant limitation is that, to date, the culturally-adaption of clinical frailty screening instruments has not occurred. Using a culturally-adapted instrument establishes the meaningfulness of the concept in other cultures and languages, and also enables one to investigate difference among cross-cultural populations, enhancing the ability to generalize (Beaton et al., 2000; Hambleton, 2005). Hence, the factors in monitoring frailty in clinical settings may depend not only on multidimensional assessment and clinical resources, but also the cultural context. To overcome these challenges, there is a need to

develop a valid, culturally-sensitive frailty screening measure that is simple, inexpensive, safe, precise, and quick to administer, particularly in hospitalized older adults in non-Western settings.

There has been an increase in the number of studies about frailty, and yet there are discrepancies in what we know about frailty and its importance in different countries, including Thailand. Currently, there have been no studies of either frailty in hospitalized Thai older adults or evaluation of frailty instruments in the Thai language. Thus, there is a priority to test a culturally-adapted clinical frailty screening instrument that can bridge this gap in order to strengthen care in Thai older adults. Additionally, for Thai clinical settings and other similar settings with limited resources, a practical frailty screening measurement—one that is simple, rapid, inexpensive, and precise—is necessary. The Reported Edmonton Frail Scale (REFS) (Hilmer et al., 2009) may be an efficient frailty assessment to use in this situation. The REFS was chosen as it has the benefit of being a quick, reliable measurement, and multiple-dimension health assessment. The validity and reliability of the original REFS have previously been validated in a hospital setting using standard measurements—the Geriatrician’s Impression of Frailty, Mini-Mental State Examination (MMSE), Charlson Comorbidity Index, and Katz Daily Living Scale; the REFS demonstrated a good validity and acceptable reliability (Cronbach’s $\alpha = 0.68$) even when administered by non-geriatric trained personnel (Hilmer et al., 2009). Hence, the REFS might be a better choice compared to other frailty instruments in evaluating frailty in clinical settings. A culturally-adapted frailty screening instrument is crucial not only for promoting health, but also for strengthening clinical-decision making and modeling appropriate care planning. Further, effective frailty screening serves the fifth priority area in the World Health Organization (WHO) 2020 vision of improving screening measurement for delaying care

dependency and enhancing the quality of care to aging populations (WHO, 2015) within the Thai population.

1.2 Aims

The purposes of the study were to: 1) translate and culturally-adapt the REFS instrument into the REFS-Thai for use with Thai older adults; and 2) evaluate the psychometric properties, specifically validity and reliability, of the REFS-Thai in hospitalized older adults.

2 METHODS

2.1 Study design and setting

A cross-sectional study design was employed. Thai older adults admitted to the Ramathibodi Hospital, Mahidol University—a tertiary care university hospital—Thailand, were invited to participate in this study.

2.2 Participants

Eligible participants were aged 60 years or older who were able to read and speak Thai fluently, and scheduled for elective surgery from February to July 2018. This included older persons undergoing general surgery, neurological surgery, vascular surgery, urology surgery, and orthopedic surgery. Exclusion criteria were patients who had emergency surgery, cognitive impairment (Mini-Cog score of less than 3), acute psychiatric condition, history of stroke, brain injury or Parkinson's disease, and bedridden or receiving therapy (e.g., mechanical ventilation or cervical traction). The sample size calculation followed the practical recommendation; the cognitive interviews were conducted 10 participants (Paul & Willis, 2007; Peterson, Peterson, & Powell, 2017) and inter-rater were validated with another group of 31 participants (Hilmer et al., 2009). For the psychometric testing, it was validated in 100 participants which based on the

recommendation as cited in Sousa and Rojjanasrirat (2011) for a small sample size for psychometric validation.

2.3 Ethical considerations

Following IRB approval [University of Washington (STUDY00003624) and Mahidol University (MURA2017/796)], trained Registered Nurses (RNs) recruited older inpatients who were scheduled for elective surgery at a tertiary care hospital in Thailand. All participants signed written informed consent forms before engaging in study procedures. In situations where a participant had a visual impairment, a verbal agreement to participate in the study was accepted.

2.4 Data collection

The data collection was conducted in two stages: 1) translation and cognitive interview (n = 10); and 2) reliability evaluation: inter-rater reliability testing (n = 31) and psychometric testing (n = 100).

Stage 1. Translation and cognitive interview. After receiving copyright permission from the owner of the REFS, we applied the WHO's guideline for instrument translation and cross-cultural adaptation to develop the REFS-Thai (Beaton et al., 2000; Sousa & Rojjanasrirat, 2011). The WHO guidelines for translation (WHO, nd) suggest four steps: 1) forward translation, 2) expert panel back-translation, 3) pre-testing and cognitive interviewing, and 4) and creating the final version. For step three, we used small group interviews to complete the cross-cultural translation and refinement of the frailty screening instrument. Cognitive interviewing methods (Izumi, Vandermause, & Benavides-Vaello, 2013) were used to focus on the content and meaning of the items to the respondents, and to explore how much difficulty the respondent had in completing the instrument. The discussions of ambiguity and suggestions for improvement

were also noted. Finally, expert agreement methods were applied to evaluate the content validity index (CVI) of the REFS-Thai.

Stage 2. Reliability evaluation. For equivalence reliability evaluation, inter-rater reliability was determined between two health care personnel who did not have geriatric training. For the psychometric testing, based on heuristics for cross-cultural translation validation, a group of study participants scheduled for elective surgery ($n = 100$) was recruited to evaluate internal consistency of the REFS-Thai and to inform its' reliability and validity.

2.5 Measures

2.5.1 Mini-Cog (Thai-version)

The Mini-Cog-Thai version (Trongsakul, Lambert, Clark, Wongpakaran, & Cross, 2015) is translated from the original Mini-Cog which is used for cognitive impairment or dementia screening. Mini-cog test is scored in 2 parts: the 3-items recalled and clock drawing. The total possible score is 5; the score of less than 3 is considered as more likely to have cognitive impairment or dementia. The Mini-Cog-Thai version shows a good interrater reliability ($K=0.80$, 95%CI 0.50-1.00, $p<0.001$), and positive concurrent validity with the Mini Mental Status Exam Thai 2002 (MMSE) ($r = 0.47$, 95%CI 0.37, 0.55, $p=0.007$).

2.5.2 The Reported Edmonton Frail Scale (REFS)- Thai version (REFS-Thai)

The REFS-Thai, a self-report instrument, was translated from the original REFS, which defines frailty using the accumulation deficit model (Hilmer et al., 2009). The REFS-Thai evaluates nine domains: general health status, cognitive function, functional independence, continence, medication uses, nutrition, mood, social support, and self-performance. Maximal score is 18; the level of frailty is classified as severe frailty (score 12-18), moderate frailty (score 10 - 11), mild frailty (score 8 - 9), apparent frailty (score 6 - 7), and non-frail (score 0 - 5).

Content validity index (CVI), rating scale, is the method applied to verify the items of REFS-Thai (Item-level CVI: I-CVI) regarding their relevance to the frailty construct. Based on recommendation, the rating scale was a 4-point scale: not relevant (1 point), item needs some revision (2 points), relevant but needs minor revision (3 points), and very relevant (4 points) (Polit & Beck, 2006). Three experts including a gerontologist (physician), geriatric nurse (PhD), and surgeon (physician) were asked to rate each REFS-Thai item for content validity.

2.6 Data Analysis

The R 3.0.1 software was used for data analysis. Descriptive summaries were used to report number of participants screened, eligible, and enrolled in the study, as well as their demographic characteristics. The CVI by three experts using the standard 4-point scale (Polit & Beck, 2006) was reported to confirm the relevant content based on Thai context. Based on the standard recommendation (Bolarinwa, 2015; Polit & Beck, 2006), the CVI value equal to or greater than 0.78 was considered as excellent with respect to the REFS-Thai readability and clarity.

The inter-rater reliability (Kappa coefficient) was evaluated by two raters (non-gerontology trained) in another sample of 31 hospitalized older adults. The Kappa coefficient value of 0.60 or greater was considered as a moderate level of concordance between the raters. The higher the Kappa value, the higher concordance between the raters; contrary, the value closer to zero (0.00) indicates the lack of concordance. The Cronbach's alpha value from 100 patients was reported to verify the internal consistency reliability of the translated REFS-Thai. Cronbach's alpha of at least 0.70 was considered as acceptable reliability for the REFS-Thai.

3 RESULTS

The total of one hundred and forty-one hospitalized older adults participated: cognitive interview (n = 10), reliability and validity (n = 100), and inter-rater reliability (n= 31). The majority of

study participants were female (72%), the average age was 69 (range 60 to 92), had comorbidities (90%), and scheduled for major surgeries.

Content validity and the expert's agreement of translation showed a high agreement regarding the meaning of the REFS-Thai items. The content validity index for items (I-CVI) was 0.97, and content validity index for scale/the universal agreement (S-CVI/UA) was 0.92 (Table 3.1), which were excellent internal validity estimates. Pre-testing using cognitive interviews were conducted with 10 participants (male = 4, female = 6), the median of age was 69 years (range 63-75 years). Five participants requested assistance: 3 participants had misplaced their glasses and needed reading assistance, and 2 participants had musculoskeletal conditions (rheumatoid arthritis and shoulder impingement syndrome) and both reported acute pain/discomfort at their hand and wrist while drawing the clock (item 1). Most male participants expressed hesitancy when asked about functional independence items, especially meal preparation, housekeeping, and laundry (item 3). All participants reported easily understanding the meaning of each item. There were very few wording changes in the REFS-Thai; the changes were pronoun-specific which were purposefully revised to pay respect to Thai elders based on the traditional culture. Useful suggestions for more practical evaluation of functional independence (item 3) and self-reported performance (item nine, sub-item three: item 9-3) relating to particular situations are presented in Table 3.2.

For the reliability evaluation, 100 hospitalized older adults participated in this study (Table 3.3). The majority of participants were female (n=72, 72%) with an average age of 69.9 years (SD=7.0 years; range 60-92 years). All were scheduled for major surgeries. The frailty status—vulnerability, mild frailty, moderate, and severe frailty—were all determined at pre-operative assessment. The average REFS-Thai score was 4.9 points (SD=2.9 points; range 0-13

points). The average time to complete the instrument was 6.5 minutes (SD=3.8 minutes; range 3-30 minutes). The Cronbach's alpha of the REFS-Thai was 0.73, which is considered satisfactory for internal consistency as presented in Table 3.4. On item analysis, all items showed Cronbach's alpha higher than 0.65 (range 0.66-0.73). Chiefly corrected item-total correlation was higher than 0.3, while the values of item one and item four were 0.039 and 0.024 respectively. The inter-rater reliability of the REFS-Thai in the 31 participants was notable for substantial agreement; unweighted Kappa was 0.78 and the linear weighted Kappa was 0.87 ($p < 0.001$).

4 DISCUSSION

The purpose of this study was to employ culturally-sensitive procedures and evaluate the psychometric properties of the REFS-Thai. Overall, the REFS-Thai was easy and quick to administer for evaluating frailty in Thai hospitalized older adults scheduled for surgery. Reducing cross-cultural barriers in health assessments is a crucial concern in instrument development and translation. Information from the cognitive interviews allowed for the correction of unclear items that ensure the validity and reliability of the self-reported assessment (Beaton et al., 2000; Paul & Willis, 2007; Peterson et al., 2017).

Our findings identified several relevant cultural issues. The Thai language has various dialects based on different geographical areas in Thailand. Thus, selecting the one most appropriate language to usage is a challenge. In Thailand, words and phrases may have different meanings in various cultural groups. With five distinct regions in Thailand, there are many sub-culture groups. For instance, the Northern Thai language is quite different from Southern or Central Thai language regarding structure, pronunciation, and meaning. Additionally, there are many religions in Thailand: Buddhism, Hill Tribes religions, traditional Chinese (Taoism or Confucianism), Islam, and Christianity—that might influence thoughts and belief. Thus, intra-

cultural factors might interfere with semantic equivalence. In this study, despite the diversity of geographical areas represented, all participants were able to understand the questions in the cognitive interview process. Further, experts also agreed that the formal Thai wording was the most appropriate.

The findings of the study also identified a significant traditional belief of Thai culture which influenced the response to the REFS-Thai related to gender roles—as presented on the functional dependence item (item 3), especially meal preparation, housekeeping, and laundry. All of the males in the cognitive interview were hesitant to answer this question due to the perception of these activities as being a female’s role. The traditional belief was essential to responses to the REFS-Thai interview and is congruent with the gender role of many countries in Asia. The findings underlined the importance of a cognitive interview as a vehicle to capture the considerable cultural issues such as the traditional belief in gender roles.

Our findings revealed that the participant’s social environment and/or personal experiences influenced individual perceptions. The findings showed that half of the participants requested an explanation of the 1-kilometer distance (item 9-3); to make sure their perception of the distance was correct. Accurately determining what constituted 1-kilometer was intangible for many participants. In our study, relating it to their current environment was the most practical and preferable for all participants. For example, in hospitalized older adults, we described 1-kilometer as being four times the distance from the front door of the unit to the end of the hospital unit.

The original REFS testing indicated that hospitalized older adults spent approximately 4 minutes, to complete the questions (Hilmer et al., 2009); however, participants in the present study took longer to complete the instrument (average 6.5 minutes). One of the reasons for the

difference is that four participants took much longer (25 to 30 minutes) than others to complete the REFS-Thai. There are many factors in the hospital that might interfere with older adult's ability to focus, which could influence completion times. Acute symptoms or severity of illness may play a significant role. In the present study, this phenomenon was observed during performance of clock-drawing test (item one) when participants with pain and discomfort due to musculoskeletal conditions of the hand/wrist indicated that their ability to complete the item was impaired. Our findings revealed that pain experience impeded functional ability, which was consistent with the recently modified REFS version (mod-REFS). One group of investigators recently revised the mod-REFS in order to change the clock-drawing test to self-report to overcome some challenges related to functional impairment seen in older adults (Rose, Yang, Welz, Masik, & Staples, 2018). This modification should be considered for future evaluation of the REFS and REFS-Thai in other samples. Additionally, level of education may be another factor related to the amount of time to complete the REFS-Thai. More than half of the participants in this study attended primary school; consequently, the patients may put more effort into reading resulting in spending more time to complete the REFS-Thai. Despite the longer time for completion than that of the original REFS, the REFS-Thai remains able to be completed by the vast majority of individuals in less than 7 minutes, making it a practical tool to use for frailty assessment.

Considering the reliability and validity of clinical frailty assessment, the original REFS showed excellent reliability when benchmarking with standard clinical measurement for detecting frailty evaluated by personnel without medical training (Hilmer et al., 2009). The prior study applying REFS to screen frailty in forty-seven cardiology-inpatients who had percutaneous pulmonary intervention, aged average greater than 78.2 years; the reliability showed substantial

agreement (Cohen's Kappa= 0.70) (Hii, Lainchbury, & Bridgman, 2015). The REFS-Thai showed better reliability and validity than the previous studies. Overall reliability was satisfied; however, the findings of this study found that item one and item four had poor item analysis values. Investigating each item, we found a right skew of response to both items, which might diminish the value of the items. Item one (clock-drawing), nearly seventy percent of participants completed drawing the clock correctly. Nevertheless, factors such as pain or type of treatment might influence that time it would take to complete the instrument. For item four (social support), almost ninety percent of participants reported that having someone to help when needed. These results were in line with the traditional Thai culture; older adults usually lived with family or other relatives. While we considered deleting these items, all items were kept as per the original REFS because of the complexity of frailty; multidimensional evaluation might be crucial for precisely detecting frailty (Buta et al., 2016; Theou et al., 2018).

Identifying frailty, in this study, classified as the extent of frailty status—vulnerability to severe frailty—was detected in the Thai hospitalized older adults similarly to recent studies using REFS in reporting the prevalence of frailty in clinical settings (Hii et al., 2015; Rose et al., 2018). Moreover, participant characteristics, namely multiple comorbidities, polypharmacy, falls history, and malnutrition, were congruent with many studies exploring frailty characteristics in clinical settings (Buigues et al., 2015; Dent et al., 2016; Theou et al., 2018). Due to the lack of consensus of a gold standard for frailty (Buta et al., 2016; Cesari & Vellas, 2015; Sutton et al., 2016), the REFS-Thai is a potentially useful instrument in evaluating frailty in the Thai context. Moreover, participating hospitalized Thai older adults showed a strong interest in frailty; all enrolled participants completed the study procedures. Further use of the REFS-Thai may shed

light on the significance of detecting frailty and ability to assess frailty-related outcomes in this population.

4.1 Limitations and recommendations for further study

This study has some limitations. The study was conducted in a single tertiary care university hospital in the center of Thailand and most of participants lived in urban areas. Thus, the participants may not be representative of all Thais either different geographical areas or receiving care in other hospitals. Further research using a large and more diverse sample with multiple clinical settings along with exploring frailty in individuals residing in rural areas is necessary. Moreover, evaluating frailty in participants with functional limitations and/or lower health literacy population, and using a proxy to identify frailty may pave the way to improve quality of care in older population.

5 CONCLUSIONS

This study is the first step towards enhancing the understanding of clinical frailty in Thailand. The REFS-Thai is reliable and valid risk stratification tool in identifying frailty in hospitalized older adults. We believe that applying the REFS-Thai into daily clinical care can provide patient-centered care based on culturally sensitive and improve the equity and quality of care of Thai older adults who are frail or at risk of frailty. Furthermore, the REFS-Thai allowing for a simple and rapid assessment may be a practical risk stratifying tool for evaluating frailty and strengthening care quality in hospitals.

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The REFS-Thai is available on request. Please contact Inthira Roopsawang.

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Table 3.1: Content Validity Index (CVI) of the judgement of three experts

REFS-Thai (Items)	Number giving rating of 3 or 4 to relevancy of item	I-CVI*	pc**	Interpretation
Item 1	3	1	0.125	Excellent
Item 2				
Item 2-1	3	1	0.125	Excellent
Item 2-2	3	1	0.125	Excellent
Item 3	3	1	0.125	Excellent
Item 4	3	1	0.125	Excellent
Item 5				
Item 5-1	3	1	0.125	Excellent
Item 5-2	3	1	0.125	Excellent
Item 6	3	1	0.125	Excellent
Item 7	3	1	0.125	Excellent
Item 8	2	0.67	0.375	Fair
Item 9				
Item 9-1	3	1	0.125	Excellent
Item 9-2	3	1	0.125	Excellent
Item 9-3	3	1	0.125	Excellent
Average I-CVI = 0.97			S-CVI/UA*** = 0.92	

Note: I-CVI*: item-level content validity index; pc**: probability of chance occurrence was computed using a formula as cited in Polit and Beck (2006): $pc = [N!A!(N-A)!] * 0.5^N$, where N = Number of experts and A = Number agreeing on good relevance; S-CVI/UA***: scale-level content validity index, the universal agreement among experts.

Table 3.2 Coding of problems detected by cognitive interviewing on item 3 and item 9-3

REFS-Thai (item)	Response process: Problem type:	Understanding	Decision/Recommendation
<p>Item3: Functional Independence <i>“How many of the following activities do you require help? Meal preparation/ Shopping/ Transportation/ Telephone/ Housekeeping/ Laundry/ Managing money/ Taking medication”.</i></p>	<p>Hesitate to answer some activity: <i>“Meal preparation/ Housekeeping/ Laundry.”</i></p>	<p>Traditional belief of gender’s role: Thai male does not perform female’s role.</p>	<p>Acknowledged the Thai’s traditional role. Then, give an example to explain: If no female is taking care of those activities, are you able to do these activities without requiring help?</p>
<p>Item9-3: Self-reported Performance <i>“Two weeks ago, were you able to walk 1 kilometer without help?”</i></p>	<p>Lack of confidence for determine the correct distance of <i>“1 kilometer”.</i></p>		<p>Connected with a person’s experiences or environment and asked. <u><i>Environment: In a hospital setting</i></u> Could you walk with a comfortable pace—forth and back 4 times without stopping—from the front door to the end of the unit? <u><i>Personal experienced: Tracking exercise</i></u> Could you walk with an easy pace about 13 minutes without stopping?</p>

Table 3.3: Participants' characteristics (n=100)

Characteristic	n (%)	Mean (SD)	Range
Age, years		69.98 (7.03)	60-92
Mini-Cog score		4.18 (0.95)	2-5
REFS score		4.93 (2.88)	0-13
Time to complete REFS (minute)		6.46 (3.82)	3-30
BMI (kg/m ²)		24.91 (4.09)	16.17-35.50
Pain score		1.48 (2.49)	0-9
Gender, n (%) of Female	72 (72%)		
Religion			
Buddhism	97 (97%)		
Islamic	2 (2%)		
Christian	1 (1%)		
Educational level			
Did not attend school	3 (3%)		
Primary school	51 (51%)		
Middle and/or High school	7 (7%)		
Diploma degree	7 (7%)		
Bachelor's degree	30 (30%)		
Master's degree or higher	2 (2%)		
Income			
Income, n (%) with insufficient income	17 (17%)		
Occupation			
Not working/ Retired	63 (63%)		
Agriculture	13 (13%)		
Merchant	9 (9%)		
Employed	8 (8%)		
Savings	4 (4%)		
Other	3 (3%)		

Characteristic	n (%)	Mean (SD)	Range
Medical payment			
Government/State Enterprise	62 (62%)		
Universal Coverage Scheme (UC 30 baht)	22 (22%)		
Personal payment	16 (16%)		
Comorbidity			
Comorbidity, n (%) report comorbidity(s)	90 (90%)		
ASA* classification			
Class I	1 (1%)		
Class II	39 (39%)		
Class III	55 (55%)		
Class IV	5 (5%)		
Type of surgery			
Surgical	61 (61%)		
Orthopedic	23 (23%)		
Traumatic	10 (10%)		
Vascular	6 (6%)		
Living location after discharge			
Home	82 (82%)		
Moved to			
Relative's home	16 (16%)		
Other: Unplanned	2 (2%)		

*Abbreviation: ASA: The American Society of Anesthesiologists

Table 3.4 Item analysis and Cronbach's Alpha coefficient of the REFS-Thai (n=100)

REFS-Thai (Items)	Scale mean if item deleted	Scale variance if item deleted	Corrected item- Total correlation	Squared multiple correlation	Cronbach's alpha if item deleted
Item 1	5.25	11.139	0.039	0.150	0.736
Item 2					
Item 2-1	4.84	9.065	0.439	0.288	0.678
Item 2-2	4.88	9.299	0.392	0.375	0.687
Item 3	5.20	9.838	0.325	0.356	0.697
Item 4	5.48	11.464	0.024	0.185	0.725
Item 5					
Item 5-1	5.19	9.671	0.573	0.430	0.665
Item 5-2	5.23	10.421	0.323	0.293	0.695
Item 6	5.29	10.430	0.330	0.385	0.695
Item 7	5.35	9.826	0.560	0.539	0.668
Item 8	5.34	10.590	0.290	0.403	0.699
Item 9					
Item 9-1	5.17	10.486	0.300	0.362	0.698
Item 9-2	5.51	10.071	0.627	0.544	0.670
Item 9-3	5.43	10.591	0.330	0.243	0.695
Cronbach's Alpha coefficients of total scale	0.728				

Note: *Inter-rater reliability of REFS-Thai (n= 31): Unweighted Kappa = 0.78***, Linear Weights Kappa = 0.87*** (p-value < 0.001***)

Chapter 4. Predicting Hospital Outcomes of The Reported Edmonton Frail Scale-Thai Version
in Orthopedic Patients

Target journal: International journal of nursing studies

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Abstract

Background: Frailty is a common geriatric condition with impact on surgical outcomes. No research has been published on frailty assessment in hospitalized orthopedic patients in Thailand. The development of a valid frailty measure has the potential to improve screening and could enhance quality of care.

Objectives: To test the ability of the Reported Edmonton Frailty Scale-Thai version (REFS-Thai) to predict hospital outcomes compared with two standard preoperative assessment measures, the American Society of Anesthesiologists physical status classification (ASA) and the Elixhauser Comorbidity Measure (EMC) in older Thai orthopedic patients.

Design: Prospective cohort study.

Setting: A university hospital in Bangkok, Thailand

Participants: Two hundred hospitalized patients aged 60 years or older scheduled for elective orthopedic surgery.

Methods: Frailty was evaluated by using the REFS-Thai. Multiple Firth logistic regression modeled the effect of frailty on postoperative complications, postoperative delirium (POD), and discharge disposition (unable to be discharged home), while length of stay (LOS) was examined by Poisson regression. The area under the receiver operating characteristic curve (AUC) and mean squared errors (MSE) were used to compare predictive ability of the instruments.

Results: Participants mean age was 72 (range 60-94 years), 78% were female, 23% were frail and underwent knee (58%), spine (24%), and hip (18%) surgeries; of which 26.5% (n = 53) had postoperative complications, 12.5 % developed POD (n = 25), and were unable to be discharged home (11%, n = 22). Average LOS was 6 days (range 3-84 days). Adjusting for other variables, frailty measured by the REFS-Thai was significantly associated with postoperative complications

(odds ratio [OR] = 2.38, $p = 0.049$), POD (OR = 3.52, $p = 0.034$), and prolonged length of stay (relative risk [RR] = 1.42, $p = 0.043$). Applying the REFS-Thai alone shows good performance in predicting postoperative complication (AUC = 0.81, 95% confidence interval [CI] = 0.74-0.88) and POD (AUC = 0.81, 95% CI = 0.72-0.90). The combination of REFS-Thai with ASA and EMC demonstrates improvement in predicting postoperative complications (AUC = 0.81, 95% CI = 0.75-0.88 and 0.82 95% CI = 0.75-0.88) and POD (AUC = 0.80, 95% CI = 0.71-0.89 and 0.81 95% CI = 0.72-0.90).

Conclusion: Assessment of frailty using the REFS-Thai was useful in predicting selected adverse outcomes in older adults undergoing orthopedic surgery. Integrating the REFS-Thai for preoperative frailty assessment may be useful for enhancing quality of care in this population.

Keywords: *Acute care; Frailty; Older adults; Orthopedic; Surgical outcomes*

What is already known about the topic?

- Frailty is associated with adverse postoperative outcomes in older adults surgical populations
- There has been limited emphasis on frailty assessment in people with musculoskeletal (MSK) conditions, especially in limited-resource countries.
- There has been no published studies on frailty assessment in Thai orthopedic patients.

What this paper adds

- Provide unique information on frailty assessment and relation to adverse surgical outcomes in Thai orthopedic patients
- REFS-Thai shows good performance in identifying frailty and predicting adverse outcomes.

- Combining the REFS-Thai with standard preoperative assessment provides improved ability to prognosticate postoperative complications, POD, discharge disposition, and prolonged length of stay.

1. INTRODUCTION

In aging societies, promoting healthy aging and improving quality of care are significant global goals (Briggs et al., 2016). Therefore, promoting early detection of decline and delaying the onset of loss of independence are priorities in orthopedic and geriatric care. Musculoskeletal (MSK) conditions are common comorbidities in older adults and impact their quality of life. Developing MSK conditions is highly related to increased age, and may result in disability with higher disability-adjusted life years (DALYs) (Briggs et al., 2016; Briggs and Dreinhofer, 2017). Specific MSK conditions—rheumatoid arthritis (RA), osteoarthritis (OA), osteoporosis, as well as musculoskeletal pain significantly impact the health of individuals as well as the costs associated with care (Briggs and Dreinhofer, 2017; Cross et al., 2014). One treatment option for certain MSK conditions to regain functional ability in older adults is surgical intervention, although there are both risks and benefits of surgery. Although some postoperative complications are preventable, in-hospital adverse events as well as unpleasant surgical outcomes are still widely reported in orthopedic surgery even with simple procedures (Flexman et al., 2016; Lin et al., 2016; Ondeck et al., 2018a).

Frailty may be a contributing factor that creates more risk for patients to develop postoperative complications (Lin et al., 2016; Sieber, 2017). Frailty, a condition of increased vulnerability and susceptibility to stressors as well as reduced ability to sustain homeostasis, is related to adverse surgical outcomes (Cesari and Vellas, 2015; Lin et al., 2016; Sieber, 2017).

Frail older adults suffering from MSK conditions have higher risk concerning postoperative complications, disability, fall-related injury, mortality, and readmission when compared with those without frailty (Ali et al., 2016; Kua et al., 2016; Ondeck et al., 2018a). Preoperative frailty screening plays a key role in preventing adverse outcomes and improving quality of care. However, it is challenging to detect frailty in MSK conditions. There are concerns that the main characteristics of MSK conditions — physical limitations to accomplish activities of daily living, severe pain, joint stiffness, or chronic fatigue, along with sarcopenia — may cause misclassification of frailty status (Beaudart et al., 2015; McGuigan et al., 2017). Until recently, there has not been a gold standard to screen for frailty (Dent et al., 2016; Theou et al., 2018). Additionally, frailty instruments are not available in all languages (Dent et al., 2016; Theou et al., 2018). Thus, using reliable and culturally-adapted instruments are important to precisely measure frailty and identify the risk of adverse outcomes in different countries and geographical areas.

In Thailand, there has been no published study investigating frailty in Thai orthopedic patients. The increased prevalence of MSK conditions adversely impacts upon health in older adults. Orthopedic surgery may be an acute stressor which triggers or exacerbates frailty and its downstream processes, so early detection of frailty or risk for frailty is important to optimize outcomes. To improve quality of care, using a valid instrument to assess frailty may be practical for making clinical decisions and preparing for appropriate pre-operative management in frail Thai older adults with MSK conditions. The Reported Edmonton Frail Scale: Thai version (REFS-Thai) is a validated clinical frailty instrument in hospitalized surgical older patients. It has been shown to be useful to apply in the clinical setting, and takes on average, 7 minutes to complete, without need for additional equipment or training to use (Roopsawang, under review).

In this study, we evaluated the predictive ability of the REFS-Thai compared with the standard of care pre-operative screening [American Society of Anesthesiologists physical status classification (ASA) and the Elixhauser Comorbidity Measure (EMC)] to evaluate frail Thai older adults before undergoing elective major orthopedic surgery (hip, knee, or spine surgery) for postoperative complications, postoperative delirium (POD), length of stay (LOS), and discharge disposition.

2. METHODS

2.1 Study design and setting

This was a prospective cohort study. Hospitalized older adults scheduled for an elective orthopedic surgery (hip, knee, or spine surgery) were recruited from a tertiary care, university hospital in Thailand. The aims of this study were to: 1) assess the ability of the REFS-Thai version compared to the standard of care pre-operative assessment (ASA scoring and EMC) administered pre-operatively to predict the occurrence of any postoperative complications (from surgery to hospital discharge), POD, and discharge disposition following major orthopedic surgery, and 2) assess the ability of the REFS-Thai version administered pre-operatively to accurately predict LOS compared to the ASA scoring instrument and the EMC in patients undergoing major orthopedic surgery.

Following Institutional Review Board (IRB) approval, this study was conducted from July-November 2018. Trained research assistants reviewed the daily surgery schedule for patients meeting study criteria and then approached the patient to discuss study participation. All participants signed written informed consent forms before engaging in study procedures. If a participant had a visual impairment, verbal agreement to participate in the study was accepted. Participants were followed from study enrollment until discharge from hospital. Participants

could refuse to consent or withdraw at any time without detriment to their surgical care or treatment.

2.2 Participants

Individuals were eligible to participate in this study if they were: 60 years of age or older; spoke and read Thai; were scheduled for major elective orthopedic surgery (hip, knee, or spine surgery). Exclusion criteria were: undergoing emergency surgery; undergoing minimally invasive surgery; had cognitive impairment [assessed using Mini-Cog <3 (Trongsakul et al., 2015)]; current psychiatric disorder with ineffective treatment; history of stroke, brain injury or Parkinson's disease; currently bedridden or with evidence of severe disabilities (i.e. paraplegia, and quadriplegia).

2.3 Procedures

This study was approved by the IRB from the University of Washington, Seattle (UW) (STUDY00003625) and Mahidol University (MURA2017/796). Following consent, data collection started on the first day of admission and continued through to the day of discharge from the orthopedic ward.

Day of admission: Participant demographic information, ASA scoring, and the EMC were extracted from medical records. Participants completed the self-report REFS-Thai. Delirium screening by 4AT (Thai version) was evaluated pre-operatively by trained research assistants.

Post-operative period to hospital discharge: Data on types of surgery, postoperative treatments, and postoperative complications were extracted from the medical record. Daily delirium screening by 4AT (Thai version) was assessed by trained research assistants. In case the participant was discharged or transferred from the orthopedic ward for any medical reason, the

discharge disposition data were documented. At discharge, the total LOS was documented. All participant information extracted from the medical record was done by either the first author or the two prepared master's orthopedic nurse research assistants trained on the study protocol.

2.3.1 Measures

2.3.1.1 Mini-Cog (Thai-version): The Mini-cog Thai version (Trongsakul et al., 2015) was translated from the original Mini-cog, that is used for cognitive impairment and dementia screening. Mini-cog test is scored by 2 parts: a) a 3-item recall with b) clock drawing. The total possible score is 5; and a total score less than 3 means a patient is more likely to suffer cognitive impairment or dementia, and the higher scores mean lower likelihood to suffer cognitive impairment or dementia. The Mini-Cog-Thai version has shown good inter-rater reliability ($K = 0.80$, 95% CI 0.50-1.00, $p < 0.001$) with positive concurrent validity to the Mini-Mental Status Exam Thai 2002 ($r = 0.47$, 95% CI 0.37, 0.55, $p = 0.007$).

2.3.1.2 The Reported Edmonton Frailty Scale (REFS)–Thai version (REFS-Thai): The REFS-Thai, a self-report instrument, is translated from the Reported Edmonton Frail Scale (REFS) which defines frailty using accumulation deficit model. This tool has previously been validated to use in Thai inpatient settings (Author, in review), The REFS-Thai evaluates nine domains: general health status, cognitive function, functional independence, continence, medication use, nutrition, mood, social support, and self-performance. A total possible score on the REFS-Thai version is 18. Frailty is classified as severe frailty (score 12-18), moderate frailty (score 10-11), mild frailty (score 8-9), apparently frail (score 6-7), and non-frail (score 0-5). The REFS-Thai shows good inter-rater reliability (linear weights $K = 0.87$, $p < 0.001$) when applied by non-geriatric trained individuals. The internal consistency of REFS-Thai also indicates acceptable reliability (Cronbach's Alpha = 0.73).

2.3.1.3 American Society of Anesthesiologists (ASA) physical status classification: ASA scoring (Sankar et al., 2014) is a subjective assessment for a patient's overall health, categorized into six classes (I to VI). Anesthesiologists assess the ASA scoring before anesthesia to assess the risk of anesthesia and surgery. The ASA score is recorded in the patient's medical record. Classification of the ASA score comprises: ASA class I: normal healthy patient, ASA class II: patient with mild systemic disease, ASA class III: patient with severe systemic disease, ASA class IV: patient with severe systemic disease that is a constant threat to life, ASA class V: moribund patient who is not expected to survive without the operation. ASA class VI, a declared brain dead person, were not included in this study.

2.3.1.4 The Elixhauser Comorbidity Measure (EMC): The EMC is an assessment for a patient's comorbid conditions or their diagnoses at each admission (van Walraven et al., 2009). The 30 comorbid conditions are each determined as dichotomous (present/absent), and are weighted in order to predict in-hospital complications and mortality. The total EMC scale score ranges from -19 (lesser disease burden) up to +89 (higher disease burden). A higher score means more likely to suffer adverse outcomes or higher mortality rate. In an orthopedic surgery population, EMC has good reliability to predict in-hospital mortality (AUC value = 0.86; 95% CI = 0.86-0.86) (Menendez et al., 2014).

2.3.1.5 The Thai-version of 4 "A's Test (4AT)": The 4AT, Thai version (Kuladee and Prachason, 2016), is a short screening instrument for diagnosing delirium in hospitalized older adults. The 4AT has four aspects in evaluating delirium and cognitive impairment: alertness, abbreviated mental test-4 (AMT4), attention, and acute change or fluctuating course. A total possible score on the 4AT is 12. Scores range from possible delirium and/or cognitive impairment (score 4 or above), cognitive impairment (score 1-3), and unlikely delirium or

severe cognitive impairment (score 0; but delirium is still possible if the acute change or fluctuating course information is incomplete). For reliability and validity, the Thai-4AT has been shown to be satisfactory in screening delirium with 83.3% diagnostic sensitivity (95% CI = 62.6%-95.3%), and 86.3% specificity (95% CI = 76.3%-93.2%). Also, the area under the receiver operating characteristic curve (AUC) is 0.92. The 4AT is simple to apply even in those older adults who are unable to do cognitive testing or an interview and does not require specific training to administer.

2.3.2 Outcomes assessment

Outcomes of this study were obtained from daily chart and medication record review during admission through discharge. The POD occurrence was evaluated daily by a research assistant using the 4AT. The LOS (total length of hospital stay in days) and discharge disposition (home discharge versus to places other than home) were extracted from medical records. Postoperative complications or adverse events were extracted from medical records. For specific postoperative complications — respiratory failure, surgical site infection, deep vein thrombosis (DVT)/pulmonary embolism (PE), bleeding, renal insufficiency, stroke, unplanned-ICU, cardiac complication (myocardial infarction, new congestive heart failure, new arrhythmia, and heart block) — were extracted and verified by ortho-geriatric nurse specialists and orthopedic surgeons.

2.4. Data analysis

The baseline demographic characteristics, prevalence of preoperative frailty and rates of postoperative health events were calculated. Logistic regressions were used to examine associations between frailty and postoperative events. Frailty was classified into three categories (non-frail, vulnerable, and frail). The ability of the REFS-Thai, ASA and EMC to predict

development of postoperative complications, POD, and discharge disposition was evaluated by using Firth logistic regression. LOS was analyzed by using robust Poisson regression (Aim 1). Models were adjusted for age, gender, type of surgical procedures, and comorbidity. Cross-validation of a predictive model of the standard of care assessment (ASA class and the EMC) with and without REFS-Thai, and the AUC from the receiver operating characteristic (ROC) curves were examined for binary outcomes, while cross-validation comparing the mean squared errors (MSE) was investigated for LOS (Aim 2). Considering predictive power, the AUC values ranged from 0 to 1.0. An AUC value of 0.5 is equal to chance, 0.5-0.6 indicates a failed test, 0.6-0.7 indicates a poor test, 0.7-0.8 indicates a fair test, 0.8-0.9 indicates a good test, and 0.9-1.0 indicates an excellent test (Menendez et al., 2014). Considering the MSE cross-validation, a lower MSE score indicates a better prediction model of the outcome variable (LOS). A p-value less than 0.05 was considered as the level of significance for all analyses. The RStudio version 3.5.1 was used for statistical analysis.

3. RESULTS

Two hundred and three hospitalized older adults who were scheduled for orthopedic surgery agreed to participate in the study. Of these, three participants were excluded from the analysis due to cancellation of their surgeries. A total of 200 participants were included in the final analysis (Table 4.1). The majority of the participants were female, mean age was 72 years (range 60-94 years), most were not frail (n = 114, 57%), and were retired/not working (n = 160, 80%). On average, the REFS-Thai assessment was completed in five minutes.

3.1. Clinical characteristic of the participants and outcomes

Most participants were pre-obese, had moderate to severe systemic diseases with preoperative ASA class of III and IV (n = 127, 63.5%) and average EMC score was 0 (SD =

5.12) (See Table 4.1). Pre-operatively, most experienced mild pain and no cognitive impairment at admission. Knee surgery was the most common surgery (n = 116, 58%). The average LOS was less than 7 days (range 3-84); and approximately 10% (n = 22) of the participants were discharged to other health care facilities. Postoperative complications or life-threatening events occurred in 27% of participants (n = 53). The most common complications and adverse events were respiratory failure requiring intubation (24.5%), neurogenic bladder (22.6%), urinary tract infection (UTI) (20.8%), pressure ulcer (18.9%), and unplanned-ICU admission (13.2%) (Supplemental data 4.1). Notably, one participant assessed to be frail pre-operatively died on the fourth day after hip surgery. POD was identified in 12.5% of participants (n = 25); and of these individuals, 52% (n = 13/25) developed delirium at 24-hours after surgery, while 48% (n=12/25) experienced delirium at time of discharge. There was no strong association between preoperative health evaluation — ASA class and EMC scoring — and postoperative complication, POD, discharge disposition, or longer LOS.

3.2. Impact of preoperative frailty on outcomes

Approximately twenty percent of participants (n = 46, 23%) were frail at pre-operative assessment. Compared to the non-frail group and without controlling for other variables, frailty significantly increased the risk of developing postoperative complications (OR= 5.01, 95% CI: 2.40-10.72), POD (OR= 7.21, 95% CI: 2.57-22.84), and prolonging LOS (RR= 1.63, 95% CI: 1.23-2.15), while vulnerable participants were more likely to develop POD (OR= 5.20, 95% CI: 1.69-17.34). Notably, there was no strong association between frailty status and discharge disposition (Table 4.2).

In the multiple Firth logistic regression model the impact of preoperative frailty on outcomes was analyzed, adjusting for age, gender, type of surgery, and comorbidity (Table 4.2).

Compared to non-frail participants, controlling for age, gender, type of surgery and comorbidity (Table 4.2), frail participants were 2.38 times more likely to develop postoperative complications (OR= 2.38, 95% CI: 1.00-5.64), while vulnerable participants were 18% less likely to develop postoperative complications (OR= 0.82, 95% CI: 0.30-2.10). For POD, vulnerable (OR=3.75, 95% CI: 1.14-13.15) and frail groups (OR=3.52, 95% CI: 1.09-12.26) were found to be significantly more likely to experience POD post-operatively compared to the non-frail group. Being frail (RR= 1.42, 95% CI: 1.01-2.00) was significantly associated with a higher likelihood of increased LOS after surgery compared to non-frail participants.

3.3. Predictive ability of the REFS-Thai compared to the standard assessments

The comparison of AUC (area under the curve) area of ROC curve was analyzed for predictive ability of ASA class, EMC scoring, and REFS-Thai to the outcomes (Table 4.3). Age, gender, type of surgery, and comorbidity were treated as covariates and adjusted for in the model.

Considering a single assessment (Figure 4.1), the AUC area for predicting model of postoperative complication or adverse events according to EMC scoring, ASA (class III and IV), and REFS-Thai (three categories) were 0.79 (95% CI: 0.73-0.87), 0.80 (95% CI: 0.73-0.87) and 0.81 (95% CI: 0.74-0.88), respectively. The REFS-Thai performed better at predicting POD (AUC = 0.81; 95% CI: 0.72-0.90) compared to the other standard assessments. For LOS, the EMC scoring showed the best predictive ability (MSE bias corrected = 51.93). All three tools demonstrated poor predictive ability for discharge disposition.

When combining frailty assessment with other pre-operative assessment tools for predicting postoperative complications, the combined standard assessment with REFS-Thai indicated better prediction than using REFS-Thai alone: EMC scoring with REFS-Thai (AUC =

0.82, 95% CI: 0.75-0.88) and ASA class with REFS-Thai (AUC = 0.81, 95% CI: 0.75-0.88). For predicting POD occurrence, the REFS-Thai showed a good ability to predict (AUC = 0.81, 95% CI: 0.72-0.90). Most instruments demonstrated poor ability to predict discharge disposition, although the AUC area of the combination of EMC and REFS-Thai was 0.68 (95% CI: 0.55-0.80) which was higher than the other combinations tested. The combination of EMC scoring with REFS-Thai (MSE bias corrected = 53.60) showed slightly better predictive ability for prolonged LOS than other combinations (Table 4.3).

4. DISCUSSION

The present study might be the first to estimate frailty prevalence in Thai hospitalized older adults undergoing orthopedic surgeries. Study participants who were classified as frail in an orthopedic acute setting were older, female, and had moderate to severe comorbid health conditions. This study highlights the importance of preoperative frailty assessments in this population. The REFS-Thai has demonstrated good performance in predicting postoperative complications and POD. This study also highlighted that the REFS-Thai increased the precision in predicting postoperative complications, POD, and discharge disposition when combined with the standard preoperative assessment—ASA class or EMC.

The findings of this study were in line with previous reports regarding the characteristics of frailty and the impact of frailty on health in hospitalized older adults. Frail hospitalized older adults have risk to develop postoperative complications, prolonged LOS, adverse events, and inpatient mortality (Cooper et al., 2016; Gleason et al., 2017; Ondeck et al., 2018b; Shin et al., 2016; Walters et al., 2016). Our findings are consistent with other studies in which frailty was found in older adults with MSK conditions such as osteoporotic fracture, hip or knee OA, and degenerative spine diseases (McGuigan et al., 2017; Zlobina et al., 2015). Although previous

studies had indicated that the prevalence of frailty in MSK conditions was relatively low (approximately 10%) (Choi et al., 2015; Nguyen et al., 2015), our findings demonstrated a higher prevalence of frailty (n = 46, 23%) in Thai hospitalized older adults with MSK conditions. Moreover, our findings substantiate previous research concerning the association of frailty with being female (de Labra et al., 2018; Lee et al., 2018).

The present findings substantiate previous studies in orthopedic populations regarding the association among preoperative frailty, adverse events or postoperative complications, inability to discharge home, POD, and increased lengths of stay (Cooper et al., 2016; Gleason et al., 2017; Ondeck et al., 2018a; Shin et al., 2016; Walters et al., 2016). These findings showed that frail patients who had hip surgery were at risk for developing postoperative complications with increased LOS, which was consistent with other frailty studies in total hip replacement (Bellamy et al., 2017; Ondeck et al., 2018a). Complications from surgery in the current study were 26.5% including minor to life-threatening which was similar to previous studies (Flexman et al., 2016; Kua et al., 2016; Ondeck et al., 2018a; Vu et al., 2017). Notably, in-hospital mortality was shown in frail older adults who had total hip replacement. These findings support the evidence that frail patients who have surgery are at higher risk of adverse outcomes (Buigues et al., 2015; Lin et al., 2016; Shin et al., 2016).

Findings from this study share similarities with other studies that show increased risk of having POD with orthopedic surgery. The POD occurrence in this study (12.5%) was episodic and unpredictable. The POD occurred most frequently at 24 hours post-surgery (52%). Interestingly, 48% of POD occurred on the day of discharge although there was no documentation of active delirium in the medical record. Delirium is difficult to identify and diagnose, particularly if it is hypoactive or mixed delirium (Pollard et al., 2015). Undetected or

late diagnosis of POD during hospital admission can result in increased dependency, poor functional recovery, and lowered quality of life following discharge (Pollard et al., 2015). POD during hospital admission increases risk of 1-year mortality (Hamilton et al., 2017; Ruggiero et al., 2017). Furthermore, older adults who experience POD without dementia may be at higher risk of later development of preclinical dementia or Alzheimer's disease (Davis et al., 2012; Idland et al., 2017). We found that vulnerable and frail patients alike developed POD. Therefore, effective detection of POD and prompt treatment is vital to prevent poor health outcomes (Pollard et al., 2015). Our findings underscore the significance of early detection of POD in orthopedic patients including monitoring from admission to post discharge and until POD resolves.

Although the present study revealed no association between preoperative frailty and discharge disposition, it may be due to the small percentage (10%) of participants who were transferred to other care facilities. Further, the sample consisted of participants scheduled for elective surgery, which may have led to selection bias, contributing to the lack of an association with discharge disposition. However, our results were similar to previous study results which found preoperative frailty in orthopedic patients may result in the inability to discharge to home and their ongoing need for personal care assistance (Cooper et al., 2016; Gleason et al., 2017; Ondeck et al., 2018b; Shin et al., 2016; Walters et al., 2016). Noticeably, orthopedic patients undergoing hip and spinal surgery require time and continuing care in order to regain optimal physical function. The consequences of post-surgery physical or functional limitations may increase frailty severity so requiring long-term care (McGuigan et al., 2017; Zlobina et al., 2015). Since MSK conditions are chronic, additional research on transitional or continuing care post-surgical interventions is needed.

Preoperative frailty is significantly associated with greater LOS, these findings are consistent with previous studies in orthopedic patients (Cooper et al., 2016; Gleason et al., 2017; Wang et al., 2018). Additionally, LOS might be raised due to other factors for example type of surgery and/or postoperative adverse events or intraoperative incidence. Hip, knee, and spine surgery are frequently complicated surgeries resulting in adverse events or post-operative complications and extended-LOS in frail patients are well documented (Ondeck et al., 2018a; Wang et al., 2018). Intraoperative complications such as a dural tear, nerve damage, bleeding, anesthesia-related events, and cardiopulmonary events might increase LOS. The present findings identified various postoperative complications and adverse events from minor to life-threatening complications, such as respiratory failure required intubation, UTI, DVT/ PE, stroke, unplanned-ICU, and acute cardiac arrest. These findings were also in agreement with previous studies regarding adverse events and common postoperative complications in orthopedic patients (Ali et al., 2016; Kua et al., 2016; Ondeck et al., 2018a). This supports previous evidence in which frail individuals may experience unpleasant outcomes resulting from a trigger stressor like orthopedic surgery (Fried et al., 2001).

Due to the lack of standard assessment of frailty, many instruments including REFS have been developed to measure frailty (Dent et al., 2016; Kua et al., 2016). The current study demonstrated that REFS-Thai, is a valid and easy to administer (< 5 minutes) instrument to detect frailty and predict adverse outcomes in older Thai orthopedic patients. Although the standard preoperative assessment—ASA and EMC scoring—demonstrated good prediction of adverse outcomes, the REFS-Thai was better than these standard assessments for POD. Moreover, REFS-Thai improves the predictive ability for other postoperative outcomes when combined with ASA and EMC scoring. Our findings reinforce the usefulness of REFS-Thai in

detecting frailty when compared with the standard assessments in the Thai context. Integrating REFS-Thai in preoperative assessment may be beneficial for early detection of frailty and so providing better care, in particular identifying those with risk for developing delirium. As a result of the complexity of frailty, the identification and management of frailty should include evaluation of various health dimensions (Dent et al., 2016; Theou et al., 2018). Moreover, routine preoperative identification of frailty will be useful for improving surgical planning, enhancing patient-centered discharge planning, and strengthening transition and continuity of care in this population.

This prospective cohort study provides additional information and may be the first published study to apply preoperative frailty assessment in older adults undergoing orthopedic surgery in Thailand. However, this study has limitations. The sample was recruited from one university hospital with the majority of participants residing in urban areas, and as such, the findings might have limited generalizability. Several variables that might be relevant to the evaluation of frailty were not included (e.g., muscle and fat mass, grip strength, Interleukin-6, C-reactive protein, and 25-hydroxyvitamin-D) and these variables may warrant further study. Investigating frailty in other orthopedic settings, expanding frailty evaluation and validation in rural hospitals, including a larger number of hip and spine surgery, including both emergency and elective cases, and re-evaluating frailty after discharge are reasonable next steps for this research. Furthermore, extending research on cross-cultural validation should provide better understanding of frailty in other countries. Ultimately this should support development of proactive interventions for preoperative or long-term care.

5. CONCLUSIONS

Findings from this study provide evidence about frailty in Thai hospitalized older adults undergoing orthopedic surgery. Integrating REFS-Thai into preoperative routines to identify frailty earlier will be useful for risk modification, improving surgical decision-making, patient-centered discharge planning, and quality of care in this patient population.

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Table 4.1: Pre- and post-operative characteristics of the sample (N=200)

Characteristics	n (%)	Mean (SD)	Range
Age, years		72 (7.5)	60-94
Mini-Cog score		4 (0.9)	3-5
Time to complete REFS-Thai (minute)		5 (1.7)	2-11
EMC score		0 (5.12)	-9 - 19
4AT score at admission		0 (1.07)	0-6
4AT score at 24 hour post-surgery		1 (1.49)	0-12
4AT score at discharge		0 (1.38)	0-12
BMI (kg/m ²)		25.90 (4.12)	17.13-39.52
Pain score at preoperational		3 (2.95)	0-10
LOS (days)		7 (7.26)	3-84
Gender, n (%) of Female	156 (78)		
BMI classification (kg/m²)			
Underweight	6 (3)		
Normal	39 (19)		
Overweight	44 (22)		
Pre-obese	78 (39)		
Obese	33 (16.5)		
Frailty category			
Not frail	114 (57)		
Vulnerability	40 (20)		
Mild frail	19 (9.5)		
Moderate frail	19 (9.5)		
Severe frail	8 (4)		
Religion			
Buddhism	195 (97.5)		
Christian	3 (1.5)		
Islamic	2 (1)		

Characteristics	n (%)	Mean (SD)	Range
Educational level			
Did not attend school	16 (8)		
Primary school	103 (51.5)		
Middle and/or High school	26 (13)		
Diploma degree	11 (5.5)		
Bachelor's degree	35 (17.5)		
Master's degree or higher	9 (4.5)		
Income			
Income, n (%) with insufficient income	20 (10)		
Occupation			
Not working/ Retired	160 (80)		
Merchant	19 (9.5)		
Agriculture	8 (4)		
Employed	7 (3.5)		
Government/State Enterprise officers	3 (1.5)		
Other	3 (1.5)		
Medical payment			
Government/State Enterprise	122 (61)		
Universal Coverage Scheme (UC 30 baht)	54 (27)		
Personal payment	21 (10.5)		
Social Security payment	3 (1.5)		
Comorbidity			
Comorbidity, n (%) report comorbidity(s)	180 (90)		
ASA* classification			
Class I	3 (1.5)		
Class II	70 (35)		
Class III	119 (59.5)		
Class IV	8 (4)		

Characteristics	n (%)	Mean (SD)	Range
Type of surgery			
Knee	116 (58)		
Spine	48 (24)		
Hip	36 (18)		
Complications/adverse events, n (%)	53 (26.5)		
Postoperative delirium (POD), n (%)			
24 hour-postoperative	13 (52)		
Discharge day	12 (48)		
Discharge disposition, n (%) of inability to discharge home	22 (11%)		

Abbreviation: REFS-Thai = the Report Edmonton Frailty Scale-Thai version; EMC scoring = Elixhauser Comorbidity Measure; 4AT = The Thai-version of 4 “A’s Test; LOS = length of hospital stay; ASA = American Society of Anesthesiologists (ASA) physical status classification

Table 4.2: The estimated odds ratios (OR) and Relative Risks (RR) from logistic regression of preoperative frailty levels using REFS-Thai measure on postoperative outcomes in a sample of 200 orthopedic patients.

Outcomes/ Frailty	Univariate (95% CI)	p value	Adjusted* (95% CI)	p value
Postoperative Complication				
- Not frail	1 (reference)		1 (reference)	
- Vulnerable	1.39 (0.56-3.25)	0.462	0.82 (0.30-2.10)	0.697
- Frail	5.01 (2.40-10.72)	< 0.001**	2.38 (1.00-5.64)	0.049*
Postoperative Delirium (POD)				
	OR (95% CI)		OR (95% CI)	
- Not frail	1 (reference)		1 (reference)	
- Vulnerable	5.20 (1.69-17.34)	0.004*	3.75 (1.14-13.15)	0.029*
- Frail	7.21 (2.57-22.84)	< 0.001**	3.52 (1.09-12.26)	0.034*
Discharge Disposition				
	OR (95% CI)		OR (95% CI)	
- Not frail	1 (reference)		1 (reference)	
- Vulnerable	0.64 (0.16-2.00)	0.471	0.60 (0.14-1.96)	0.420
- Frail	1.11 (0.38-2.91)	0.834	0.85 (0.25-2.55)	0.779
Length of Stay (LOS)				
	RR** (95% CI)		RR** (95% CI)	
- Not frail	1 (reference)		1 (reference)	
- Vulnerable	1.63 (0.99-2.66)	0.051	1.55 (0.90-2.53)	0.113
- Frail	1.63 (1.23-2.15)	< 0.001**	1.42 (1.01-2.00)	0.043*

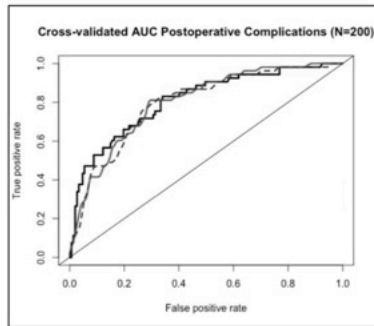
*The multiple Firth logistic regression and Poisson regression was applied with adjusted variables: age, gender, type of surgery, comorbidity. RR** = Relative Risk of robust Poisson regression.

Table 4.3. Estimates of the diagnostic ability of the preoperative REFS-Thai and other standard assessment to predict postoperative health events among a sample of 200 orthopedic patients

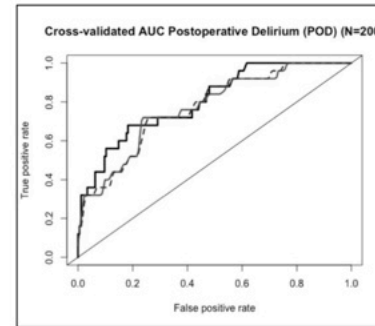
*Predictors	Postoperative Complications (AUC) (95%CI)	POD (AUC) (95%CI)	Discharge disposition (AUC) (95%CI)	LOS (MSE) (biased corrected)
ASA class 3 and over	0.80 (0.73-0.87)	0.77 (0.67-0.87)	0.62 (0.50-0.75)	52.39 (52.04)
EMC scoring	0.79 (0.73-0.87)	0.77 (0.68-0.87)	0.67 (0.54-0.79)	52.25 (51.93)
REFS-Thai	0.81 (0.74-0.88)	0.81 (0.72-0.90)	0.65 (0.53-0.77)	54.58 (53.93)
ASA class 3 and over + REFS-Thai	0.81 (0.75-0.88)	0.80 (0.71-0.89)	0.64 (0.53-0.76)	54.35 (53.76)
EMC scoring + REFS-Thai	0.82 (0.75-0.88)	0.81 (0.72-0.90)	0.68 (0.55-0.80)	54.16 (53.60)

**Adjusted for: age > 60 years, gender, comorbidity, and type of surgery; Poisson regression was analyzed for LOS, while the Firth logistic regression was used for the others.*

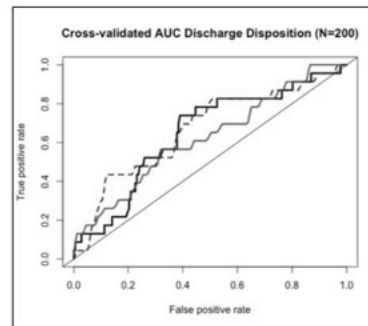
ASA = American Society of Anesthesiologists (ASA) physical status classification; EMC scoring = Elixhauser Comorbidity Measure; REFS-Thai = the Report Edmonton Frailty Scale-Thai version; POD = postoperative delirium; LOS = length of stay; AUC= Area Under the Curve; MSE = Standard Mean Squared Errors; CI = Confidence interval.



A. Area under the curve (AUC) for REFS-Thai: 0.81, 95% CI = 0.74-0.88



B. Area under the curve (AUC) for REFS-Thai: 0.81, 95% CI = 0.72-0.90



C. Area under the curve (AUC) for REFS-Thai: 0.65, 95% CI = 0.53-0.77

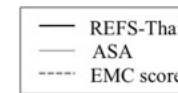


Figure 4.1. Prediction of outcomes by pre-operative REFS-Thai scores and other standard instruments

*ROC = Receiver Operating Characteristic

Supplement data

Supplement 4.1: Postoperative complications and adverse events (listed in order of frequency)
(N=200)

List of complications and events	n (%)
Respiratory failure	13 (24.5)
Neurogenic bladder	12 (22.6)
Urinary tract infection	11 (20.8)
Pressure ulcer	10 (18.9)
Unplanned-ICU	7 (13.2)
Deep vein thrombosis	4 (7.5)
Reoperation	3 (5.7)
Septicemia	2 (3.8)
Gastrointestinal bleeding	2 (3.8)
Acute pulmonary embolism	2 (3.8)
Dural tear	2 (3.8)
Surgical site infection	1 (1.9)
Meniscus tear	1 (1.9)
Stroke	1 (1.9)
Atrial fibrillation	1 (1.9)
Acute myocardial infraction	1 (1.9)
Anaphylactic shock	1 (1.9)
Cardiac arrest	1 (1.9)
Death	1 (1.9)

Supplement 4.2: The association of clinical characteristics of participants, preoperative frailty and outcomes (N=200)

Variables	Complication and Adverse events (ORs)	POD (ORs)	Discharge disposition (ORs)	LOS** (RRs)
Age ≥ 60 years	1.03 (0.98-1.09) p = 0.179	1.04 (0.98-1.12) p = 0.129	1.00 (0.94-1.07) p = 0.860	0.99 (0.97-1.02) p = 0.0370*
Female	0.63 (0.28-1.43) p = 0.268	0.99 (0.37-2.96) p = 0.988	1.92 (0.64-7.73) p = 0.262	0.99 (0.71-1.40) p = 0.984
Preoperative chronic diseases	1.21 (0.89-1.67) p = 0.218	1.79 (1.19-2.80) p = 0.004*	1.27 (0.87-1.88) p = 0.216	0.98 (0.870-1.11) p = 0.795
Types of surgery				
Spine surgery	Reference			
Hip surgery	1.25 (0.48-3.29) p = 0.642	0.62 (0.15-2.24) p = 0.467	0.44 (0.10- 1.72) p = 0.247	0.87 (0.58-1.29) p = 0.476
Knee surgery	0.17 (0.04-0.40) p < 0.001**	0.61 (0.20-1.88) p = 0.386	0.65 (0.23-1.99) p = 0.446	0.64 (0.42-0.97) p = 0.037*
ASA class				
1-2	Reference			
3 and higher	1.77 (0.81-4.00) p = 0.151	0.99 (0.40-2.57) p = 0.989	1.99 (0.77- 5.84) p = 0.157	0.86 (0.68-1.08) p = 0.186

Variables	Complication and Adverse events (ORs)	POD (ORs)	Discharge disposition (ORs)	LOS** (RRs)
EMC score	0.97 (0.89-1.04) p = 0.435	0.98 (0.92-1.10) p = 0.877	1.05 (0.97-1.15) p = 0.195	1.01 (0.99-1.03) p = 0.156
REFS-Thai (Frailty)				
Not frail	Reference			
Vulnerable	0.77 (0.28-2.00) p = 0.604	3.68 (1.12-12.76) p = 0.031*	0.57 (0.14-1.87) p = 0.370	1.54 (0.92-2.57) p = 0.100
Frail	2.69 (1.10-6.60) p = 0.030*	3.39 (1.03-11.97) p = 0.044*	0.76 (0.22-2.42) p = 0.654	1.37 (0.73-1.13) p = 0.069

Abbreviation: REFS-Thai = the Report Edmonton Frailty Scale-Thai version; EMC score = Elixhauser Comorbidity Measure; ASA = American Society of Anesthesiologists (ASA) physical status classification; POD= Postoperative delirium; LOS = length of stay; OR = odd ratio; RR = relative risk.

*LOS using Poisson regression, other outcomes used Firth logistic regression analysis

*p < 0.05; **p < 0.001

Chapter 5. Conclusions and Future Directions

The purpose of this chapter are fourfold. First, I will summarize the importance of improving clinical care for older adults who are frail or at risk for frailty. Second, I will summarize key issues facing investigators regarding the current measurement of frailty. Third, I will highlight the key findings from each of my three dissertation research studies. Lastly, I will close with future directions for frailty research in older adults with musculoskeletal (MSK) conditions.

With an increase in the aging population, there are more people with chronic illnesses, geriatric syndromes, and disabilities worldwide. Frailty, a common, serious, and complex geriatric syndrome, is a significant factor contributing to an individual's increased vulnerability to adverse health events due to age-related changes. Among hospitalized patients, frail older adults are prone to increased postoperative complications, institutionalization, morbidity, and mortality. MSK conditions are strongly associated with frailty leading to disability or care dependency. Age-related MSK conditions such as osteoarthritis (OA), rheumatoid arthritis (RA), and sarcopenia may intensify the progression of frailty. Frailty also has the potential to influence functional limitations and/or disabilities. Hence, frailty, MSK conditions, and disability may be conceived as a vicious cycle resulting in decreasing quality of life in older adult populations. The burden of care for frail older adults with MSK conditions might directly and/or indirectly affect health-care costs. Therefore, prevention and early identification of frailty with a reliable frailty screening instrument is beneficial in clinical care for risk stratification, treatment decision-making, and surgical planning in the older adult population.

Identifying those who are frail has significant challenges, yet screening for clinical frailty has limitations. One limitation is that there is no reliable instrument to measure frailty that currently serves as a gold standard. To date, many reliable frailty instruments have been

developed for evaluating frailty. However, existing frailty instruments range from simple to complex assessment, and the requirements to complete the assessment also vary depending on concepts of frailty, specific equipment usage, and number of items or complexity of such instruments. Thus, selecting a frailty instrument might be problematic in any setting, but more so in limited-resource settings. Another limitation is that identifying clinical frailty based on disability or comorbidity is challenging in some populations, particularly in those with MSK conditions. Clinical characteristics of MSK conditions such as physical limitations of daily activity, joint stiffness, severe pain or chronic fatigue, and sarcopenia may lead to a frailty misclassification. Thus, evaluation and detection of clinical frailty particularly in populations with MSK conditions is a formidable challenge. The final limitation is that there is a lack of frailty instruments in languages other than English. For example, there have been neither studies about frailty in hospitals nor frailty instruments published in the Thai language, and this includes an absence of work in orthopedic patients. Hence, a culturally-adapted frailty screening instrument is crucial not only for enhancing cross-cultural frailty assessment generally in Thai populations, but also for promoting older Thai orthopedic patients' health. To promote healthy aging, provide equity of care, and serve World Health Organization (WHO) priorities, applying a practical screening frailty instrument such as the REFS-Thai into routine preoperative care is needed.

This dissertation consists of a series of three studies developed from the study results. I will describe studies related to each of the research studies including the purpose, research design, key findings, and implications.

The first study that is a scoping review guided by Arksey and O'Malley framework, focused on frailty instruments used in older orthopedic patients. Main databases including

PubMed, CINAHL, PsycINFO, Scopus, and EMBASE were searched to identify relevant studies. The review methods consisted of five steps: 1) identified the research question; 2) identified relevant studies; 3) selected the studies; 4) charted the data; and 5) assembled, summarized and reported the results. Twenty-one articles were identified to compare and explore the quality of frailty instruments. Fourteen unique and reliable instruments measuring frailty were identified. The average time to complete the frailty instruments ranged from 1-10 minutes. Ninety percent (19) of the articles were from Western countries. The Frailty Index (6 articles) and Fried's frailty phenotype (3 articles) were the most widely used instruments. Preoperative frailty was associated with adverse outcomes. Although evidence was lacking for the single best-performing frailty instrument, the REFS was identified as a particularly practical instrument as no specific equipment is required to complete it, there are no specific training needs to administer it, and it takes less than 5 minutes to complete it. This scoping review provided additional evidence concerning challenges in frailty screening in patients with MSK conditions. Findings of the first study highlighted the needs for further research in clinical frailty for populations with physical limitation. For limited-resource settings, we recommended selecting frailty instruments which would be consistent with the clinical context, resources requirement, and instrument quality to minimize the gaps in care and provide quality of care.

The second study conceptualized from the results of a cross-sectional study, which was deployed in a tertiary care university hospital in Thailand. The multidimensional clinical frailty instrument—the REFS—was chosen to translate based on the assessment of instruments in the first research study. The REFS was chosen since it had good reliability and validity, quick assessment and time efficiency, less resource requirement, and no training needs for the personnel administering the instrument. The WHO's methods and cognitive interview for cross-

cultural translation were applied for improving semantic equivalence of the REFS-Thai version. Validity testing was provided via three experts and a cognitive interview with 10 participants. Reliability was examined by inter-rater testing with 31 participants and internal consistency with 100 participants. The findings demonstrated that the REFS-Thai was a reliable instrument: content validity index was 0.97, Cronbach's alpha was 0.73, and inter-rater reliability (linear weighted Kappa) was 0.87 ($p < 0.001$). None of the participants reported difficulties in interpreting the REFS-Thai, although 5 participants with physical limitation at wrists and upper arms due to MSK conditions expressed difficulties with the drawing-clock test. The REFS-Thai could be completed, on average, within 7 minutes. Although this study used a small sample of Thai older adults, the cognitive interview captured cultural differences in gender roles along with various personal and social experiences in Thai older adults. This research extended practical information for giving an example of the self-reported performance of the REFS-Thai. Perception of the 1-kilometer distance might depend on individuals' experience, as accurately determining what constituted 1 kilometer was intangible for many participants. In this study, we additionally provided additional an example of that distance by relating it to the participants' current environment (Table 3.2). Findings from this study suggested that the REFS-Thai is a practical and valid tool for frailty evaluation and could guide inpatient care in a middle-income country.

The third study was created by the results of a prospective cohort study conducted in orthopedic units of a tertiary care university hospital in Thailand. The study aimed to test the ability of the REFS-Thai to predict hospital outcomes compared with two standard preoperative assessment measures, the American Society of Anesthesiologists (ASA) physical status classification and the Elixhauser Comorbidity Measure (EMC), in older Thai patients undergoing

major orthopedic surgeries. Two hundred hospitalized patients, aged 60 years or older scheduled for elective major orthopedic surgery, participated in this study. Multiple Firth logistic regression was applied to investigate the effect of frailty on postoperative complications, postoperative delirium (POD), and discharge disposition (unable to be discharged home), while length of stays (LOS) was examined by using Poisson regression. The area under the receiver operating characteristic curve (AUC) and mean squared errors (MSE) examined the predictive ability on outcomes. Findings of the study given the results for the third research study revealed that participants' mean age was 72 (range 60-94 years), 78% were female, 23% were frail and underwent knee (58%), spine (24%), and hip (18%) surgeries; of which 26.5% (n = 53) had postoperative complications, 12.5 % (n = 25) developed POD, and 11% (n = 22) were unable to be discharged home. Average LOS was 6 days (range 3-84 days). Adjusted for other variables, frailty measured by the REFS-Thai was significantly associated with postoperative complications (OR = 2.38, $p = 0.049$), POD (OR = 3.52, $p = 0.034$), and prolonged-LOS (RR = 1.42, $p = 0.043$). Applying the REFS-Thai alone showed good performance in predicting postoperative complications (AUC = 0.81, 95% CI = 0.74-0.88) and POD (AUC = 0.81, 95% CI = 0.72-0.90). The combination of REFS-Thai with ASA and EMC demonstrated predictability increase in postoperative complications and POD. The empirical findings of the study provided a new understanding of clinical frailty in the orthopedic population, in Thailand. Findings also demonstrated various postoperative complications and adverse events from minor to life-threatening complications in frail participants. One of the most significant findings was that more almost half of vulnerable and frail participants developed POD at 24 hours post-surgery (52%, n = 13/25) and at the time of discharge (48%, n = 12/25). Interestingly, nearly 50% of those participants were underdiagnosed for POD during hospital admission and discharged home and

so did not receive treatments. As such, there is a need in comprehensive postoperative cognitive dysfunction monitoring for improving care quality. This study highlighted that assessment of frailty using the REFS-Thai was useful in predicting adverse hospital outcomes in older adults undergoing orthopedic surgery. Integrating the REFS-Thai for preoperative frailty assessment will be useful for enhancing the quality of care in this population. Future research should, therefore, concentrate on the investigation of clinical frailty and postoperative cognitive dysfunction, and transitional care or long-term monitoring to enrich the quality of life in this population.

This dissertation is the first step towards enhancing the understanding of clinical frailty in Thailand. The REFS-Thai is the reliable and valid risk stratification tool in identifying frailty in hospitalized older adults. I believe that applying the REFS-Thai in daily care can provide patient-centered and culturally-sensitive care and improve the equity and quality of care of Thai older adults who are frail or at risk of frailty. Results from these three studies have identified questions in need of further investigation regarding feasibility and acceptability of frailty instruments, preoperative care interventions for frailty, care transition/continuing care, and the link between postoperative cognitive dysfunction and frailty. Longitudinal studies of clinical frailty and its consequences in Thai older adult populations are recommended.