

## **Title**

Does extreme age involve the selection of the non-frail for surgery? A secondary analysis of the peri-interventional outcome study in the elderly in Europe.

## **Background**

The elderly population is increasing. According to the World Health Organization, the number of persons aged 80 years or older is expected to triple within the next 30 years and reach up to 426 million in 2050 (1). As the population ages, the rate of surgical procedures in the older population is rising (2). It seems that advanced age is associated with an increased risk of complications after surgery (3,4). Nevertheless, recent publications show that patient's chronological age is not an independent risk factor, and clinicians may also consider the functional status of the patients when selecting the extreme elderly for surgery (5,6,7). One study concluded that outpatient thyroid surgery is safe in appropriately selected elderly patients, hence age should not be a contraindication to surgery in these patient groups (8). However, this study refers to a patient group of elderly  $\geq 80$  years of age and does not include the group of extreme elderly patients  $\geq 90$  years old. Another study compared centenarian hip fracture patients with a group of younger hip fracture patients between 70 to 99 years, and found that centenarians had fewer comorbidities, although mortality was higher at each follow-up timepoint (9). It seems that most data is limited to elderly patients and centenarians having specific types of surgery e.g., thyroid surgery and orthopaedic surgery. General data on the group of extreme elderly patients undergoing anaesthesia for various surgical procedures is limited.

The peri-interventional outcome study in the elderly in Europe (POSE) is a multicentre, prospective, cohort study that contains perioperative data on 9497 European surgical patients above 80 years old. Our study is a secondary analysis of the POSE study.

## **Purpose**

Our aim is to compare the prevalence of frailty in the extreme elderly POSE patients ( $\geq 90$  years) with elderly patients 80-89 years old.

## *Hypothesis:*

1. Frailty occurs with a significant lower frequency in extreme elderly ( $\geq 90$  years) as compared to patients aged 80-89 years old.

2. Frailty is associated with all cause 30-day mortality.

### **Materials and methods**

We will include patients above 80 years old, who underwent anaesthesia for various surgical procedures and with available baseline data on age, sex, most recent blood results (haematocrit and albumin level), functional status (independent, partially dependent, totally dependent), comorbidity and frailty assessments (history of falls during the last six months and Mini-Coq). Furthermore, we will include data on surgical urgency (urgent, emergency, elective), severity of surgery (minor, intermediate, major) and surgical category (orthopaedic, gynaecologic/abdominal, vascular, cardiothoracic, neurosurgical, other (ENT, plastic, ophthalmologic)). Finally, we will include postoperative data regarding all cause 30-day mortality.

### **Primary analysis**

Frailty as defined in the primary article. The POSE frailty assessment was based on the accumulation of deficits model (10) and frailty was scored as present if at least four of the following six markers were present.

1. Mini-Coq total score  $\leq 3$  points.
2. Albumin level  $\leq 3.3$  g/dL.
3. Fall in the last six months.
4. Haematocrit level  $< 35\%$ .
5. Preoperative functional status (partially dependent or totally dependent).
6. Three or more comorbidities using the Charlson Comorbidity Index.

**Secondary analysis:** All cause 30-day mortality.

### **Statistics**

We will use R for all statistical analyses.

The primary variable is dichotomised frailty (yes/no) and our primary null hypothesis of no difference in frailty between the two age groups ( $\geq 90$  years versus 80-89 years) will be analysed using Fisher's exact test/Chi-squared test. The frequency of frailty in the various types of surgical categories (surgical urgency, severity of surgery, surgical category) will be presented as well. For all statistical analyses, a p-value of less than 0.05 will be considered statistically significant.

The number of patients analysed in the original POSE study was 9497 patients. The specific pre-interventional geriatric assessment revealed frailty in 1336 patients (14.1%) and an estimated number of 1000 patients were  $\geq 90$  years old. With a power of 90% at the 0.05% significance level, we will be able to detect a difference in frailty of 3,5 % between the extreme elderly patients ( $\geq 90$  years) and the patients aged 80-89 years old.

### **Project participants**

#### Responsible for the project:

Liva Thoft Jensen, Medical student, University of Copenhagen, Denmark.

#### Main consultant

Jacob Steinmetz, MD, Ph.D. and Clinical Professor, Aarhus University and Rigshospitalet, Denmark, Center of Head and Orthopaedics, Department of Anaesthesia.

#### Other participants

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### **Timeline**

It is expected that data analysis and writing of first draft of manuscript will be 6 months from data receipt.

### **Funding**

Departmental funding via Copenhagen University Hospital, Rigshospitalet, Centre of Head and Orthopaedics, Department of Anaesthesia.

### **Ethics**

This is a non-interventional secondary analysis based on prospectively collected data from the POSE study, which we gain access to via a data transfer agreement with the University Hospital RWTH Aachen. The proposal for this analysis is approved by the POSE study Steering Committee (SC) and we will follow the POSE secondary analysis guideline. This guideline covers the approval

of this secondary analysis, why there are no further ethical concerns regarding the included patients. When submitting our final manuscript, we will include the POSE study original paper as a reference and incorporate all relevant individuals from the POSE study group as coauthors.

### **Publication**

As stated in the POSE secondary analysis guideline, our final manuscript must be approved by the POSE study SC before submission to a journal. We aim to publish in an international peer-reviewed journal in compliance with the ICMJE criteria for authorship as stated in the Vancouver recommendations.

### **Perspective**

This study will provide information on an emerging group of the extreme elderly patients in Europe. Since age is a well-known risk factor, the indication for surgery in these patients might be dependent on other important factors. Conservative treatment is often recommended for the extreme elderly patients. Those patients we however do select for operation might be in a very good shape. This study will describe this patient group and subsequently contribute to an understanding of age and frailty, and how we based on these factors select the non-frail for surgery.

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