

# Disease Severity, Volume Status, Cognition and Delirium in Older Patients in the Emergency Department, a Pilot Study

✉ Jacinta Anna Lucke<sup>1</sup>, ✉ Eva Lubbers<sup>1</sup>, ✉ Karlijn van Stralen<sup>2</sup>, ✉ Bas de Groot<sup>3</sup>

<sup>1</sup>Spaarne Gasthuis Hospital, Clinic of Emergency Medicine, Haarlem, Netherlands

<sup>2</sup>Spaarne Gasthuis Hospital, Clinic of Science, Haarlem, Netherlands

<sup>3</sup>Radboud University Medical Center, Department of Emergency Medicine, Nijmegen, Netherlands

## Abstract

**Objective:** Cognitive impairment and delirium occur frequently in older emergency department (ED) patients and could be caused by low volume status and acute disease severity. Unfortunately, frail older patients can be difficult to include in clinical trials due to problems with informed consent and the burden of participation. To assess the feasibility and acceptability of obtaining informed consent, cognitive impairment, frailty, volume status and disease severity of older ED patients. Secondly, to assess disease severity and volume status in the patients with or without cognitive impairment and delirium.

**Materials and Methods:** A prospective study including ED patients  $\geq 70$  years who were hospitalized with a suspected infection or hip fracture was conducted. We assessed the Modified Early Warning score (MEWS; acute disease severity) and inferior vena cava (IVC) collapsibility with ultrasound; low volume status. Primary outcomes were the feasibility of obtaining informed consent and the experienced burden. Secondary outcomes were cognitive impairment in the ED [4 'A's test (4AT) score] and delirium (Delirium Observation Screening score) on the ward.

**Results:** Health-care professionals found the study feasible, and all 28 included patients experienced no burden. Eighteen of 28 (64%) patients had  $>50\%$  vena cava inferior-collapsibility, despite fluids being hardly administered. Patients with a 4AT  $\geq 1$  had higher MEWS. Nine of 28 (32%) patients developed delirium during hospitalization, of whom 56% had 4AT  $\geq 1$  and all had IVC  $< 2.1$  cm.

**Conclusion:** The study was feasible and acceptable for health care professionals and older ED patients. Acute disease severity in these patients was associated with impaired cognition, which was highly prevalent in those who developed delirium during hospitalization. Low volume status was also observed in these patients.

**Keywords:** Fluid resuscitation, geriatrics, geriatric emergency medicine, cognitive function, delirium

## Introduction

Cognitive impairment is a common problem in older emergency department (ED) patients. It may be caused by dementia, delirium, and primary neurologic disorders, but could also be a subtle sign of occult hypoperfusion of the brain [1,2]. For this reason, cognitive impairment might be used as an endpoint in fluid resuscitation. If this is the case, improvement of brain perfusion, i.e., by improving cardiac output with fluid

resuscitation, should then lead to improvement of cognitive status.

This relationship between the heart and brain has been studied in long-term settings [3], but not in the acute ED setting. Especially in older ED patients, recognition of hypoperfusion is notoriously difficult because of non-specific disease presentation and different interpretation of vital signs; i.e., a systolic blood pressure of 120 mmHg is normal in younger



**Address for Correspondence:** Jacinta Anna Lucke, MD, PHD, Spaarne Gasthuis Hospital, Clinic of Emergency Medicine, Haarlem, Netherlands

**E-mail:** jacintalucke@gmail.com **ORCID-ID:** orcid.org/0000-0002-0098-0833

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patients but may indicate hypotension in older patients, which is often not recognized as such [4]. The impaired recognition of hypoperfusion in addition to the fear of fluid overload in, for example, older patients with sepsis, may lead to delayed and inappropriate fluid resuscitation in older patients [5] who are already more prone to dehydration because of an impaired thirst mechanism [6]. The use of cognition as an endpoint for resuscitation might improve both short-term outcomes by preventing further hemodynamic deterioration and may also prevent the development of delirium and its sequelae during hospitalization.

However, testing this may be difficult because older patients are frequently excluded from large RCTs because of their multimorbidity, difficulty obtaining informed consent, and burden of participation [7,8]. Assessment of informed consent is even more difficult in older ED patients with time-sensitive medical conditions like sepsis or severe trauma, who often experience hypoperfusion. In addition, disease severity, volume, and cognitive status should be assessed before ED treatment, potentially causing unethical time delays. Previous studies have shown difficulties understanding consent forms, the complexity of the consent process, limited accessibility of information, and concerns about cognitive capacity, underscoring the ethical need to balance research burden with potential benefits.

Therefore, the aim of this pilot study was twofold. First, we aimed to assess the feasibility and acceptability (for patients and professionals) of obtaining informed consent, as well as evaluating cognitive impairment, frailty, volume status, and disease severity of older ED patients who were hospitalized with a suspected infection or hip fracture within a 20-minute timeframe. Secondly, we aimed to assess disease severity and volume status in the aforementioned patients with or without cognitive impairment and delirium.

## Materials and Methods

### Study Design and Setting

This was a single-centre prospective observational pilot study, performed during a two-week period in January 2023 in the ED of Spaarne Gasthuis Hospital, which has an annual census of approximately 45,000 visits. The study was evaluated by the medical ethical committee of the Amsterdam University Medical Center, who decided that it did not fall under the “Medical Research in Humans Act (approval number: 2022.0075, date: 17.06.2022)”. Oral and written informed consent was obtained.

### Participants

ED patients aged 70 years and older who were hospitalized with either a suspected infection but no clinically apparent signs of acute organ failure, and those with hip fractures, were included. In the patients with suspected infection, we expected abnormal

vital signs, elevated Early Warning scores (EWSs), and low volume status. The patients with a hip fracture served as a control group in which we expected normal vital signs and EWS, and normal volume status. In both groups impaired cognition and frailty were expected to be prevalent. Patients were recruited and included between 16/1/2023 and 27/1/2023.

Patients triaged as most urgent (category red/U0), known to have any form of dementia or cognitive decline, requiring acute medical or surgical interventions (<1 hour of ED arrival), having with fluid overload, a known LVEF <25%, receiving more than 250 mL of fluid in the ambulance, having meningitis or other suspected CNS infection and those who were excluded.

### Data Collection

During the inclusion period, a physician researcher was available during the daytime shift (10:00-19:00 h) to monitor announcements from the ambulance about potential patients. The physician researcher obtained informed consent and collected the data described below in a structured case report form.

Demographic characteristics, medication use, urgency, vital parameters, Modified EWS scores (MEWS) [9], and predisposition-infection-response-organ dysfunction (PIRO) [10] scores were measured as indicators of disease severity. Results of routine blood tests were registered. Frailty was assessed with the Clinical Frailty score (CFS) [11] and morbidity with the Charlson Comorbidity score (CCI) [12]. Patients and healthcare staff completed questionnaires to assess implementation feasibility, acceptability, and perceived burden.

### Outcome Measures

The primary outcomes were the feasibility, quantified by the number (%) of patients from whom informed consent was obtained and scores were assessed within 20 minutes, as well as the number (%) of healthcare workers who found the implementation of the study feasible. Feasibility was defined as at least 75% consent for participation by patients and at least 75% approval by healthcare staff. The secondary outcomes were number (%) of patients with low volume status, [inferior vena cava (IVC) <2.1 cm and/or >50% collapsibility] [13], cognitive impairment [4A's test alertness, AMT4, attention, acute change (4AT) score  $\geq 2$ ] [14], and delirium on the ward [Delirium Observation Scale (DOS)] [15].

### Sample Size

This pilot study was not powered to find significant differences in cognitive status and delirium incidence between groups but it should be able to show whether there are potential differences.

### Statistical Analysis

Baseline characteristics were reported as mean standard deviation (SD) for normally distributed data and as median interquartile range (IQR) when skewed. Categorical data were

reported as number (%). Differences between groups (suspected infection vs. hip fracture; 4AT =0 vs. 4AT  $\geq$ 1; delirium vs. no delirium on ward) were tested using chi-square tests, Mann-Whitney U test, and/or independent t-test, as appropriate.  $P < 0.05$  was considered significant. IBM SPSS Statistics package version 24 (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp. USA) was used for statistical analyses.

## Results

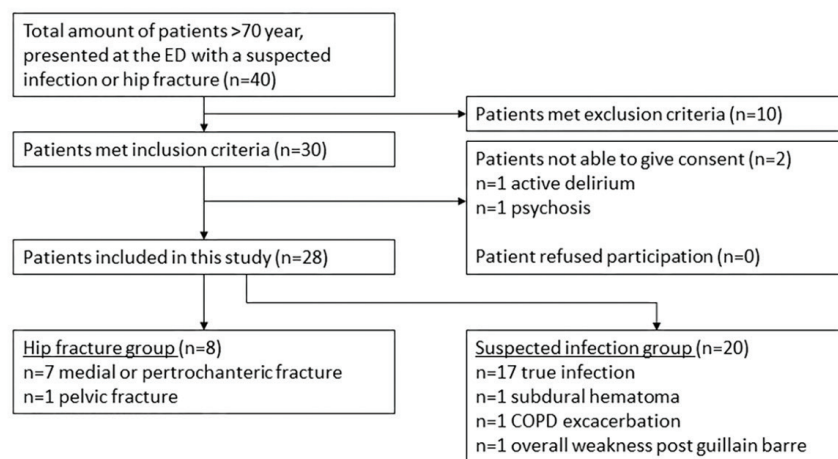
We included 28 patients (Figure 1). Patients in the infection group were younger and more often male. Furthermore, they more frequently had a high MEWS score (MEWS score  $>3$  points,  $n=7$  (35%), in the infection group versus 0 in the hip fracture group). The Charlson Comorbidity score had a mean of 7 (SD 2.2) in the infection group and 4.9 (SD 1.2) in the hip fracture group. Both groups were equally frail, with a median CFS of 4 (IQR 3.3-5.0) in the infection group, and 5 (IQR 4.0-5.0) in the hip fracture group (Table 1). Length of stay in the ED did not differ between

groups. Most patients were admitted to the hospital (80% vs. 87.5%,  $p=0.64$ ). Patients with suspected infection received more antibiotics (35% vs. 0%,  $p=0.05$ ), while those with hip fractures received more opiates (5% vs. 50%,  $p=0.01$ ).

Table 2 shows that bedside time for inclusion was similar between groups and were all within 20 minutes. All approached patients provided informed consent and were not subjected to any undue hardship. All healthcare professionals considered the study feasible and reported no interference with patient care (Supplementary Table 1).

In Table 3, it is shown that MEWS and PIRO score tended to be higher in patients with a 4AT  $\geq$ 1, i.e. impaired cognition, while IVC collapsibility and diameter and urea/creatinine were similar in patients with normal and impaired cognition.

Finally, Table 4 shows that delirium during hospitalization occurs more frequently in patients who were experiencing frailty (CFS  $\geq$ 5) and had impaired cognition in the ED (4AT  $\geq$ 1).



**Figure 1.** Patient flow through study

COPD: Chronic obstructive pulmonary disease, ED: Emergency department

**Table 1. Patient characteristics**

|                                    | Suspected infection (n=20) | Hip fracture (n=8) |
|------------------------------------|----------------------------|--------------------|
| <b>Demographic data</b>            |                            |                    |
| Age, mean (SD)                     | 82.2 (8.1)                 | 84.0 (5.1)         |
| Gender, male (%)                   | 14 (70)                    | 4 (50)             |
| Nursing home resident (%)          | 0 (0)                      | 1 (12.5)           |
| <b>Clinical features</b>           |                            |                    |
| Triage code                        |                            |                    |
| U1 (%)                             | 2 (10)                     | 0 (0)              |
| U2 (%)                             | 4 (20)                     | 7 (87.5)           |
| U3 (%)                             | 14 (70)                    | 1 (12.5)           |
| <b>Vital parameters, mean (SD)</b> |                            |                    |
| MAP                                | 99 (15.9)                  | 100 (16.6)         |
| Temperature                        | 37.2 (1.1)                 | 36.2 (0.5)         |
| Heart rate                         | 84 (19.4)                  | 75 (13.4)          |

| Table 1. Continued                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                            |                    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------|--------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Suspected infection (n=20) | Hip fracture (n=8) |
| Respiratory rate                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 19 (6.5)                   | 15 (1.4)           |
| <b>Disease severity</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                            |                    |
| MEWS score                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                            |                    |
| score 0-2 (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 13 (65)                    | 8 (100)            |
| score 3 or higher (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 7 (35)                     | 0 (0)              |
| MEWS score, median (IQR)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 2 (0-3)                    | 0 (0-1)            |
| PIRO score, median (IQR)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 5 (2.3-8.8)                | 2 (1-2)            |
| PI score, median (IQR)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 4 (2-5.8)                  | 2 (1-2)            |
| RO score, median (IQR)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 2 (0-3)                    | 0 (0-0)            |
| IVC diameter in cm before fluid, mean (95% CI)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 1.61 (1.30-1.92)           | 1.28 (0.95-1.60)   |
| Collapsibility >50% before fluid, number (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 12 (66.7)                  | 6 (75)             |
| IVC diameter in cm after fluid, mean (95% CI)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 1.64 (1.33-1.95)           | 1.29 (0.91-1.67)   |
| Collapsibility >50% after fluid, number (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 12 (63.2)                  | 5 (71.4)           |
| <b>Geriatric characteristics</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                            |                    |
| Charlston comorbidity score, mean (SD)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 7 (2.2)                    | 4.9 (1.2)          |
| Clinical frailty score, median (IQR)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 4 (3.3-5.0)                | 5 (4.0-5.0)        |
| 4AT score before fluid, mean (95% CI)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 0.95 (0.18-1.72)           | 0.13 (0-0.42)      |
| 4AT score after fluid, mean (95% CI)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 0.90 (0.22-1.58)           | 0.13 (0-0.42)      |
| DOS score at time of admission, mean (95% CI)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 1.1 (0.4-1.9)              | 0.1 (0-0.5)        |
| Delirium during admission, number (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 5 (31.3)                   | 4 (57.1)           |
| <b>Medication use</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                            |                    |
| Antihypertensives (n,%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 17 (85)                    | 5 (62.5)           |
| Diuretics (n,%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 6 (30)                     | 1 (12.5)           |
| Antibiotics (n,%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 9 (45)                     | 0 (0)              |
| Number of medications, mean (SD)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 11 (5.4)                   | 6 (3.0)            |
| <b>Laboratory results</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                            |                    |
| Leukocytes, mean (SD)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 11.1 (3.7)                 | 9.6 (3.1)          |
| Sodium, mean (SD)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 136 (4.6)                  | 136 (4.4)          |
| Creat, median (IQR)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 101 (72-137)               | 73 (68-101)        |
| CRP, mean (SD)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 80 (86.6)                  | 18 (30.2)          |
| <b>ED treatment</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                            |                    |
| Fluid in liters, mean (95% CI)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0.26 (0.13-0.39)           | 0.18 (0-0.35)      |
| Medication                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                            |                    |
| Opiate, number (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 1 (5)                      | 4 (50)             |
| Paracetamol, number (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 3 (15)                     | 3 (37.5)           |
| NSAID, number (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 1 (5)                      | 0 (0)              |
| Furosemide, number (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 1 (5)                      | 0 (0)              |
| Antibiotics, number (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 7 (35)                     | 0 (0)              |
| Corticosteroids, number (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 1 (5)                      | 0 (0)              |
| None, number (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 12 (60)                    | 3 (37.5)           |
| Missing data: temperature n=2 (hip fracture), respiratory rate n=5 (infection) and n=6 (hip fracture), leukocytes n=1 (infection), CRP n=1 (infection), sodium n=2 (infection) and n=1 (hip fracture), creat n=1 (infection) and n=1 (hip fracture), c DOS score n=1 (infection) and n=1 (hip fracture), delirium during admission n=4 (infection) n=1 (hip fracture), missing data first ultrasound n=1 (infection), first collapsibility n=2 (infection), second ultrasound n=1 (infection) and n=1 (hip fracture), second collapsibility n=1 (infection) and n=1 (hip fracture). |                            |                    |
| n: number, SD: Standard deviation, IQR: Interquartile range, CI: Confidence interval, MEWS: Modified Early Warning score, PIRO: Predisposition infection response organ dysfunction CRP: C-reactive protein, MAP: Mean arterial pressure, NSAID: Non-steroidal anti-inflammatory drug, IVC: Inferior vena cava, 4AT: 4A's test (alertness, AMT4, attention, acute change) DOS: Delirium Observation Scale, ED: Emergency department                                                                                                                                                 |                            |                    |

**Table 2. Primary outcome-feasibility**

|                                             | Suspected infection (n=20) | Hip fracture (n=8) | p    |
|---------------------------------------------|----------------------------|--------------------|------|
| Minutes at the patient's bedside, mean (SD) | 17 (2.3)                   | 18 (2.1)           | 0.60 |
| Participation was experienced as a burden   | 0 (0)                      | 0 (0)              | NA   |
| Opinion healthcare staff: nurse             | n=13                       | n=7                |      |
| Feasibility, yes                            | 13 (100)                   | 7 (100)            | NA   |
| Interfere with acute care, no               | 13 (100)                   | 7 (100)            | NA   |
| Opinion healthcare staff: doctor            | n=15                       | n=3                |      |
| Feasibility, yes                            | 15 (100)                   | 3 (100)            | NA   |
| Interfere with acute care, no               | 15 (100)                   | 3 (100)            | NA   |

Minutes at the patient's bedside is the spend at the patients bedside to gain informed consent and perform all study measurements. P value calculated using independent t test and chi-square test. Missing data nurses n=8, missing data doctor n=10.

n: number, SD: Standard deviation

**Table 3. 4AT during ED stay and signs of acute disease**

|                                        | 4AT = 0<br>(total n=19) | 4AT = >1<br>(total n=9) | p    |
|----------------------------------------|-------------------------|-------------------------|------|
| IVC collapsibility ≤50% (n,%)          | 6 (33.3)                | 3 (37.5)                | 0.84 |
| IVC collapsibility >50% (n,%)          | 12 (66.7)               | 5 (62.5)                |      |
| IVC >2.1 cm (n,%)                      | 2 (11.1)                | 1 (12.5)                | 0.92 |
| IVC ≤2.1cm (n,%)                       | 16 (88.9)               | 7 (87.5)                |      |
| MEWS 0-2 (n,%)                         | 16 (84.2)               | 5 (55.6)                | 0.10 |
| MEWS ≥ 3 (n,%)                         | 3 (15.8)                | 4 (44.4)                |      |
| PIRO (mean, SD)                        | 4.05 (3.58)             | 6.44 (3.4)              | 0.11 |
| Ureum/creatinine ratio (mean, SD)      | 0.89 (0.03)             | 0.10 (0.04)             | 0.53 |
| SBP/HR ratio (shock index) (mean, SD)  | 1.82 (0.56)             | 2.05 (0.31)             | 0.27 |
| Saturation/resp. rate ratio (mean, SD) | 5.89 (1.6)              | 5.37 (1.96)             | 0.56 |

IVC collapsibility missing n=2, ureum/creatinine ratio missing =15, saturation/respiration missing =11. P-values are calculated using chi-square and t-test.

IVC: Inferior vena cava, 4AT: 4A's test (alertness, AMT4, attention, acute change), MEWS: Modified Early Warning score, SBP: Systolic blood pressure, HR: Heart rate, resp. rate: Respiratory rate, SD: Standard deviation, PIRO: Predisposition infection response organ

**Table 4. Delirium during hospitalization and geriatric factors**

|                                        | No delirium during<br>hospitalisation<br>(total n=14) | Delirium during<br>hospitalisation<br>(total n=9) | p     |
|----------------------------------------|-------------------------------------------------------|---------------------------------------------------|-------|
| IVC collapsibility <50% (n,%)          | 5 (38.5)                                              | 2 (25.0)                                          | 0.53  |
| IVC collapsibility >50% (n,%)          | 8 (61.5)                                              | 6 (75.0)                                          |       |
| IVC >2.1 cm (n,%)                      | 3 (23.1)                                              | 0 (0)                                             | 0.14  |
| IVC <2.1cm (n,%)                       | 10 (76.9)                                             | 8 (100.0)                                         |       |
| CFS <4 (n,%)                           | 11 (78.6)                                             | 2 (22.2)                                          | 0.008 |
| CFS ≥5 (n,%)                           | 3 (21.4)                                              | 7 (77.8)                                          |       |
| 4AT ≥1 (n,%)                           | 3 (21.4)                                              | 5 (55.6)                                          | 0.094 |
| Charlston Comorbidity Index (mean, SD) | 6.86 (2.35)                                           | 5.33 (1.41)                                       | 0.096 |
| DOS score at admission (mean, SD)      | 0.43 (0.94)                                           | 1.88 (1.89)                                       | 0.025 |

Patients with missing delirium scores (n=5) were not included in this table. P-values are calculated using chi-square and t-test. Missing DOS score n=1.

IVC: Inferior vena cava, 4AT= 4A's test (alertness, AMT4, attention, acute change), CFS: Clinical Frailty Scale, DOS: Delirium Observation Scale, n: number, SD: Standard deviation



## Discussion

This study shows that it is feasible and acceptable for health care professionals to obtain informed consent and assess the 4AT, CFS, IVC, vital signs, and disease severity scores of older ED patients with suspected infection or a hip fracture before ED treatment within 20 min. In addition, our preliminary results suggest that in ED patients with elevated MEWS or PIRO as measures of acute disease severity, signs of cognitive impairment and delirium (4AT) are more frequently present, which are subsequently associated with the development of delirium during hospitalization, as is frailty (high CFS). Elevated MEWS or PIRO per se is not associated with the development of delirium during hospitalization. Finally, the majority of ED patients with suspected infection but also with a hip fracture have a small IVC or elevated collapsibility, suggesting low volume status. However, this was not associated with 4AT, although all patients who developed delirium during hospitalization had a small IVC with a tendency for higher collapsibility in the ED.

Obtaining informed consent in acute patients can be difficult, especially in frail older people. The literature shows problems due to the accessibility of information, including font size and reading level of patient information leaflets, difficulties in hearing verbal information understanding the project, and loss of cognitive agility or confidence to make an autonomous decision [7]. In a review published by Gobat et al. [16], different papers investigating consent models in acute care research are described and show prospective informed consent, third party consent, and deferred consent as possible options. In studies in patients with acute myocardial infarction, only 19-28% of patients read the information sheet, and a mismatch between the educational level and the level required to comprehend the information sheet existed. This review also shows that patients in the ED might have negative views about third-party consent. In low-risk studies, patients found deferred consent acceptable, but as risk increased, patients preferred to make the decision themselves or involve a family member. In a review performed by Southerland et al. [17] it was shown that in older patients in the ED who participated in a study requiring informed consent, it was assessed in only 4.3% whether patients had the capacity to make decisions and 5.1% used a legal representative. In acute care settings, it has been shown that it is possible to obtain prospective informed consent in adults; we now find that this also applies to older adults in the ED. Prusaczyk et al. [18]. Describe the challenges and opportunities of performing research in patients with cognitive impairments and show that it is also unethical not to perform research in this group; they are a large and growing population, with specific problems that also need to be investigated. While older patients, especially those with lower formal learning, show less comprehension of consent information, they tend to make the same decision

as younger patients [19]. One of the possible solutions to gain informed consent is proper timing, a factor we also found to be significant in our study. During the wait time in the ED, patients had no problem participating in the study. Doctors and nurses agreed that the study did not interfere with their work, showing that it is possible to perform this study on a larger scale. While it would be best to give patients time to extensively review all options, the setup requires the study to be performed in the ED, and we show that it is possible to obtain informed consent. However, screening for competency using a formal tool might be a future step in the research process if we perform a larger study.

The association between elevated MEWS and PIRO and 4AT are in line with findings of a previous study showing that vital signs are associated with impaired cognition [1]. In contrast to what we expected, low volume status was not associated with signs of impaired cognition, which may partially be explained as by the previous observations that especially oxygen saturation and respiratory rate are associated with impaired cognition, while hemodynamic parameters like blood pressure and heart rate have a much weaker association. Since IVC is mainly considered a hemodynamic parameter, it may not be surprising that we did not find a strong association with cognition in the ED.

The high frequency of older patients with a collapsing IVC and the scarce fluid administration correspond with findings of a previous study suggesting insufficient fluid resuscitation in older patients with a suspected infection, and suggests that more fluids may need to be administered. Interestingly, all the patients who developed delirium during hospitalization had a small IVC. It would be interesting to investigate if increasing the IVC with administration of more fluids may have the potential to reduce delirium incidence on the ward [20]. The amount of fluids administered in patients with suspected infection and hip fracture in this study was too small to draw conclusions about the immediate impact of fluids on cognition and development of delirium.

The high frequency of low volume status in older ED patients with a hip fracture was an unexpected finding in the present study, even though these patients did not have a high MEWS score. Although we do not have an explanation for this observation, it would be interesting to investigate in future studies whether the low volume status contributed to the fall in this patient group. In addition, these patients may also benefit from fluid administration. Larger studies could help to assess the influence of possible confounders on volume status, such as the use of medication.

This study has several limitations. It is a small, single center study, limiting external validity. Not all healthcare providers could be interviewed due to other clinical care obligations or

shift-changes, possibly introducing selection bias. However, 64% of doctors could be interviewed and 71% of the nurses could be interviewed. Not all patients had family members with them in the ED, so the reliability of using the 4AT score to assess cognitive fluctuations over the past two weeks varied.

## Conclusion

In the ED, obtaining informed consent and assessing cognitive impairment, frailty, disease severity, and volume status in older acutely ill or injured patients before treatment is feasible and acceptable. The present study shows a high frequency of low volume status and delirium in older ED patients with a suspected infection and hip fracture. The complex interplay among acute disease severity, cognitive impairment, frailty, and the development of delirium warrants larger future studies investigating the impact of early fluid resuscitation on cognitive function and delirium incidence in this patient group.

## Ethics

**Ethics Committee Approval:** The study was evaluated by the medical ethical committee of the Amsterdam University Medical Center, who decided that it did not fall under the “Medical Research in Humans Act (approval number: 2022.0075, date: 17.06.2022)”.

**Informed Consent:** Oral and written informed consent was obtained.

## Footnotes

### Authorship Contributions

Concept: B.d.G., Design: J.A.L., B.d.G., Data Collection or Processing: E.L., Analysis or Interpretation: J.A.L., E.L., K.v.S., B.d.G., Literature Search: J.A.L., E.L., Writing: J.A.L., E.L., B.d.G.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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| Supplementary Table 1. Responses to questionnaires from healthcare personnel regarding feasibility |                      |                       |                       |                        |                                                                                                                                                      |                                                                                                                                                                                           |
|----------------------------------------------------------------------------------------------------|----------------------|-----------------------|-----------------------|------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                    | Feasible?<br>(nurse) | Feasible?<br>(doctor) | Interfere?<br>(nurse) | Interfere?<br>(doctor) | Suggestions or comments*<br>(nurse)                                                                                                                  | Suggestions or comments* (doctor)                                                                                                                                                         |
| Patient 1                                                                                          | Yes                  | Yes                   | No                    | No                     | As you already do: be aware of when you can step into the patient room, please in consultation with nurse and/or when nurse is ready                 | Use time when patient is waiting for results, this feels like extra attention for the patient                                                                                             |
| Patient 2                                                                                          | Yes                  | Yes                   | No                    | No                     | Went fine                                                                                                                                            | Can imagine that during a very busy shift, your examination could possibly be delayed if the doctor cannot get to the patient because investigator is busy. however, was not the case now |
| Patient 3                                                                                          | Yes                  | Missing               | No                    | Missing                | None                                                                                                                                                 | Missing                                                                                                                                                                                   |
| Patient 4                                                                                          | Yes                  | Yes                   | No                    | No                     | None                                                                                                                                                 | Coordinate with the treating physician how long you think you will need as a researcher                                                                                                   |
| Patient 5                                                                                          | Yes                  | Missing               | No                    | Missing                | You can tell nurse in advance how long you expect to be with the patient, take your ultrasound machine into the room only after patient's permission | Missing                                                                                                                                                                                   |
| Patient 6                                                                                          | Yes                  | Yes                   | No                    | No                     | You checked carefully whether there was place to go into the patient's room                                                                          | Fine I didn't see you                                                                                                                                                                     |
| Patient 7                                                                                          | Yes                  | Yes                   | No                    | No                     | None                                                                                                                                                 | None                                                                                                                                                                                      |
| Patient 8                                                                                          | Yes                  | Yes                   | No                    | No                     | Went fine                                                                                                                                            | May consider wearing a white coat as a researcher, patient may experience the research as even more confidential                                                                          |
| Patient 9                                                                                          | Yes                  | Missing               | No                    | Missing                | None                                                                                                                                                 | Missing                                                                                                                                                                                   |
| Patient 10                                                                                         | Yes                  | Yes                   | No                    | No                     | None                                                                                                                                                 | None                                                                                                                                                                                      |
| Patient 11                                                                                         | Missing              | Yes                   | Missing               | No                     | Missing                                                                                                                                              | None, just went smoothly                                                                                                                                                                  |
| Patient 12                                                                                         | Missing              | Yes                   | Missing               | No                     | Missing                                                                                                                                              | None, patient is waiting a long time anyway                                                                                                                                               |
| Patient 13                                                                                         | Yes                  | Missing               | No                    | Missing                | You ask politely if it's a good time, communication is important                                                                                     | Missing                                                                                                                                                                                   |
| Patient 14                                                                                         | Yes                  | Yes                   | No                    | No                     | Went fine, especially if it's a quiet shift                                                                                                          | None                                                                                                                                                                                      |
| Patient 15                                                                                         | Yes                  | Yes                   | No                    | No                     | None                                                                                                                                                 | No, when I had to go into the room for needed patient care you went out of the room and waited your turn                                                                                  |
| Patient 16                                                                                         | Yes                  | Yes                   | No                    | No                     | None                                                                                                                                                 | No, you have not obstructed me                                                                                                                                                            |
| Patient 17                                                                                         | Yes                  | Missing               | No                    | Missing                | Given the long duration of ED time a feasible study, keep an eye on the admission time                                                               | Missing                                                                                                                                                                                   |
| Patient 18                                                                                         | Missing              | Yes                   | Missing               | No                     | Missing                                                                                                                                              | None                                                                                                                                                                                      |
| Patient 19                                                                                         | Yes                  | Yes                   | No                    | No                     | As long as you communicate with healthcare personnel, much is possible                                                                               | None                                                                                                                                                                                      |
| Patient 20                                                                                         | Missing              | Yes                   | Missing               | No                     | Missing                                                                                                                                              | Fine                                                                                                                                                                                      |
| Patient 21                                                                                         | Missing              | Yes                   | Missing               | No                     | Missing                                                                                                                                              | None                                                                                                                                                                                      |
| Patient 22                                                                                         | Yes                  | Missing               | No                    | Missing                | None                                                                                                                                                 | Missing                                                                                                                                                                                   |
| Patient 23                                                                                         | Missing              | Yes                   | Missing               | No                     | Missing                                                                                                                                              | None                                                                                                                                                                                      |



