Research Proposal

Clinical and **H**ealth Economic **O**utcomes in Geriatric **P**atients with an **O**perative **F**ractured Neck of **F**emur **(ChopOff** Study**)**

Background

NOF fracture is a serious cause of morbidity and mortality. In 2013, approximately 24,000 Australians had fractured NOF, a figure projected, as the population ages, to exceed 32,000 by 2022 (1). This rise of NOF fractures will accordingly increase the associated costs. The direct health care cost alone accounted for $762 Million in 2013 and it is expected to be over $1 billion in 2022 (1), of which, nearly three quarters (72%) are hospital treatment costs (2).

Nevertheless, clinical outcomes may be improved by identifying risk factors and then adopting strategies to manage or modify these risks (3,4,5). In older surgical patients, the 30-day mortality is related to increasing age, high American Society of Anaesthesiologists (ASA) score, low preoperative plasma albumin, non-scheduled surgery, acute renal impairment, unplanned intensive care unit (ICU) admission and systemic inflammation (3).

For the fractured NOF patients, a few risk-scoring tools have been developed and claimed to accurately predict (and thus, risk adjust) the in-hospital, 30-day and one-year mortalities (4,5). Unfortunately, several well-recognized perioperative variables were either omitted or ill-defined in these studies, *e.g.,* timing of surgery, anemia, ASA status, ICU admissions and acute kidney injury (AKI).

However, it is important to first standardize or clearly define these to-be-assessed variables (Appendix A), since there exist mixed definitions for certain entities, for example, “early surgery” is recommended in the current guidelines, but its definition varies from 24 hours (6), 48 hours (7) to 72 hours post-admission (8). This is a concerning problem as such inconsistence could lead to different interpretations, and thus, inconclusive results, as in this case, the effect of “early surgery” on mortality benefits is still open to question with conflicting results reported in the literature (9,10). Therefore, new studies in this cohort are essential in order to specify some perioperative variables and then to determine if they are independent risk factors.

While the early mortality rates have been declining (11,12,13), there were significant differences between centres and countries, which could reflect the large diversities in the treatment of NOF fractures (11,13). As such, more detailed international comparisons are required to determine if the differences in outcome were due to variations in the demographics and/or the management of this population.

Indeed, a recent editorial (14) further underlines the need to carry out high-quality large observational studies worldwide so that CER is possible. CER (15) analyses distinctions in both outcome and

management in these studies and then, using advanced statistical models, to synthesize what works best in the "real world", *i.e.,* improving health, avoiding unnecessary costs or both.

Given that NOF fracture imposes such heavy medico-economic burden on the health system (16) but the evidence base is disappointingly weak (17), particularly its financial implications (18), CER in geriatric NOF patients is therefore urgently called for (14).

In Australia, comparable data are regrettably scarce and only a few small studies reported an inpatient mortality of 4.7 - 7.7% (19,20) and one-year mortality of 21.6 – 24.9% (21,22). To make matters worse, besides lacking of data on economic outcomes, one of the main outcome measures for geriatric surgical patients (3,11), 30-day mortality, has hardly ever been studied locally (21).

As such, it is necessary for Australian researchers to conduct large observational studies in older NOF patients that are designed to identify and evaluate unfavorable variables that could impair clinical and/or economic outcomes. This may not only assist risk stratification but may also help develop evidence-based hospital efficiency-cost control measures, *i.e.,* the hospital can provide quality service in the most cost-effective manner.

Aims:

The primary outcome of this study is to determine the post-operative 30-day all-cause mortality in older patients with an operative fractured NOF. The secondary outcomes are: to estimate the associated hospital costs for each fracture; to identify and specify unfavorable perioperative variables in terms of their impact on outcomes, being increased mortality risks, greater hospital costs or both.

Methods

Study Design

This is a retrospective observational study of patients aged 70 years or older (3), who were admitted to a metropolitan hospital during the period July 2011 to July 2015 for surgical fixation of NOF fractures.

Data Collection

After institutional ethics approval, the hospital diagnostic related group (DRG) database identified 1163 eligible patients and provided with the activity-based hospital costs for each patient, including total DRG hospital cost up to 1st August 2016, the first year DRG hospital cost, total initial admission cost and its activity-based costs.

Prior to commencing data collection, a pilot study (n = 62) was conducted, which assisted the calculation of sample size and established the feasibility of data collection.

The investigators will then examine the electronic patient records and noting: age, gender, ASA status, length of hospital stay, the number of inpatient transfers, the number of hospital admissions, pre-operative and post-operative 5 days' lowest haemoglobin levels, pre-operative and post-operative 5 days' renal

function. In addition, the following elements will be examined: whether the patients underwent an arthroplasty surgery, ICU admissions planned or unplanned, and the timing of surgery which includes 'the time of day' and 'how soon after the orthopaedic admission' when the operation took place. Inpatient, 30-day and 1-year mortality will be checked against the records from Victorian Registry of Births, Death and Marriages. Based on the mortality data, the postoperative survival days and the days alive out of hospital can be calculated.

All the collected data will be de-identified and then entered in a customised data entry form (Epi Info™ 7, *Version 3* 2016; CDC Software, USA).

Sample Size

The required sample size will be based on the primary research aim, which is the 30-day all-cause mortality fraction. The number of patient records that need to be reviewed depends on the expected mortality fraction and the desired band of the 95% confidence interval estimate (23).

Assuming the mortality fraction to be 13%, 149 patients would be required to achieve a 95% confidence level with a width of 10%. For a narrower confidence error margin of 5%, 411 patients would be needed.

Statistical Analysis

The mortality fractions and the 95% confidence levels will be estimated as percentages of the total number of patients who have died in a specified time period. In order to examine the association between patient factors and mortality, a survival analysis (such as proportional hazards regression) will be used to estimate the hazard ratios (or similar measures of association) taking into account the time until death and censoring (23).

Feasibility

This study itself is a feasibility study, with a view to developing into a larger scale study.

It is feasible to conduct and complete within the study timeframe, and the set objectives are achievable on account of the following aspects:

A strong research team:

The Chief Investigator (Dr Aihua Wu) has extensive research experience and published a number of original articles, review articles and one editorial in peer-reviewed journals. Since she was appointed as a full-time staff anaesthetist at Maroondah Hospital in early 2010, she has been very active in research and completed several research projects with great achievements at the Anaesthetic Department, including RELIEF Trial.

In addition, there are a number of enthusiastic in-house associate investigators and collaboration partners from external expert panels with different expertise:

1. Research Mentor and Supervisor – Professor David Story, Head of Anaesthesia, Perioperative and Pain Medicine Unit of Melbourne Medical School and Director of Melbourne Clinical and Translational Sciences Research Platform
2. Biostatistician – Dr Michael Fahey from Epworth Prostate Cancer Research Centre, Epworth HealthCare
3. Data Support – Mr Peter Long from Data Analyst, Decision Support, Eastern Health

Pilot Study

A pilot study (n = 62) was conducted before the commencement of data collection, which has assisted the calculation of sample size and established the feasibility of data collection.

Data Entry Form

Epi Info™ 7 (*Version 3* 2016, CDC Software, USA) was recommended by the statistician (Dr Fahey), hence, a user-friendly data entry form has been created, enabling researchers to conveniently enter and analysis data (http://wwwn.cdc.gov/epiinfo/). This form has been personally trialed with success, and each would take approximately 20-30 minutes to complete.

Data Collection

Currently, the required data are all available to enter in the EpiInfo form, including demographic and perioperative data from electronic patient records, hospital costs from DRG database and mortality data from Victorian Registry of Births, Death and Marriages.

Study Timeframe

After ethics approval, as the required data are readily available, most time would be spent on entering and analyzing data.

Now that this customized EpiInfo form has been specifically designed and validated for this study, data entry is straightforward. However, about half hour is needed to complete each form, so this study could consume two part-time researchers 6 months to enter the data and another 6 months to analyze the data.

Take into account the time spent on writing and presenting which could take another year, it is suggested to allow two years for completion of the study after ethics approval.

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Appendix A. Definitions

1	**Inpatient Mortality**		Patient died as an inpatient
2	**30-day Mortality**		Patient died within 30 days postoperatively
3	**Early Surgery**		Operation occurred within 48hrs following orthopaedic admission
4	**Operation Time**		Anaesthetic start time
5	**After-Hour Surgery**		Transferring patient to Operating Suite is after 17:00 o'clock
6	**Number of Hospital Admissions**		Number of NOF-related admissions to the Primary Hospital (MH) due to either postop complications or second NOF during the study period
7	**Number of In-Hospital Transfers**		Number of NOF-related ward transfers within the primary hospital (MH) due to either postop complications or rehabilitation during the study period
8	**ASA Status**		American Society of Anaesthesiologists (ASA) physical status classification system, which is classified into five categories.
9	**DAOH** (Days Alive Out of Hospital after Surgery)	**DAOH** within 30 Days	If survive 30 days: DAOH-30d = 30days – (length of MH stay) If 30-day mortality: DAOH-30d = date of death – (date of MH discharge)
		DAOH within a Year	If survive one year: DAOH-1yr = 365days – (length of MH stay) If 1-yr mortality: DAOH-1yr = date of death – (date of MH discharge)
10	**Haemoglobin**	Preoperative	Lowest haemoglobin level before the operation (lowest preop)
		Postop 5-day	Lowest haemoglobin level within postoperative 5 days
		Perioperative use	Whether blood products (excluding albumin) was administered during intraop and/or within postop 5 days
11	**AKI** (Acute Kidney Injury)	Preop Creatinine	Baseline Creatinine Level before the operation (highest preop)
		Postop 5-day Creatinine	Highest Creatinine level within postop 5 days
		Postoperative AKI	Creatinine increase > 20% of pre-operative value or, admission to ICU for renal replacement therapies
12	**ICU Admission**	Planned	ICU/HDU was requested for before the operation
		Unplanned	ICU/HDU was requested for during or after the operation
13	**Hospital Costs**	Initial Admission Costs	Costs to the hospital for the initial admission (from hospital admission to hospital discharge)
		1st year Costs	NOF-related hospital costs for the first year after the initial hospital admission (the cost was spent on NOF fracture during the 1st year)
		Total Costs	Total costs to hospital from initial admission till 1/8/2016 which was spent on all the hospital admissions due to NOF fracture

Note:

NOF: Neck of Femur Fracture; MH: Maroondah Hospital; ICU/HDU: Intensive Care Unit or High Dependency