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TREATMENT OF COMMUNITY-ACQUIRED PNEUMONIA: A THERAPEUTIC PERSPECTIVE

EARLY MOBILISATION DYSPHAGIA

BY DORTE MELGAARD

DISSERTATION SUBMITTED 2017



Treatment of community-acquired pneumonia:

A therapeutic perspective

EARLY MOBILISATION

DYSPHAGIA

by

Dorte Melgaard / Region Nordjylland



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PREFACE

The present thesis is based on an interest in patients hospitalised because of community-acquired pneumonia. Many patients have pneumonia, and these patients represent an economic burden because of their large numbers, relatively long length of stay, rehospitalisation, and death. Nonetheless, pneumonia does not receive significant attention in Danish hospitals. Few studies have focused on physiotherapeutic and occupational therapeutic interventions for this group of patients.

This thesis is based on the following papers:

Melgaard, D.; Baandrup, U.; Bøgsted, M.; Bendtsen, M.D; Kristensen, M. T.: *Early mobilisation of patients with community-acquired pneumonia reduces length of hospitalisation: a clinical intervention study*. Physiotherapy Theory and Practice (Submitted)

Melgaard, D.; Baandrup, U.; Bøgsted, M.; Bendtsen, M.D; Hansen, T.; *The prevalence of oropharyngeal dys-phagia in Danish patients hospitalised with community acquired pneumonia.* Dysphagia (Accepted)

Melgaard, D.; Baandrup, U.; Bøgsted, M.; Bendtsen, M.D; Hansen, T.: *Rehospitalization and mortality after hospitalization for Orapharyngeal Dysphagia and Community-Acquired Pneumonia: a 1-year prospective fol- low-up study.* The Journals of Gerontology Series B (Submitted).

Abbreviations

CAP	Community-acquired pneumonia
CAS	Cumulated Ambulation Score
CCI	Charlson Comorbidity Index
CG	Control group
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CURB65	Severity scores for community-acquired pneumonia
EM	Early mobilisation
ICF	International Classification of Functioning, Disability and Health
ICU	Intensive Care Unit
IG	Intervention group
IQR	Interquartile range
LOS	Length of stay
MRS	Modified Rankin Scale
NMS	New Mobility Score
OD	Oropharyngeal dysphagia
SD	Standard deviation
VVS-T	Volume Viscosity Swallow Test
30-s cst	30-second chair-stand test

ENGLISH SUMMARY

Community-acquired pneumonia (CAP) is one of the most common causes of admission to Danish hospitals, and despite the existence of suitable methods of treatment, many people die every year from CAP. The elderly are the most common group affected by CAP, and the risk increases in men, nursing home residents, and physically weakened individuals. The most common treatment is antibiotics. The severity of the illness and the overall health of the patients are essential to determining whether the treatment will occur in the patients' homes or through hospital admission. The numerous and frequent long admissions are a burden to the economy of the so-ciety. In addition, the course of the illness has significant consequences for patients because they often become weakened and experience a decline in their ability to function over longer periods, thus making it critical to limit the disease course as early as possible. The majority of the patients admitted with CAP are elderly, and therefore, they often have other diseases and illnesses, and hence an increased risk of developing oropharyngeal dysphagia (OD). Untreated OD can result in repeated cases of pneumonia, dehydration, and unwanted weight loss.

The objectives of this thesis were 1) to determine whether a standardised and structured effort in relation to early mobilisation can optimise the admission progress and 2) to determine the prevalence of OD in patients admitted with CAP and to identify the factors that influence readmission and mortality.

The studies were performed in the Department of Respiratory Medicine in the North Denmark Regional Hospital, and patients who were admitted with CAP were included.

In the winter of 2012/2013, 97 patients who were admitted with CAP were included in this study. Physiotherapists mobilised patients within 24 hours after their admission. Compared with a similar group of patients who were admitted in the winter of 2011/2012, the results showed that early mobilisation resulted in a reduction of admission by 1.5 days.

In the winter of 2013/2014, 154 patients who were admitted with CAP were checked for OD, and 34.4% were found to have OD. Patients with CAP and OD had a significantly longer duration of admission and higher readmission frequency and mortality than those of patients with only CAP. The one-year mortality rate for patients with CAP and OD was 71.7% versus 19.8% for patients with CAP.

This thesis supports the need for a standardised and systematic effort with regard to the early mobilisation of patients with CAP; similarly, an early report of OD in patients with CAP may serve as a foundation for a standardised multisector effort with regard to OD. Such an effort could improve patients' quality of life, reduce the number of admissions and reduce the high mortality

DANSK RESUME

Lungebetændelse er en af de hyppigst forekommende årsager til indlæggelse i Danmark og til trods for gode behandlingsmuligheder er der stadig hvert år mange danskere, der dør af lungebetændelse. Ældre mennesker får oftere lungebetændelse og der er desuden en øget risiko for at få lungebetændelse hvis man er mand, plejehjemsbeboer og i øvrigt fysisk svækket. Behandlingen er oftest medicinsk med antibiotika. Sygdommens sværhedsgrad og patientens almentilstand er afgørende for om behandlingen foregår i hjemmet eller under indlæggelse på hospital. De mange, og ofte relativt lange indlæggelser er belastende for samfundsøkonomien. Sygdomsforløbene har desuden store konsekvenser for patenterne, da sygdommen ofte medfører, at de bliver svækkede og får faldende funktionsevne over en længere periode, og det er vigtigt at begrænse dette fald i funktionsevne så tidlig som muligt. En stor del af de patienter der bliver indlagt med lungebetændelse er ældre og har andre sygdomme, dermed øges risikoen for, at de har dysfagi. Ubehandlet dysfagi kan medføre gentagne lungebetændelser, dehydrering og uønsket vægttab.

Formålene med denne afhandling var 1) at belyse hvorvidt en standardiseret og struktureret indsats i forhold til tidlig mobilisering kunne optimere indlæggelsesforløbene, 2) at afdække prævalensen af dysfagi hos patienter der bliver indlagt med lungebetændelse samt beskrive hvilke faktorer der har indflydelse i forhold til genindlæggelser og mortalitet.

Studierne blev gennemført på Lungemedicinsk afsnit, Regionshospital Nordjylland, og patienter, der blev indlagt på grund af lungebetændelse blev inkluderet.

I vinteren 2012/13 blev der inkluderet 97 patienter, der var indlagt med lungebetændelse. De blev mobiliseret af fysioterapeuter inden for 24 timer efter indlæggelsen. Sammenholdt med en sammenlignelig gruppe patienter der var indlagt vinteren 2011/12 viste resultaterne at tidlig mobilisering medførte en reduktion i indlæggelsestiden på 1,5 dag.

I vinteren 2013/14 blev 154 patienter, der blev indlagt med lungebetændelse undersøgt for dysfagi og 34.4% havde dysfagi. Patienter med lungebetændelse og dysfagi havde en signifikant længere indlæggelsestid, højere genindlæggelsesfrekvens og mortalitet end gruppen af patienter med lungebetændelse. Etårs mortaliteten for patienter med lungebetændelse og dysfagi var 71.7% versus 19.8% for patienter med lungebetændelse.

Denne afhandling understøtter en standardiseret og systematisk indsats i forhold til tidlig mobilisering af patienter med lungebetændelse. En tidlig udredning af dysfagi hos patienter med lungebetændelse vil ligeledes kunne danne grundlag for en systematisk, tværsektoriel indsats i forhold til dysfagi og dermed højne patienternes livskvalitet, reducere antallet af indlæggelser og nedsætte den meget høje mortalitetsraten hos denne gruppe patienter.

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1. INTRODUCTION

Community-acquired pneumonia (CAP) remains a leading cause of mortality worldwide. In Denmark, it is the fifth highest reason for acute admission ¹ and the third highest reason for readmission ². Admission and readmission result in considerable clinical and economic burdens ³⁻⁷. The prevalence among elderly patients is high, up to four times the prevalence in younger populations ⁸. Elderly patients are more likely to be treated in inpatient settings. A Dutch registry study has documented that 80% of patients with CAP aged 80-84 years were treated in an inpatient setting compared with 56% of patients aged 50-54 years ⁴. In the elderly, pneumonia may present with fewer respiratory symptoms but with delirium, and worsening of chronic confusion, and falls ⁹. The elderly also complain of fewer symptoms than younger patients ¹⁰. In Denmark, the incidence of patients hospitalised with CAP increased from 288 per 100 000 person-years to 442 per 100 000 person-years from 1994 to 2003. Age, comorbidity, and male gender were prognostic factors for admission ¹¹.

Studies have documented that the length of stay (LOS) in the hospital increases with age ^{12,13}. A Danish study has reported a median LOS of 6 days for patients hospitalised with CAP in the age \geq 65 years ¹⁴.

The rate of readmission in patients with CAP is relatively high, and a Danish study has reported that 12.3% of patients are readmitted within 30 days after discharge ¹⁴. These results are in line with international studies reporting a rehospitalisation rate for patients with CAP from 1% to 20% ⁶.

The mortality rates in-hospital and within 30 days after discharge range from 0-18% and from 1% - 23%, respectively, 6,15,16 . A Danish registry study including 11.332 patients aged ≥ 65 years has demonstrated an in-hospital mortality of 11.5% and a mortality of 8.6% within 30 days after discharge for patients with CAP ¹⁴.

The economic burden and the costs to treat CAP requiring hospitalisation are high ⁷. Only a few studies have presented the financial burden of CAP, but a Dutch registry study has found that the majority of costs are generated by the elderly, and 76% of the total CAP cost is related to patients aged 50 years and older. The mean cost per CAP case treated in a general ward is approximately $5000 \in 4$.

Validated national and international guidelines exist for the management of patients with CAP ¹⁷⁻¹⁹. These guidelines focus on when to hospitalise the patient and the rapidity of the administration of the first antibiotic dose, but there is limited or no focus on the effect of early mobilisation, nutrition, and swallowing disorders. Studies show that compliance with these guidelines can reduce unnecessary hospitalisations, LOS, costs, and mortality ^{20,21}. A Danish study has found a lack of compliance with the national Danish guidelines, especially relating to mobilisation and nutritional status ²².

2. BACKGROUND

2.1. DEFINITION

CAP is defined as an acute respiratory tract illness acquired outside of hospitals. CAP is associated with radiographic shadowing in admission chest radiographs and clinical symptoms such as coughing, sputum production, pleuritic chest pain, fever, tachypnoea, and rales ¹⁹.

2.2. INCIDENCE

The incidence of adults hospitalised with CAP has increased during the past several decades ^{11,23}. The risk factors for CAP are age, male gender, a general decrease in functional level, and malnutrition ^{9,24}. The rate of discharge for CAP increases with age. An American study has reported 33.4 per 10.000 for the ages of 45-64 and 189.0 per 10.000 for ages \geq 65 years ¹². A Danish study has found an incidence rate of 127 per 10.000 for patients with CAP for ages \geq 65 years ¹⁴.

2.3. EARLY MOBILISATION

Mobility is closely related to the functional level and CAP, and admission to the hospital is often followed by immobilisation during the hospitalisation and by an irreversible decline in the functional level and quality of life after discharge ²⁵. People of all ages are affected by being immobilised, but hospitalisation and immobilisation are especially major risks for older persons ²⁶.

More factors are associated with immobilisation and hospitalisation. Muscle strength is reduced with age, and decreased muscle strength and muscle atrophy follow immobilisation ^{26,27}. Muscle strength decreases by 5% per day when there is no contraction, and the lower extremities are especially affected; for elderly people, this reduction affects the functional level within a short time ²⁸.

The respiratory system undergoes more changes with age. The maximum inspiratory pressure decreases by up to 25%, the transdiaphragmatic pressure decreases by 13%, and the maximum voluntary ventilation decreases by 12% ²⁴. Muscle atrophy and a decrease in size in fast twitch fibres are likely explanations for the reduced diaphragmatic strength ²⁴. The level of exercise capacity is an individual variable that depends on age, fitness, and regular physical activity ²⁴.

Recovery is prolonged in elderly patients ⁹, and hospitalisation, which results in immobility, is followed by a loss of functional levels in 25-60% of the patients ^{29,30}.

Several studies have documented the effects of the early mobilisation (EM) of patients in intensive care and surgery units ³¹⁻³⁶, but a systematic review has included only a single study documenting this effect in patients with CAP ³⁷. This multicentre study included 458 patients with CAP, and the patients were randomised to EM or standard care in different settings. The study has shown that the patients in the EM group had a LOS in the hospital decreased by an average of 1.1 days compared with the standard care group ³⁸. However, this study did not report data for the level of mobilisation during hospitalisation, and a study investigating these findings has, to our knowledge, not been conducted, despite recommendations.

A Danish study has reported that the Danish guidelines are followed with respect to medical treatment but not to mobilisation to a chair and the assessment of functional levels ²².

2.4. OROPHARYNGEAL DYSPHAGIA

It is essential for humans to eat and drink, and dysphagia describes difficulties in meeting these basic needs. There are more definitions of dysphagia, and one is "difficulties moving food from the mouth to the stomach," ³⁹ but the International Classification of Functioning, Disability, and Health (ICF) classifies swallowing as "functions of clearing the food and drink through the oral cavity, pharynx and oesophagus into the stomach at an appropriate rate and speed ⁴⁰. Eating and drinking is a daily activity that includes the additional phases pre-oral, oral, pharyngeal, and oesophageal phase ⁴¹.

Dysphagia is divided into oropharyngeal and pharyngeal dysphagia. Difficulties in the phases mentioned above may lead to impairment in eating or drinking. The impairment can be addressed as a lack of safety and/or efficiency, as illustrated in figure 1.

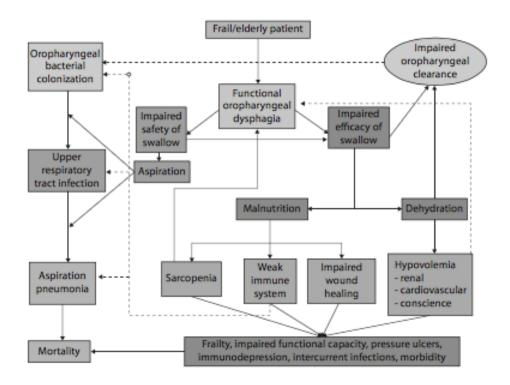
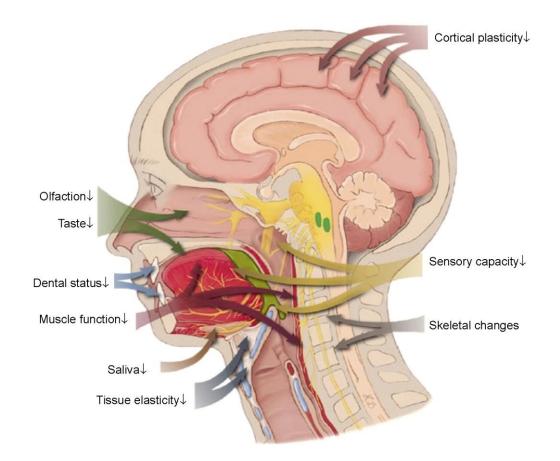
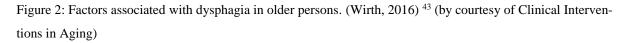


Figure 1: Nutritional and respiratory complications associated with oropharyngeal dysphagia in older patients. (Clave, 2012) ⁴² (by courtesy of Nestlé Healthcare)

As illustrated in figure 1, OD can lead to lung infections, frailty, malnutrition, loss of quality of life, and finally, death.

OD is highly prevalent in elderly patients, and the prevalence is 47% in frail elderly hospitalised for acute illness⁴². As illustrated in figure 2, additional factors are associated with OD. Loss of muscle mass, impaired dental status, reduction of saliva production, and changes of the cervical spine all affecting swallowing function ⁴³.





Only one study has documented a prevalence in patients with CAP, providing a value of 91.3% ⁴⁴. OD is not mentioned in the Danish guidelines for CAP ⁴⁵, but awareness of OD and its consequences is increasing in Denmark. In 2012, the Danish Patient Safety Authority published a recommendation for protocols for OD in hospitals and municipalities ⁴⁶. The recommendation was based on the occurrence of several adverse events and a lack of screening, and the recommendation has led to the national clinical guidelines "National Clinical Guideline for Oropharyngeal Dysphagia", published in 2015 ⁴⁷. These guidelines recommend a systematic, clinical assessment of OD. In Denmark, OD is not systematically explored in patients with CAP.

3. AIMS

On the basis of the described background, the overall aim of this study was to investigate the effect of early mobilisation on patients with CAP and the influence of OD in relation to CAP.

The specific aims were the following:

Study I

The primary aim was to evaluate whether the early mobilisation of patients with CAP reduces the LOS. The secondary aims were to systematically document the level of mobilisation during hospitalisation, to evaluate the deaths during hospitalisation and within 30 days after discharge, and to assess the prevalence of rehospitalisation within 30 days after discharge.

Study II

The aim was to assess the prevalence of OD in Danish patients hospitalised with CAP. The secondary aims were to identify the risk factors for OD in patients with CAP and to investigate the association of OD in patients with CAP and LOS, rehospitalisation within 30 days after discharge, mortality during hospitalisation, and mortality within 30 days after discharge. The long-term effect of OD was investigated by reporting the frequency of rehospitalisation 180 and 360 days after discharge and the mortality rates 180 and 360 days after discharge.

4. MATERIALS

All included patients \geq 18 years old were diagnosed with CAP and hospitalised in the Department of Respiratory Medicine in the North Denmark Regional Hospital and were discharged from this department. Patients received their first antimicrobial dosage within a few hours after hospitalisation ¹⁹. Pre-antibiotic expectorated sputum was used to specify the antibiotic treatment ⁴⁸. The medical treatments switched from intravenous to oral treatments when the patients had no signs of ileus, and when they were clinically stable ¹⁹. According to current guidelines, patients are considered to be clinically stable when their pulse is < 100/min, their respiratory frequency is < 24/min, their temperature is < 38°C, their systolic blood pressure is > 90 mm Hg, and their blood saturation level is > 90% ¹⁹.

The severity of the pneumonia was determined via the CURB-65 system, a validated index measuring the severity of pneumonia and predicting the mortality. The CURB-65 score is a part of the initial standard assessment procedure performed by the physician and consists of five factors: confusion, urea, respiratory rate, blood pressure, and age \geq 65 years. These five variables, each receiving a dichotomous one or zero score, are added to determine an overall score from 0 to 5^{49,50}.

The comorbidity was measured using the Charlson Comorbidity Index (CCI) ^{51,52}, which consists of 19 disease groups, each with a significant mortality risk (e.g., cancer, Chronic Obstructive Pulmonary Disease (COPD), or myocardial infarction); a higher score indicates a higher risk. The scores were summed to a score between 0 and 31.

Patients who received antibiotics orally and were clinically stable and independently mobile or had reached their habitual state of function were discharged ¹⁹.

Rehospitalisation is defined as rehospitalisation because of any disease in the northern region of Denmark.

5. METHODS

Study I: Early mobilisation of patients with CAP

A controlled study with longitudinal follow-up was performed. Patients hospitalised with CAP in the Department of Respiratory Medicine at the North Denmark Regional Hospital in the period from 1st September 2012 to 28th February 2013 were consecutively included and mobilised within 24 hours from admission.

A historical control group (CG) was matched with the intervention group (IG) at the case level according to gender, age (± 2 years), hospitalisation due to CAP in the same Department of Respiratory Medicine, and being discharged from this ward in the period between 1st September 2011 and 28th February 2012.

The following demographic data were recorded from the National Patient Register: age, gender, admission date, discharge date, first acute rehospitalisation within 30 days after discharge, and mortality. The following medical information was recorded from the electronic patient records: CRP, temperature, urea, respiratory rate, confusion, blood pressure at hospitalisation, time from admittance to initiation of antibiotic therapy, use of corticosteroids, and medication by discharge.

For the IG, the Cumulated Ambulation Score (CAS) ⁵³, the pre-hospital New Mobility Score (NMS) ⁵⁴, and the 30-second chair-stand test (30-s cst) ⁵⁵⁻⁵⁷ were scored at the first contact with the physiotherapist. The CAS and 30-s cst were thereafter recorded daily during the hospitalisation.

The CAS describes patient independence in three activities: 1) getting in and out of bed 2) sitting down and standing up from a chair, and 3) being able to walk with or without an appropriate walking aid. The scores for each activity were combined to provide a daily score between 0 and 6, with 6 indicating basic mobility independence.

The NMS was used to describe the patients' pre-hospital functional level, and patients reported their walking ability indoors, outdoors, and during shopping one week before they were hospitalised. Each activity was scored from 0–3, and a cumulative score between 0 and 9 was calculated, with high scores indicating a high level of activity.

The 30-s cst standardised test was performed, and patients were instructed to use the armrests. The score was the number of completed chair stands in 30 seconds ⁵⁶.

A non-standard taxonomy for mobilisation was registered daily and used for setting goals: 0 = not able to be mobilised; 1 = moved from lying in bed to sitting in a chair or to standing beside the bed; 2 = walked 1 to 10 metres; 3 = walked 11 to 20 metres; 4 = walked 21 to 35 metres; and 5 = walked 36 or more metres. Each level was with or without help from the physiotherapist. These data were not reported.

Three experienced physiotherapists who had received a training session in administering the tests mobilised the patients within 24 hours of hospitalisation. EM was defined as movement out of bed with a change from the horizontal to the upright position for at least 20 minutes that progressed during the entire hospitalisation. Physio-therapy was offered daily on weekdays.

After every intervention, the physiotherapist recorded the result of the mobilisation, and a goal was set for the next intervention.

Study II: OD in patients with CAP

A cross-sectional study with longitudinal follow-up was conducted. Patients hospitalised with CAP in the Respiratory Medicine Department in the North Denmark Regional Hospital from 1st September 2013 to 31st March 2014 were included and tested for OD.

Of the 170 patients enrolled in the study, seven were excluded because they were unable to communicate and thus were unable to participate in the test, and nine patients declined to participate in the study. Thus, 154 patients were included in the study.

Data were collected on the body mass index (BMI), circumference of the waist (2 cm above the navel), level of oral health, strength in both hands, circumference of the lower leg (15 cm above the lower edge of the patella), and circumference of the upper arm (lateral epicondyle + 10 cm). The age, gender, admission date, discharge date, and first acute readmission within 30 days after discharge were recorded from the National Patient Register.

Frailty was indicated by the following parameters: functional level before hospitalisation as reported with the Modified Rankin Scale (MRS) ⁵³, functional level at hospitalisation as assessed with Barthel-20 ⁵⁸⁻⁶¹, and comorbidity as computed with the CCI. A diagnosis of dementia, admission from a nursing home, and handgrip strength measured using a Jamar dynamometer ^{62,63} was also part of the combination of factors illustrating frailty in this group of patients.

OD was assessed using the Danish version of the clinical volume-viscosity swallow test (V-VST)^{64,65} and was administered by experienced occupational therapists. The test assesses different types of viscosity and different volumes and indicates the efficacy and safety of swallowing. The bolus volumes were 5 ml, 10 ml, and 20 ml. The bolus viscosity was a liquid viscosity; nectar viscosity was achieved by adding 1.2 g of the thickener Resource ThickenUp (Nestlé HealthCare Nutrition) to 100 ml water, and pudding viscosity was achieved by adding 6.0 g of the thickener Resource ThickenUp to 100 ml water. Mineral water at a room temperature of 25 °C was used. Boluses with each volume and viscosity were administered to the patients with a syringe during the test to ensure an accurate measurement of the volume. Before the V-VST, a pulse oximeter was placed on the index finger, and baseline readings were measured before starting the test. During the test, the following clinical signs of impaired efficacy were observed: impaired labial seal, oral or pharyngeal residue, and multiple swallows per

bolus. The clinical signs of impaired safety of swallowing were also observed: changes in voice quality, coughing, and a decrease in the oxygen saturation \geq 3%, indicating silent aspiration. The original Spanish version of V-VST has an 83.7% sensitivity and 64.7% specificity for bolus penetration into the larynx and a 100% sensitivity and 28.8% specificity for aspiration ⁶⁴.

6. STATISTICS

Statistical analyses were performed using Stata version 13.1 software (Stata Corporation, College Station, TX, USA). Throughout the analyses, 95% confidence intervals (CI) are reported, and a P-value < 0.05 was considered to be significant. Descriptive statistics included the number and percentage of patients for categorical variables, and the mean (\pm SD) or median (interquartile range (IQR)) for continuous variables. Differences between the two groups in the studies were analysed using Fisher's exact test for categorical variables and two-sample t-tests for continuous variables. Log-rank tests were applied to assess the differences in survival and rehospitalisation between the two groups in both studies. The Kaplan-Meier method was applied to estimate the mean LOS with discharge as the event and censoring for death. Z-tests were conducted to test for differences in the LOS between the two groups ⁶³.

Study I

The distributions of some clinical variables were positively skewed, but the number of observations per group was sufficiently large to justify using the t-test without a log transformation.

Study II

To compare continuous frailty parameters between the two groups, age and gender-adjusted t-tests (ANCOVA) were conducted. The suitability of these models was assessed by Q-Q plots of the residuals and scatter plots of the residuals versus the fitted values and to assess the homogeneity of the regression slopes, a visual inspection of scatter plots of the frailty parameter versus the covariate with regression lines for each group was performed. In some cases, models of the log-transformed frailty parameters were more suitable but did not alter the conclusions, and because the untransformed parameters are easier to interpret, those parameters are reported in table 8. The associations between the dichotomous frailty parameters and the two groups were estimated as age- and gender-adjusted incidence rate ratios using modified Poisson regression with robust variance estimation ⁶⁶. The variables of hand grip and BMI were so positively skewed that they are reported in table 12 and 13 with a median (IQR) and analysed with the Wilcoxon rank-sum test. Even though the distributions of some of the other clinical variables were also positively skewed, the number of observations per group was sufficiently large to justify using the t-test without a log transformation.

7. ETHICS

Study I:

The study was registered with the Danish Data Protection Authority (2008-58-0028), conducted according to the Declaration of Helsinki ⁶⁷ and approved by the local ethical committee. To mobilise patients early after admission is common practice in Denmark, and therefore, informed consent was not relevant.

Study II:

The study was presented to the North Denmark Region Committee on Health Research Ethics (N-20130058), but the committee responded that the study did not require the approval of the committee due to the fact testing for OD is common practice in Denmark. The study was conducted according to the Declaration of Helsinki ⁶⁷ and was approved by the Danish Data Protection Authority (2008-58-0028).

8. RESULTS

Study I: Early mobilisation of patients with CAP

In Study I, 111 consecutive patients were enrolled in the IG, and 14 patients were excluded because they were transferred to another department for further rehabilitation or they were transferred to the Intensive Care Unit (ICU). A historical CG was matched with the IG, and the patients in the IG and the CG were similar in age, gender, severity of pneumonia (CURB65), CCI, time from admittance to initiation of antibiotic therapy, use of corticosteroids and medication at discharge. In the IG, fewer patients had COPD (P = 0.044) as illustrated in table 1.

	Intervention group (N=97)	Control group (N=97)	P-value
Age	71.9 (±16.5)	71.9 (±16.5)	0.982
<u>≤</u> 49	10 (10.3%)	9 (9.3%)	
50-69	26 (26.8%)	26 (26.8%)	
70-79	26 (26.8%)	31 (32.0%)	
80-	35 (36.1%)	31 (32.0%)	0.872
Gender		• · · ·	
Male	51 (52.6%)	51 (52.6%)	1.000
CURB65	· · · · · ·		
Confusion	9 (9.3%)	15 (15.5%)	0.275
Urea (carbamide >7	34 (35.1%)	31 (32.0%)	0.920
Mmol/L)			
Respiratory rate \geq	10 (10.4%)	6 (6.2%)	0.310
30/min			
Blood pressure <90mmHg syst or	14 (14.6%)	18 (18.6%)	0.562
≤60 mmHg dias			
\geq 65 years	72 (74.2%)	67 (69.1%)	0.524
CURB65 score	· · · · · ·		
0	15 (18.1%)	16 (19.1%)	
1	29 (34.9%)	26 (30.9%)	
2	26 (31.3%)	30 (35.7%)	
3	13 (15.7%)	10 (11.9%)	
4	0 (0%)	1 (1.2%)	
5	0 (0%)	1 (1.2%)	
Unknown	14 (14.4%)	13 (13.4%)	0.839
Comorbidity			
Congestive heart failure	10 (10.3%)	4 (4.1%)	0.163
Cerebrovascular disease	11 (11.3%)	11 (11.3%)	1.000
Dementia	4 (4.1%)	3 (3.1%)	1.000
COPD	39 (40.2%)	54 (55.7%)	0.044
CCI	4.6 (±2.0)	4.5 (±1.8)	0.910
Time to antibiotic therapy (hours)	10.0 (±6.5)	10.0 (±7.69)	0.963
Corticosteroids	53 (54.6%)	48 (49.5%)	0.566
Medication by discharge	9.6 (±5.2)	9.5 (±6.3)	0.921
Temperature by hospitalisation	38.1 (±0.9)	37.9 (±0.9)	0.197

Table 1: Baseline data, demographic, and clinical characteristics of patients with CAP

Data are reported as number (%) for categorical variables, and as mean and SD (\pm) for continuous variables. The p-values are from unpaired t-test for continuous variables and Fisher's exact test for categorical variables. 14 patients in the IG and 13 patients in the CG have incomplete CURB65.

Patients in the IG were discharged after an estimated mean of 5.0 days (CI: 4.1; 5.9), and patients from the CG after 6.5 days (CI: 5.1; 7.9). The difference was -1.5 (CI: -3.2; 0.2) days between the IG and the CG (P=0.077). From winter 2011/2012 to winter 2012/2013, the mean LOS for all patients in the department decreased from an average of 4.8 days to 4.7 days. This difference was clinically irrelevant and statistically non-significant, and therefore it was ignored.

As presented in table 2, patients from the IG with a CURB65 score of 0-2 had a significant shorter LOS as compared with those in the CG; for example, patients with a CURB65 score of 2 in the IG had an LOS of 5.0 versus 8.1 in the CG (P=0.041). Patients in the IG with COPD had a significantly shorter LOS than those in the CG with COPD, with a mean of 2.05 (P=0.028) days.

	Intervention group (n=83)				Control group (n=84)			
CURB65	n	LOS Mean	Compliance	n	LOS Mean	Diff (IG-CG)	P-value	
0	15	3.6	14 (93.3%)	16	4.3	-0.8	0.381	
		(2.2; 4.9)			(3.2; 5.5)	(-2.6; 1.0)		
1	29	5.4	25 (82.2%)	26	7.1	-1.7	0.379	
		(3.9; 6.9)			(3.6; 10.6)	(-5.5; 2.1)		
2	26	5.0	22 (84.6%)	30	8.1	-3.1	0.041	
		(4.0; 6.1)			(5.3; 10.9)	(6.1; 0.1)		
3	13	8.9	9 (69.2%)	10	7.1*	1.8	0.419	
		(5.4; 12.4)			(4.7; 9.5)	(-2,5; 6.0)		
Total	83		70 (84.3%)	84				
COPD	39	4.3	33 (84.6%)	54	6.4	-2.1	0.028	
		(3.5; 5.1)			(4.7; 8.0)	(-3.9; -0.2)		

Table 2: Length of stay on the basis of CURB65 and COPD in patients with CAP

14 patients in the intervention group and 13 patients in the control group were not included in this table due to incomplete CURB65. *Two patients with a CURB65 score of respectively 4 and 5 included. Diff=difference in length of stay between intervention group and control group. Compliance=number of patients and percentage of patients undergoing early mobilisation. Z-tests were applied to test for differences in LOS between the two groups.

In the IG, 59 of 97 patients reached basic mobility independence on the first day after admission; additionally, 16 out of the 28 patients still hospitalised on day 4 also reached basic mobility independency on the first day after admission. In contrast, 4 out of the 5 patients who were still hospitalised on day 7 did not achieve independent mobility (table 3).

	Day 1	Day 4	Day 7
	Total (N=97)	Total (n=28)	Total (n=5)
Mob >20 min per day	80 (82.5%)	24 (85.7%)	2 (40.0%)
CAS getting in and out of bed			
Unable to perform function with human	17 (17.5%)	5 (17.9%)	3 (60%)
assistance			
Required human assistance to perform	4 (4.1%)	2 (7.1%)	1 (20%)
function			
Did not require human assistance	76 (78.4%)	21 (75.0%)	1 (20%)
CAS sitting down and standing up from	n chair		

Table 3: Mobility on days 1, 4, and 7 in patients hospitalised with CAP

Unable to perform function with human	18 (18.6%)	6 (21.4%)	4 (80%)
assistance			
Required human assistance to perform	7 (7.2%)	0 (0%)	0 (0%)
function			
Did not require human assistance	72 (74.2%)	22 (78.6%)	1 (20%)
CAS walking ability with an appropriat	te walking aid		
Unable to perform function with human	21 (21.6%)	9 (32.1%)	4 (80%)
assistance			
Required human assistance to perform	17 (17.5%)	3 (10.7%)	0 (0%)
function			
Required human assistance to perform	59 (60.8%)	16 (57.1%)	1 (20%)
function			
CAS total (min. 0, max. 6)	6 (4 - 6)	6 (4 - 6)	0 (0 - 3)
CAS=6	59 (60.8%)	16 (57.1%)	1 (20%)
	n=72	n=22	n=1
Number of sit to stand in 30 seconds	7 (0-10)	8.5 (0-10.8)	0 (0-1)

Data are presented as number (%), or as median (25-75%).

Patients in the IG who could be mobilised out of bed for more than 20 minutes within 24 hours after hospitalisation had a shorter LOS (P=0.021) than those with a lower level of mobility (table 4). Similarly, patients who were independent in basic mobility activities on day 1 (CAS score=6) were discharged earlier (P=0.002) than those who were not. As illustrated in Table 4, the primary factors influencing whether a patient was independently mobilised on day 1 appeared to be the functional level before hospitalisation (NMS) and a low CURB65 score compared with that of patients who were not early mobilised.

	Mob < 24 h		/ 1	P-value		
	Yes n=80	No n=17		Yes n=59	No n=38	
Age		•		•	•	•
<70 y	33 (41.3)	3 (17.6%)	0.097	29 (49.2%)	7 (18.4%)	0.003
>70 y	47 (58.8)	14 (82.4%)		30 (50.9%)	31 (81.6%)	
Gender						
Male	44 (55.0%)	7 (41.2%)	0.423	34 (57.6%)	17 (44.7%)	0.298
NMS						
NMS 0-8	30 (37.5%)	12 (75.0%)	0.011	13 (22.0%)	29 (78.4%)	< 0.001
NMS 9	50 (62.5%)	4 (25.0%)		46 (78.0%)	8 (21.6%)	
CURB65						
0	14 (20.0%)	1 (7.7%)		13 (26.0%)	2 (6.1%)	
1	25 (35.7%)	4 (30.8%)		19 (38.0%)	10 (30.3%)	
2	22 (31.4%)	4 (30.8%)		15 (30.0%)	11 (33.3%)	
3	9 (12.9%)	4 (30.8%)	0.416	3 (6.0%)	10 (30.3%)	0.007
LOS						
Days	4.4	7.8	0.017	3.8	6.8	0.001
	(3.6; 5.3)	(4.4; 8.8)		(2.9; 4.7)	(5.3; 8.2)	

Table 4: LOS according to patient characteristics, early mobilisation, and basic mobility status for the intervention group

Data are reported as number (%) for categorical variables, and as mean and 95% CI for continuous variables. Independent ttest for continues variables and Fisher's exact test for categorical variables. Due to incomplete CURB65 10 patients mobilised within 24 hours and 4 patients not mobilised within 24 hours were excluded. 9 patients with CAS=6 and 5 patients with CAS<6 were excluded due to incomplete CURB65. As shown in table 5, four patients (4.1%) in the IG died during hospitalisation compared with seven patients (7.2%) in the CG (P=0.351). The mortality rate 30 days from discharge was 4 out of 93 patients (4.3%) in the IG versus 3 out of 90 patients (3.3%) in the CG (P=0.738).

	Interver	ntion group	Contr	ol group
	Dead	Alive	Dead	Alive
	N=4	N=93	N=7	N=90
	(4.1%)	(95.9%)	(7.2%)	(92.8%)
Dead during hospitalisation			•	
Age				
<70 y	0 (0%)	36 (38.7%)	2 (28.6%)	33 (36.7%)
≥70 y	4 (100%)	57 (61.3%)	5 (71.4%)	57 (61.3%)
Gender	• • •		• • •	•
Male	2 (50.0%)	49 (52.7%)	4 (57.1%)	47 (52.2%)
NMS			· · · · ·	
NMS 0-8	4 (100%)	38 (41.3%)		
NMS 9	0 (0%)	54 (58.7%)		
CURB65			•	1
0	0 (0%)	15 (18.7%)	0 (0%)	16 (20.3%)
1	0 (0%)	29 (36.3%)	1 (20.0%)	25 (31.7%)
2	1 (33.3%)	25 (31.2%)	2 (40.0%)	28 (35.5%)
3	2 (66.7%)	11 (13.8%)	2 (40.0%)	10 (12.7%)
ССІ				1
	5.5±1	4.5±2.0	5.4±1.0	4.4±1.9
Dead within 30 days after discha	rge		•	1
v	N=4	N=89	N=3	N=87
	(4.3%)	(95.7%)	(3.3%)	(96.7%)
Age	,		• • •	• • •
<70 y	0 (0%)	36 (40.5%)	1 (33.3%)	32 (36.8%)
≥70 y		53 (59.6%)	2 (66.7%)	55 (63.2%)
Gender				
Male	1 (25.0%)	48 (53.9%)	2 (66.7%)	45 (51.7%)
NMS	,			• • •
NMS 0-8	3 (75.0%)	35 (39.8%)		
NMS 9		53 (60.2%)		
CURB65		/	•	•
0	0	15 (19.5%)	0	16 (21.1%)
1	2 (66.7%)	27 (35.1%)	1 (33.3%)	24 (31.6%)
2	0	25 (32.5%)	2 (66.7%)	26 (34.2%)
3	1 (33.3%)	10 (13.0%)	0	10 (13.2%)
CCI	6.5 (±3.7)	4.4 (±1.9)	4.0 (±1.7)	4.5 (±1.9)

Table 5: All causes of mortality during hospitalisation and within 30 days for patients with CPAP

Data are reported as number (%) for categorical variables, and as mean and SD (±) for continuous variables

In the IG, 19 out of 93 (20.4%) patients were rehospitalised within 30 days after discharge compared with 13 out of 90 (14.4%) in the CG (P=0.274), as shown in table 6. However, 5 of the patients in the IG were rehospitalised because of diseases other than lung-related diseases (e.g., aorta stenosis or cancer) compared with one patient in the CG who was rehospitalised because of pancreatitis.

	Intervent	ion group	P-value	Contro	P-value	
	Rehospitalised	Not		Rehospitalised	Not	
	N=19 (20.4%)	rehospitalised		N=13 (14.4%)	rehospitalised	
		N=74 (79.6%)			N=77 (85.6%)	
Age	·				• · · · •	
<70 y	6 (31.6%)	30 (40.5%)		6 (46.2%)	27 (35.1%)	
>70 y			0.600			0.537
Gender						
Male	9 (47.4%)	40 (54.1%)	0.618	10 (76.9%)	37 (48.1%)	0.073
NMS	•					
NMS 0-8	12 (66.7%)	26 (35.1%)				
NMS 9	6 (33.3%)	48 (64.9%)	0.018			
CURB65						
0	3 (15.8%)	12 (19.7%		4 (30.8%)	12 (18.2%)	
1	8 (42.1%)	21 (34.4%)		4 (30.8%)	12 (18.2%)	
2	6 (31.6%)	19 (31.2%)		5 (38.5%)	23 (34.9%)	
3	2 (10.5%)	9 (14.8%)	0.964	2 (15.4%)	8 (12.1%)	0.482
CCI						
	4.5	4.5		4.5	4.4	
	(3.55; 5.39)	(4.03; 4.99)	0.939	(3.42; 5.66)	(4.00; 4.85)	0.885
COPD						
	10 (52.6%)	28 (37.8%)	0.299	7 (53.9%)	41 (53.3%)	1.000
LOS						
Days	5.6	4.4	0.247	6.7	5.8	0.529
-	(3.8; 7.4)	(3.6; 5.2)		(4.3; 9.1)	(4.4; 7.3)	
Cause of rel	nospitalisation					
Pneumonia	14 (73.7%)			12 (92.3%)		
COPD						
Other dis-	5 (26.3%)			1 (7.7%)		
eases						

Table 6: All causes of rehospitalisation within 30 days from discharge

Data are reported as number (%) for categorical variables, and as mean and 95% CI for estimated mean LOS. Unpaired ttest for continuous variables and Fisher's exact test for categorical variables. 13 patients in the intervention group and 11 patients in the control group had incomplete CURB65.

Study II: OD in patients with CAP

As presented in table 7, 154 patients were consecutively included in study II: 54.5% were male, the mean age was 77.4 (\pm 11.5) years, and 34.4% (27.3; 42.3) of the sample was diagnosed with OD. In the group of patients over 70 years, 37.1% were diagnosed with OD. The patients with both OD and CAP were discharged after a mean of 10.6 days (8.8; 12.3) compared with 8.0 days (6.9; 9.1) (P=0.018) for patients with CAP alone. Patients with both OD and CAP had a significantly poorer tooth status (P=0.049), oral hygiene (P=0.018), and BMI (P=0.005).

	Patients with CAP and	Patients with CAP	P-
	OD	alone	value
	N=53	N=101	
	34.4%	65.6%	
Age (mean)	80.9 (±10.6)	76.0 (±11.6)	0.011
<50	0	4	
50-69	7	19	
70-79	14	38	
80+	32	40	0.075
Point of origin			
House/apartment	36 (68.9%)	98 (97.0%)	
Nursing home	17 (32.1%)	3 (3.0%)	>0.001
Volume Viscosity Swallow Test			
Impaired safety	50 (94.3%)		
Impaired efficacy	44 (83.0%)		
CURB65			
Confusion (yes)	23 (45.1%)	13 (13.5%)	>0.000
Urea (carbamide>7 Mmol/L)	36 (70.6%)	40 (41.7%)	0.001
Respiratory rate >30/min	8 (16.0%)	7 (7.3%)	0.149
Blood pressure <90 mmHg syst	6 (11.8%)	15 (15.6%)	0.625
or			
≤60 mmHg diast			
≥65 years	48 (90.6%)	89 (88.1%)	0.789
Use of oxygen		, ,	
Yes	4 (7.6%)	11 (10.9%)	
No	42 (79.3%)	85 (84.2%)	
Unknown	7 (13.2%)	5 (5.0%)	0.191
Tooth status	(1012/0)	0 (01070)	0.1771
No dentures	14 (26.4%)	41(40.6%)	
Denture on upper jaw	7 (13.2%)	17 (16.8%)	
Denture on underjaw	0 (0%)	2 (2.0%)	
Dentures	25 (47.2%)	38 (37.6%)	
Unknown	7 (13.2%)	3 (3.0%)	0.049
Oral hygiene	/ (13.270)	5 (5.070)	0.047
2 times per day	24 (45.3%)	70 (69.3%)	
1 time per day	18 (34.0)	20 (19.8%)	
3-5 times per week	1 (1.9%)	4 (4.0%)	
1-2 times per week	1 (1.9%)	2 (2.0%)	
1 time per month	0 (0%)	0 (0%)	
Never	2 (3.8%)	1 (1.0%)	
Unknown	7 (13.2%)	4 (4.0%)	0.018
Weight			0.018
0	64.8 kg (±15.2)	73.6 kg (± 22.0)	-
Height	$\frac{169.15 \text{ cm} (\pm 9.6)}{22.7 (\pm 5.1)}$	$167.5 \text{ cm} (\pm 8.7)$	0.586
BMI	22.7 (±5.1)	26.1 (±6.9)	0.005
Waist-line	101.5 (±13.3)	106.0 (±19.2)	0.124
Medication by discharge	9.4 (±4.3)	10.2 (±11.7)	0.573
Temperature by hospitalisa-	37.8 (±1.0)	38.2 (±1.1)	0.022
tion			

Table 7: Baseline data, demographic, and clinical characteristics of patients with CAP and OD.

Data are reported as number (%) for categorical variables, and as mean and SD (\pm) for continuous variables.

P-values were calculated using unpaired t-test and Fisher's exact test for the continues and categorical variables, respectively.

As illustrated in table 8, there was a significant difference between the groups of patients with both OD and CAP and that of the patients with CAP alone, on the basis of all of the frailty parameters, except comorbidity where the difference was nonsignificant.

	OD	САР	Difference	Р-	Age-adjusted difference	P-value
	and		(OD - no OD)	value	95% CI	
	CAP		95% CI			
Age	80.9	76.0	4.9	0.011		
	(10.6)	(11.6)				
Hand grip	12.7	19.6	-6.9	0.004	-5.6	0.017
•••	(11.1)	(12.1)	(2.3; 11.5)		(-10.1; -1.0)	
Leg circumfer-	32.0	38.0	-6.0	< 0.001	-5.8	0.003
ence	(4.8)	(12.6)	(-8.9; 3.0)		(-9.6; -1.9) -5.5	
Barthel-20	12.4	18.2 (2.4)	-5.7	< 0.001	-5.5	< 0.001
	(6.4)		(-7.7; -3.8)		(-7.0; -4.1)	
Modified Ranki	n Scale	•			· · · · · ·	
No symptoms	2	20				
v 1	(3.8%)	(19.8%)				
No significant	2	23				
disability	(3.8%)	(22.8%)				
Slight disability	8	25				
0	(15.1%)	(24.8%)				
Moderate disa-	13	26				
bility	(24.5%)	(25.7%)				
Moderately se-	18	6				
vere disability	34.0%	5.9%)				
Severe disabil-	8	0 (0%)				
ity	(15.1%)					
Unknown	2	1 (1.0%)		< 0.001		
	(3.8%)	× /				
CCI	5.7	5.5	0.2	0.666	-0.1	0.785
	(1.7)	(2.2)	(-0.5; 0.9)		(-0.8; 0.6)	
			Incident rate ratio		Age-adjusted relative	
					risk	
Admission to a	16	3 (3.0%)	3.2	< 0.001	2.9	< 0.001
nursing home	(30.2%)	` ´	(2.3; 4.4)		(2.0; 4.1)	
Dementia	12	4 (4.1%)	(2.3; 4.4) 2.5	< 0.001	(2.0; 4.1) 2.4	< 0.001
			(1.7; 3.7)		(1.6; 3.6)	

Table 8: Frailty (difference adjusted for age and gender)

Data are represented as number (%) for categorical variables and as mean and 95% CI for continuous variables. Independent t-test for continuous variables and relative risk is estimated by poisson regression.

In the group of patients with both OD and CAP, 7 of the 53 patients (13.2%) died during hospitalisation, as illustrated in table 9, and in the group of patients with CAP, no patients died during hospitalisation (P < 0.001). During the 30 days after discharge, 10 patients of the surviving 46 with both OD and CAP (21.7%) died, as shown in table 9. In the group of patients with CAP alone, only 2 patients out of 101 (2.0%) died (P > 0.001).

As shown in table 9, the group of patients who died during hospitalisation was characterised by a significantly higher mean age (8.6 years) and insignificantly lower Barthel-20 score and handgrip strength. No significant differences were present between the two groups regarding these variables.

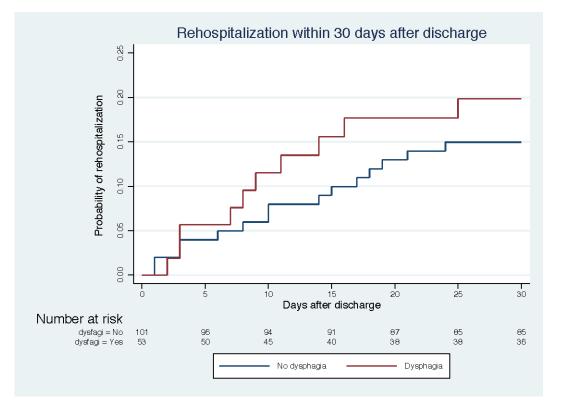
	OD and CAP	OD and CAP	P-value	
	Dead	Alive		
	N = 7 (13.2%)	N = 46 (86.8%)		
Mortality during hospitalisatio	n			
Mean age	88.3 (81.5; 95.2)	79.8 (76.6; 82.9)	0.045	
<70 y	0 (0%)	7 (15.2%)	0.575	
≥70 y	7 (100%)	39 (84.8%)		
Gender				
Male	4 (57.1%)	29 (63.0%)	1.000	
Barthel-20				
	9.8 (1.3; 18.3)	12.8 (10.9; 14.7)	0.296	
CURB65	• • • •			
Mean	2.9 (2.0; 3.7)	2.3 (2.0; 2.5)	0.091	
0	0 (0%)	0 (0%)		
1	0 (0%)	6 (14.0%)		
2	3 (42.9%)	24 (55.8%)		
3	4 (57.1%)	13 (30.2%)	0.425	
ССІ	4.8 (4.4; 5.3)	5.8 (5.2; 6.3)	0.224	
Dementia	1 (16.7%)	11 (24.4%)	0.565	
Handgrip	3.4 (1.2-18.4))	8.7 (6.9-17.4)	0.423	
Circumference under leg	33.5 (30.0; 37.0)	31.8 (30.3; 33.3)	0.419	
Nursing home	4 (57.1%)	13 (28.3%)	0.139	
Dead within 30 days after dis-				
charge	N = 10 (21.7%)	N = 36 (78.3%)		
Age				
Mean	80.8 (75.9; 83.0)	79.5 (75.9; 83.0)	0.736	
<70 y	1 (10%)	6 (16.7%)		
≥70 y	9 (90%)	30 (83.3%)	1.000	
Gender				
Male	3 (30%)	26 (72.2%)	0.025	
Barthel-20				
	11.1 (6.2; 16.0)	13.2 (11.1; 15.4)	0.364	
CURB65				
Mean	2.2 (1.5; 2.9)	2.3 (2.0; 2.6)	0.815	
0	0	0		
1	3 (30%)	3 (9.1%)	0.090	
2	3 (30%)	21 (63.6%)		
3	4 (40%)	9 (27.3%)		
CCI	6.7 (5.2; 8.3)	5.5 (4.9; 6.1)	0.060	
Dementia	4 (40.0%)	7 (20.0%)	0.187	
Hand grip	8.0 (4.4-20.0)	9.4 (7.0-17.4)	0.616	
Circumference under leg	31.6 (28.1; 35.0)	31.9 (30.1; 33.7)	0.870	
Nursing home	3 (30%)	10 (27.8%)	0.589	

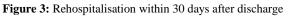
Table 9: All causes of mortality during hospitalisation and within 30 days in patients with both OD and CAP

Data are represented as number (%) for categorical variables and as mean and 95% CI for continuous variables.

P-values were calculated using unpaired t-test and Fisher's exact test for the continuous and categorical variables. Handgrip is reported with a median (IQR) and analysed with the Wilcoxon rank-sum test.

As illustrated in figure 3 patients with CAP and OD are rehospitalised more frequently than patients with CAP.





As illustrated in table 10 the rehospitalised patients with both OD and CAP exhibited a significantly higher hand grip strength compared with that of the rehospitalised patients with CAP alone, but there were no significant differences in any other variable. Patients with both CAP and OD are rehospitalised more frequently than those with CAP alone within 30 days after discharge.

days after discharge.	OD and CAP	OD and	P-	САР	САР	Р-
	Rehospitalised	CAP	value	Rehospi-	Not rehospi-	value
	N = 10	Not re-		talised	talised	
	(21.7%)	hospitalised		N = 15	N = 86	
		$\dot{N} = 36$		(14.9%)	(85.2%)	
		(78.3%)		, , , , , , , , , , , , , , , , , , ,		
Age	·					
Mean	74.1 (67.2 -87.6)	80.9 (77.5 -	0.174	74.7 (71.6-	77.4(70.8-	0.554
		89.0)		81.7)	84.6)	
<70 y	3 (30.0%)	4 (11.1%)	0.101	2 (13.3%)	21 (24.4%)	0.666
≥70 y	7 (70.0%)	32 (88.9%)		13 (86.7%)	65 (75.6%)	
Gender						
Male	7 (70.0%)	22 (61.1%)		8 (53.3%)	43 (50.0%)	0.517
Barthel-20	19 (11-19)	13 (7-17)	0.080	18 (16 -	19 (17 - 20)	0.141
				19)		
CURB65	2 (2-2)	2 (2-3)	0.362	2 (1 - 2)	2 (1 - 2)	0.572
0	0 (0%)	4 (0%)	0.759	0 (0%)	8 (9.7%)	0.475
1	2 (22.2%)	4 (11.8%)		5 (35.7%)	27 (32.9%)	
2	5 (55.6%)	19 (55.9%)		7 (50.0%)	35 (42.7%)	
3	2 (22.2%)	11 (32.4%)		2 (14.3%)	12 (14.6%)	
CCI	6 (5 – 6)	5 (5 - 6)	0.895	5 (4 – 7)	5 (4 - 6)	0.579
Dementia	0 (0%)	11 (30.6%)	0.059	1 (6.7%)	3 (3.7%)	0.495
Handgrip strength	18.3	7.9	0.017	19.2	17.9	0.614
	(8.2-27)	(5.1-12.1)		(16.2-20.7)	(11.6-23.1)	
Nursing home	1 (10.0%)	12 (33.3%)	0.240	0 (0%)	3 (3.5%)	1.000
LOS (first hospitalisation)						
Days	7.2	10.2	0.020	8.5	7.9	0.727
	(5.3; 9.03)	(8.5; 12.0)		(5.3; 11.7)	(6.7; 9.1)	

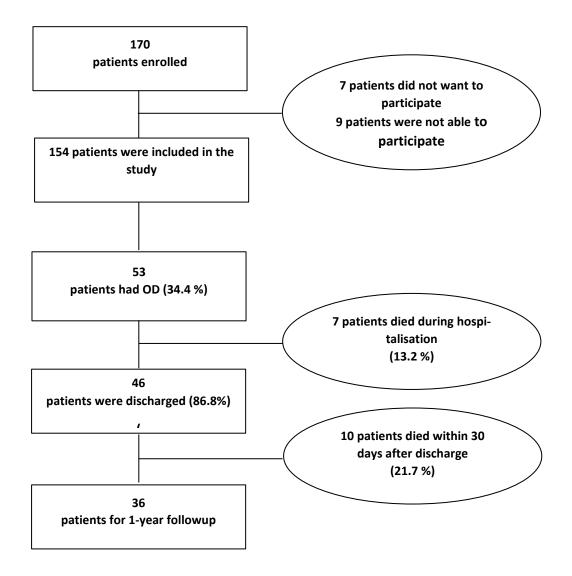
Table 10: Characteristics of patients with both CAP and OD and patients with CAP alone rehospitalised within 30 days after discharge.

Data are represented as number (%) for categorical variables and as median (IQR) for continuous variables. P-values were calculated using unpaired t-test and Fisher's exact test for the continuous and categorical variables, respectively. 3 patients in the group of patients with CAP and OD who were rehospitalised and 1 patient in group of patients with CAP and OD who were not rehospitalised had incomplete CURB65.

The reasons for rehospitalisation were lung diseases and lung-related diseases for 80% of the patients with CAP and OD versus 63% of the patients with CAP alone.

The patients with OD were followed for one year after discharge to describe the long-term consequences of OD. A group of 36 patients (72.2% male; mean age 80.9 years; SD ± 10.5) were alive 31 days after discharge and were followed (figure 4).

Figure 4: Flowchart including patients with OD



As illustrated in table 11, this group of patients was characterised by a high mean age, 27.8% of them were living in nursing homes, and 42.9% of them had COPD. Approximately 70% of the patients were moderately to severely disabled, and the mean Barthel-20 score was 13.2.

CAP 31 days after discharge.	N 26
	N=36
Gender	
Male	26 (72.2%)
Age (mean)	80.9 (±10.5)
<50	0
50-69	6
70-79	9
80+	1
Point of origin	
House/apartment	26 (72.2%)
Nursing home	10 (27.8%)
CURB65	
Confusion (yes)	15 (44.1%)
Urea (carbamide >7 Mmol/L)	24 (70.6%)
Respiratory rate >30/min	5 (15.2%)
Blood pressure <90 mmHg syst or □60 mmHg diast	63 (8.8%)
≥ 65 years	32 (88.9%)
CURB65 (mean)	2.3 (0.872)
0	0 (0%)
1	3 (9.1%)
2	21 (63.6%)
3	7 (21.2%)
4	1 (3.0%)
5	1 (3.0%)
CCI	5.5 (±1.6)
Comorbidity	5.5 (±1.0)
Dementia	7 (20.0%)
COPD	15 (42.9%)
Diabetes	3 (8.6%)
	4 (11.4%)
Hemiplegic	
CRP	95.3(82.4)
MRS	1 (2 00/)
No symptoms	1 (2.8%)
No significant disability	2 (5.6%)
Slight disability	6 (16.7%)
Moderate disability	9 (25.0%)
Moderately severe disability	11 (30.6%)
Severe disability	5 (13.9%)
Unknown	2 (5.6%)
Barthel-20	13.2 (±6.1)
Tooth status	
No dentures	10 (27.8%)
Dentures on upper jaw	6 (16.7%)
Dentures on underjaw	0 (0%)
Dentures	15 (41.7%)
Unknown	5 (13.9%)
Oral health	

Table 11: Baseline data, demographic and clinical statistic for patients with OD and CAP 31 days after discharge.

2 times per day	17 (47.2%)
1 time per day	11 (30.6%)
3-5 times per week	1 (2.8%)
1-2 times per week	0 (0%)
1 time per month	0 (0%)
Weight	65.9 kg (±15.1)
Height	169.2cm(±9.6)
BMI	22.7 (±5.2)
Waistline	101.2 (±13.0)
Circumference – upper arm	26.2 (±4.5)
Circumference – under leg	31.9 (±5.1)
Hand grip right	13.6 (±12.0)
Medication by discharge	9.1 (±4.2)
Temperature at hospitalisation	37.9 (±0.9)

Data are reported as number (%) for categorical variables, and as mean and SD (±) for continuous variable

As illustrated in table 12, 18 (50%) of the patients were rehospitalised 31-180 days after discharge, and this group of patients was characterised by a significantly higher Barthel-20 score, which indicates a higher functional level. There were insignificant differences in all of the other parameters. The group of rehospitalised patients had a lower frequency of dementia, and the patients had a 2.5-day longer LOS in the hospital.

In the period of 181-360 days, 17 (60.7%) were rehospitalised. The characteristics of these patients were a significantly higher Barthel-20 score and non-significant differences in the other parameters. The rehospitalised patients had a 1.7-day longer LOS than those who were not rehospitalised.

	31-180 days after discharge		181-360 days after discharge			
	Rehospitalised	Not rehospital-	P-	Rehospitalised	Not rehospital-	P-value
		ised	value	_	ised	
	N=18 (50.0%)	N=18 (50.0%)		N=17 (60.7%)	N=11 (39.3%)	
Age mean	80.6 (75.5; 85.7)	78.4 (72.9; 83.8)	0.528	78.5 (73.1; 84.0)	76.1	0.574
-					(68.44;83.70)	
<70 y	2 (11.1%)	4 (22.2%)	0.658	3 (17.7%)	3 (27.3%)	
≥70 y	16 (88.9%)	14 (77.8%)		14 (82.4%)	8 (72.7%)	0.653
Gender						
Male	12 (66.7%)	14 (77.8%)	0.711	11 (64.7%)	7 (63.6%)	1.000
Barthel-20	16.1 (14.1; 18.2)	10.5 (7.1; 14.0)	0.007	15.9 (13.5; 18.3)	9.7 (5.30; 14.10)	0.015
CURB65						
Mean	2.5 (2.0; 3.0)	2.1 (1.8; 2.3)	0.124	2.4 (2.0; 2.9)	2.0 (1.58; 2.42)	0.137
0	0 (0%)	0 (0%)		0 (0%)	0 (0%)	
1	1 (6.3%))	2 (11.8%)		1 (7.1%))	2 (18.2%)	
2	9 (56.3%)	12 (70.6%)		7 (50.0%)	7 (63.6%)	
3	4 (25.0%)	3 (17.7%)		6 (42.9%)	2 (18.2%)	
4	1 (6.3%)	0 (0%)		1 (7.1%)	0 (0%)	
5	1 (6.3%)	0 (0%)	0.683	0 (0%)	0 (0%)	0.707
ССІ	5.5 (4.6; 6.4)	5.5 (4.7; 6.2)	0.958	5.7 (4.6; 6.7)	4.9 (4.09; 5.73)	0.215
Dementia	2 (11.1%)	5 (29.4%)	0.228	2 (12.5%)	4 (36.4%)	0.187
Hand grip	8.5 (6.8-14.1)	13.7 (7-26)	0.632	8.5 (6.7 - 23.2)	7.3 (7.0 - 10.2)	0.991
Nursing home	5 (27.8%)	5 (27.8%)	1.000	4 (23.5%)	4 (36.4%)	0.671
MRS						
No symptoms	0 (0%)	1 (5.6%)		1 (5.9%)	0 (0%)	
No significant disability	1 (5.6%)	1 (5.6%)		1 (5.9%)	0 (0%)	
Slight disability	4 (22.2%)	2 (11.1%)		5 (29.4%)	1 (9.1%)	
Moderate disability	6 (33.3%)	3 (16.7%)		4 (23.5%)	3 (27.3%)	
Moderate severe disability	5 (27.8%)	6 (33.3%)		4 (23.5%)	3 (27.3%)	
Severe disability	1 (5.6%)	4 (22.2%)		1 (5.9%)	3 (27.3%)	
Unknown	1 (5.6%)	1 (5.6%)	0.668	1 (5.9%)	1 (9.1%)	0.654
BMI	21.6 (16.6-27.2)	25.1 (21.4-26.7)	0.186	24.5 (21.4-25.6)	26.7 (25.1-28.0)	0.232
LOS	10.7 (5.7; 14.9)	8.2 (4.8; 10.3)	0.261	9.2 (5.4; 14.9)	6.4 (4.4; 13.6)	0.541

Table 12: All causes of rehost	pitalisation within 31-180 da	ivs and 181-360 days	s after discharge for	patients with OD and CAP

Data are represented as number (%) for categorical variables and as mean and 95% CI or SD (±) for continuous variables.

P-values were calculated using unpaired t-test and Fisher's exact test for the continuous and categorical variables. Handgrip and BMI is reported with a median (IQR) and analysed with the Wilcoxon rank-sum test.

During 31-180 days after discharge, 8 (22.2%) patients died. These patients were significantly older (P=0.008), and more of them were male (P=0.076). As illustrated in table 13, there were no other significant or clinically relevant differences between the two groups.

From 181-360 days after discharge, 13 (46.4%) patients died. The patients who died in this period after discharge had a significantly higher CCI (P=0.043) and a significantly weaker handgrip (P=0.027). There were no other relevant differences between the two groups.

	31-180 days after discharge			181-360 days after discharge		
	Alive	Dead	P-	Alive	Dead	P-
			value			value
	N = 28	N = 8		N = 15	N = 13	
	(77.8%)	(22.2%)		(53.6%)	(46.4%)	
Age						
Mean	77.6	86.2	0.008	74.9	80.6	0.164
	(73.4; 81.7)	(81.2; 91.3)		(68.6; 81.3)	(89.7; 94.2)	
<70 y	6 (21.4%)	0 (0%)	0.302	4 (26.7%)	2 (15.4%)	0.655
≥70 y	22 (78.6%)	8 (100%)		11 (73.3%)	11 (86.6%)	
Gender						
Male	18 (64.3%)	8 (100%)	0.076	11 (73.3%)	7 (64.3%)	0.433
Barthel-20	13.4	12.8	0.822	15.5	13.2	0.889
	(11.0; 115.8)	(6.7; 18.8)		(10.0; 17.1)	(9.4; 17.0)	
CURB65						
Mean	2.2 (1.9; 2.5)	2.4 (1.5; 3.3)	0.744	2.1 (1.7; 2.5)	2.5 (2.0; 2.9)	0.192
0	0 (0%)	0 (0%)		0 (0%)	0 (0%)	
1	3 (12.0%)	0 (0%)		3 (21.4%))	0 (0%)	
2	14 (56.0%)	7 (87.5%)		7 (50.0%)	7 (63.6%)	
3	7 (28.0%)	0 (0%)		4 (28.6%)	4 (36.4%)	
4	1 (4.00%)	0 (0%)		0 (0%)	1 (9.1%)	
5	0 (0%)	1 (12.5%)	0.364	0 (0%)	0 (0%)	0.325
CCI	5.4 (4.7; 6.1)	5.9 (4.7; 7.0)	0.400	4.7 (4.1; 5.4)	6.1 (4.9; 7.3)	0.043
Dementia	6 (22.2%)	1 (12.5%)	1.000	2 (14.3%)	4 (30.8%)	0.385
Handgrip	8.3 (7.0-17.4)	12.1 (10.8-16.2)	0.580	17.3 (8.3-26)	6.7 (2.2-7.3)	0.039
Nursing home	8 (28.6%)	2 (25.0%)	1.000	4 (26.7%)	4 (30.8%)	1.000
MRS						
No symptoms	1 (3.6%)	0 (0%)		1 (6.7%)	0 (0%)	
No significant	1 (3.6%)	1 (12.5%)		0 (0%)	1 (7.7%)	
disability						
Slight disability	6 (21.4%)	0 (0%)		5 (33.3%)	1 (7.7%)	
Moderate disabil-	7 (25.0%)	2 (25.0%)		2 (13.3%)	5 (38.5%)	
ity						
Moderately severe	7 (25.0%)	4 (50.0%)		5 (33.3%)	2 (15.4%)	
disability						
Severe disability	4 (14.3%)	1 (12.5%)		2 (13.3%)	2 (15.4%)	
Unknown	2 (7.1%)	0 (0%)	0.615	0 (0%)	2 (15.4%)	0.143
BMI	25.1 (21.4-	17.9 (16.8-18.5)	0.225	25.1 (21.8-	21.4 (18.2-	0.764
	27.2)			27.2)	27.4)	
LOS	7.9 (4.6; 13.6)	9.8 (7.2; 12.4)	0.571	9.2 (4.8; 13.6)	6.4 (4.4; 14.9)	0.963

Table 13: All causes of mortality within 31-180 days and 181-360 days after discharge for patients with OD and CAP

Data are represented as number (%) for categorical variables and as mean and 95% CI or SD (\pm) for continuous variables. P-values were calculated using unpaired t-test and Fisher's exact test for the continuous and categorical variables. Handgrip and BMI is reported with a median (IQR) and analysed with the Wilcoxon rank-sum test.

The 1-year mortality rate for patients with both OD and CAP was 71.7% (38 patients out of 53) versus 19.8% (20 patients out of 101) for the patients in this study with only CAP.

9. DISCUSSION

The strength of these clinical studies is that the patients were consecutively included, and only a small group had to be excluded. The limitations of the studies are the relatively small sample sizes, which may have led to a type II statistical error. Another limitation is that the definition of CAP remains vague and unclear, and there is a risk that some of the patients hospitalised with aspiration pneumonia may be viewed as having a subtype of CAP ^{68,69}. In Study 1 where the IG was mobilised within 24 hours the IG was compared with a historical CG. This design is not optimal, but performing a randomised controlled clinical study in one ward is a challenge⁷⁰. The two groups were comparable in age, gender, severity of pneumonia (CURB65), CCI, time from admittance to initiation of antibiotic therapy, use of corticosteroids and they were all hospitalised with CAP in the same ward; however, the representation of COPD was higher in the CG than in the IG.

Study 1 shows a clear tendency towards a shorter LOS (by 1.5 days) after an early, progressive, physiotherapeutic mobilisation programme compared with standard care of patients with CAP.

A randomised controlled study conducted in the US has reported a reduced LOS by 1.1 days for patients with CAP after an EM programme ³⁸. Our findings are in accordance with this report, and they add to the sparse knowledge of the positive effect of early mobilisation on the LOS for patients with CAP.

LOS is related to the systematically evaluated basic mobility status of patients throughout their admittance, and there is an association between the CURB65 score and the LOS for both groups. Of interest, patients with a CURB65 score of 2 appear to benefit the most from EM, as indicated by a reduction in the LOS of 2.67 days compared with the CG. This finding appears to correspond to the findings for patients in the EM group with a Pneumonia Severity Index score of 3 in a study by Mundy et al. ³⁸. However, this comparison should be interpreted with caution, owing to the different score systems used. Nonetheless, it seems that the patients who benefit the most from EM are those classified with a low to medium severity index. The study also indicated that patients with a low prehospital NMS tends to have a longer LOS than those with a higher functional level.

Another explanation of the reduction of the LOS in the present study may be that the physiotherapist in cooperation with the patient sets goals for the treatment. A review of the literature discussing goal-setting indicates that some studies demonstrate positive effects of goal-setting, although other studies are methodologically weak and have shown no evidence of the effect of goal-setting ⁷¹. However, the design of this study makes it impossible to separate the effect of EM from the effect of goal-setting.

The mortality during hospitalisation in a study by Mundy et al. ³⁸ was lower in the IG than in the CG; however, as in the present study, no significant difference was seen for mortality during hospitalisation or 30 days after admission.

The frequency of rehospitalisation was higher in the IG, even though it was not significant, and the difference was primarily due to patients being rehospitalised for diseases not related to the lungs. Study II documents the prevalence of OD in patients with CAP and OD was observed in 37.1% of the patients over 70 years. This study found that the risk factors for OD and CAP are increased age, severe CAP, dementia, poor dental status and oral hygiene, poor level of mobility before hospitalisation, decreased hand grip strength, and living in a nursing home. Other studies have also documented this link between people living in a nursing home and OD and between independent people and OD ⁷². It is well known that frailty correlates with vulnerability, poor outcomes, and death ^{73,74}, as confirmed by the results of this study. In this study, frailty was measured by the following parameters: functional capacity, handgrip strength, dementia, and admission from a nursing home. There are some available frailty tools, such as the Clinical Frailty Scale, Frailty Index, Comprehensive Geriatric Assessment, Vulnerable Elders Survey-13, Groningen Frailty Indicator, and Geriatric 8 ⁷⁵. However, multiple studies have found that these tools are not suitable for routine use at the bedside. The diagnostic value of these instruments is poor, and their clinical value may be weak ^{76,77}.

The videofluoroscopy (VFES) and fiberoptic endoscopic evaluation of swallowing (FEES) are objective assessments of the swallow function. In our clinical setting, these were not possible, so we used V-VST because studies have shown a strong correlation between videofluoroscopy and V-VST ⁶⁴ and because an OD-screening protocol with a standardised bedside screening decreases the risk of CAP. V-VST uses a decrease in the oxygen saturation \geq 3% to detect silent aspiration. A smaller fall in oxygen saturation is not a reliable indicator of silent aspiration⁷⁸. Nonetheless, a bedside test combined with pulse oximetry is recommended ⁷⁹. Pharyngeal residue is one of the signs of swallowing disorders, and although it can be visualised by videofluoroscopy, it is impossible to visualise in bedside screening. V-VST is recommended in more reviews ^{79,80} but has not yet been validated in Denmark. Silent aspiration is prevalent in patients with pneumonia, but it is detectable only with VFES or FEES. OD may be underestimated because it was assessed with a bedside test, not with VFES or FEES.

The group of patients with both OD and CAP has a higher rehospitalisation rate than the group of patients with CAP alone. It is well known that patients with OD have a higher frequency of rehospitalisation ⁸¹. Patients with both OD and CAP who are rehospitalised compared with those who are not readmitted have a significantly stronger handgrip (P=0.004). The group of patients rehospitalised with both OD and CAP compared with the rehospitalised patients with CAP alone is characterised by non-significant differences of decreased age, higher Barthel-20 score, less dementia and origins from nursing homes. There may be multiple explanations for these findings: 1) patients living in their own residence may have more difficulty in changing their eating habits than those living in nursing homes and 2) doctor delay, which in this context implies that doctors and nurses do not hospitalise elderly people with CAP alone but instead let them stay in their nursing homes during treatment.

Patients with both OD and CAP had significantly increased in-hospital, 30-day and 1-year mortality rates compared with those of patients with CAP alone. A Danish multicentre study including elderly citizens admitted with CAP ¹⁴ has reported an in-hospital mortality of 11.5%. In our study, the group with both CAP and OD showed an in-hospital mortality of 13.5% versus a non-OD value of 0%. The multicentre study has reported a 30-day mortality of 8.6%. The present study had a 30-day mortality for patients with both CAP and OD of 19.2% versus a value for non-OD patients of 2.0%. The one-year mortality is high in patients with OD ^{82,83}, and this study confirms these results with a 1-year mortality of 71.7% for patients with both CAP and OD.

The relatively high prevalence of OD underlines the necessity of awareness about OD in patients hospitalised with CAP and indicates the need for systematic screening for OD, as is also recommended in national and international guidelines and recommendations ^{47,84}.

10. CONCLUSION

An EM programme compared with standard care reduces the LOS for patients with CAP. Patients with CAP who are mobilised within 24 hours after hospitalisation are discharged 1.5 days earlier than those not mobilised within 24 hours. We found no significant difference in the in-hospital and short-term mortality rates or in the short-term pulmonary-related rehospitalisation rate between the two groups.

More than one-third of all patients hospitalised with CAP had OD. Compared with the patients with CAP alone, the patients with both CAP and OD showed significant differences in the parameters related to frailty. This study demonstrates that patients with both OD and CAP have a high frequency of rehospitalisation and that the long-term mortality is very high (71.7%) for patients hospitalised with both CAP and OD.

The results of the studies suggest that progressive EM shall be part of the standard treatment programme offered to patients who are hospitalised with CAP and that a systematic investigation of OD in elderly patients with CAP shall be implemented in the guidelines.

11. PERSPECTIVES

These studies have made it clear that it is appropriate to expand the interdisciplinary approach towards the treatment of CAP with a systematic intervention by physiotherapists and occupational therapists. It has been confirmed that early mobilisation within 24 hours can reduce the LOS, especially in patients with a relatively high level of functioning prior to admission and with a moderately severe CAP. This group of patients in particular should be systematically mobilised as soon as possible after hospitalisation and with an individual approach. Because the majority of patients in Denmark are admitted to the emergency room, mobilisation should occur even there. It is relevant to study whether the effects of early mobilisation may be even greater, for example, within 12 hours after hospitalisation.

In Denmark, there has been no focus on the systematic screening for OD in patients with CAP. This study shows that approximately one out of three patients with CAP has OD, and those with OD are often frail and their LOS is 2 days longer than that for patients with CAP alone. This knowledge provides a basis for a systematic screening for OD very early after admission to uncover whether such a protocol may reduce hospitalisation time and the number of readmissions. At the North Denmark Regional Hospital, in the spring of 2017, we will launch a research project wherein, for 6 months, we will perform OD screening in all patients admitted in the emergency room. We expect to include 5,500 patients, and with this project, we will be able to predict the prevalence in the population and in subpopulations, e.g., patients with COPD, diabetes or alcoholism. That study should also demonstrate the importance of the awareness of OD in an acute hospital. Another initiative is a video about the signs of OD and the interventions to reduce the consequences of OD. This video is an obligatory introduction to all staff with patient contact. A multidisciplinary focus on OD is important, and in North Denmark Regional Hospital, the kitchen staff is continually developing food for this group of patients on the basis of the contributions of dieticians as well as nurses, physiotherapists and doctors. The study of OD has attracted attention from other hospitals, but, especially from municipalities where there is awareness of the relation between OD and a high risk of CAP and hospital admissions. In Denmark the municipalities are financing a part of the costs of the hospitalisations. In spring 2017 we will present the total financial burden in patients with OD and CAP compared to patients with CAP. The calculation will include the total costs calculated for 12 months prior to admission to 3 months after discharge.

FEES has been implemented as a routine assessment in critically ill patients at risk to develop aspiration following extubation. In 2017 we plan to implement FEES as a possible assessment for e.g. patients with signs of silent aspiration.

In general, the awareness of OD in patients other than neurological patients has increased significantly in Denmark during the past 2-3 years. In autumn 2016, the Danish Society of Dysphagia was founded. The board represents a multidisciplinary and intersectoral group, and the undersigned was selected as chairman of the society.

The results of this study support the conclusion that systematic early mobilisation and systematic screening for OD in elderly patients with CAP can optimise treatment outcomes. Because only limited resources would be required in conjunction with other treatments, it would be appropriate to include early mobilisation and screening for OD in the guide-lines for CAP.

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