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Preoperative dehydration identified by serum calculated osmolarity is associated with severe frailty in patients with hip fracture

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Abstract

Background & Aims

Preoperative dehydration is a well-known predictor of in-hospital complications and poor functional outcomes in older patients with hip fractures. In an orthopedic and geriatric cooperative setting, we aimed to investigate whether preoperative dehydration was associated with frailty, prolonged hospital stays and short-term mortality in older patients with hip fractures.

Methods

This retrospective cohort study was conducted in a Danish university hospital. The study population consisted of patients 65+ years surgically treated for hip fracture. Dehydration was defined as serum calculated osmolarity above 295 mmol/L. Outcomes were frailty at discharge measured by the Multidimensional Prognostic Index, hospital stay of 7 days or more and 90-day mortality.

Results

In total, 214 patients were consecutively included in the study from March 11, 2018, to August 31, 2020. The mean age was 81.2 (SD: 7.6) and 69% of the patients were women. The prevalence of preoperative dehydration was 40%. It was associated with severe frailty (Odds Ratio (OR): 2.08 [95% confidence interval (CI): 1.11-3.90]; p=0.02) and prolonged hospital stay (OR: 2.28 [95% CI: 1.29-4.04]; p=0.02). Seven percent died when dehydrated compared to 5% in the non-dehydrated (p=0.91).

Conclusion

Prevalence of preoperative dehydration is high among older patients with hip fractures and is associated with severe frailty and length of hospital stay. Systematic screening for dehydration on admission is advisable and may contribute to more adequate fluid management in the perioperative phase.
Introduction

Preoperative dehydration is a well-known factor of in-hospital complications, hospital readmission, and poor functional outcomes in older patients with hip fractures [1,2]. Previous studies report that up to 50% of patients with hip fractures show signs of dehydration [3,4]. Several extrinsic and intrinsic factors potentially contribute to this condition, including age-related pathophysiological changes such as increased thirst threshold and decreased renal function, which may lead to insufficient fluid intake and excessive loss of fluid [5]. Moreover, older patients have an increased risk of low-intake dehydration due to comorbidities, polypharmacy, and physical and mental disabilities [5].

Many patients receive inadequate fluid treatment upon hospitalization due to physicians misdiagnosing dehydration [6]. Physicians often use clinical signs and symptoms such as confusion, skin turgor, and mouth dryness to diagnose dehydration, but no evidence supports the use of noninvasive clinical signs and symptoms [6]. Thus, according to ESPEN Guideline on clinical nutrition and hydration in geriatrics, the use of osmolarity (>295 mmol/L) or osmolality (>300 mOsm/kg) is recommended in diagnosing low-intake dehydration [7].

Like dehydration, previous studies have identified several other risk factors impacting morbidity, mortality, and functional outcomes after hip fracture [2,8]. Among others, this includes medical factors such as the presence of comorbidities and sarcopenia, as well as demographic, social, and functional factors [8]. The combination of these factors can be expressed as frailty, which is characterized by the accumulation of multiple deficits and loss of harmonic interaction between multiple domains [9]. Previous studies show a prevalence of frailty of up to 55% among older patients with hip fractures [10,11]. In these patients, frailty is associated with prolonged length of hospital stay, postoperative complications, and mortality [10-12], which is why a standardized
orthogeriatric approach based on perioperative risk evaluation is necessary.

Orthogeriatric management has proven to reduce the length of hospital stay, morbidity, and mortality and improve functional recovery in patients with hip fracture [13-16]. Although low-intake dehydration and frailty are frequent in older patients with hip fractures, it is unclear whether early identification of preoperative dehydration by serum-calculated osmolarity is associated with poor outcomes and serum osmolarity can be used as a screening tool for frailty.

Thus, the study aimed was to investigate whether preoperative dehydration on admission is associated with adverse outcomes such as frailty at discharge, prolonged hospital stay, and short-term mortality in older patients with hip fracture.

Materials & Methods

Study design and patients

This retrospective cohort study is based on data from the Frailty Database. The database contains information on approximately 3,700 patients aged ≥65 years living in the municipality of Aarhus who were admitted to the Geriatric Department at Aarhus University Hospital, Denmark, due to acute illness from March 11, 2018, to August 31, 2020 [17]. The database was established to systematically assess all patients admitted to our wards by the Multidimensional Prognostic Index (MPI) based on Comprehensive Geriatric Assessment [9]. The purpose was to identify frailty and, thereby, the need for early geriatric follow-up visits in the patients' homes after discharge [17]. Multidisciplinary teams performed the bedside assessment routinely on the day of discharge and stored it in the Frailty database [18].

Only patients with hip fractures who underwent surgery were included in this present study. They were identified by one of the following codes in the International Classification of Diseases, 10th Revision: S72.0 (femoral neck fracture), S72.1
(pertrochanteric femoral fracture), and S72.2 (subtrochanteric femoral fracture).

According to a collaboration between Geriatric Department and Orthopedic Department, an outgoing multidisciplinary geriatric team visits the nursing home residents after discharge from the post-anaesthetic care unit to the nursing homes. Consequently, the residents are preferably managed in the nursing homes by the geriatric team; and therefore, the central part of the nursing home residents is not included in the Frailty database [14].

The following patients from the Frailty database were excluded: 1) those with hip fracture caused by malignancy or arthrosis not related to falling, 2) those misclassified with the abovementioned ICD-10 codes, 3) those misclassified living in Aarhus municipality, and 4) those with a missing or a partially assessed frailty score.

The study complied with the STROBE guidelines [19].

**Data collection**

Fluid values of potassium, sodium, urea, and glucose are routinely measured on admission to the Emergency Department within the first 24 hours of admission. By the patients' Civil Registration System number, the blood test results were collected post hoc from the patients’ electronic health records. The values were merged with the data from the Frailty database. Patients with insufficient data on blood samples to calculate serum osmolarity were excluded. Data on length of hospital stay and date of death were obtained from the Danish National Patient Registry. The merged data set was managed using Research Electronic Data Capture (REDCap), a safe software tool for research studies recommended by Aarhus University [20].

**Dehydration**

According to the ESPEN guideline on clinical nutrition and hydration in geriatrics, we
chose serum-calculated osmolarity to assess and define low-intake dehydration. The Khajuria and Krahn’s equation [21], based on routine blood measures, has been proven to be the best for predicting serum osmolarity in older people [22], independently of diabetes status [23]:

\[
\text{osmolarity} = 1.86 \times (Na^+ + K^+) + 1.15 \times \text{glucose} + \text{urea} + 14 \text{ (all measured in mmol/L)}.
\]

Patients with serum-calculated osmolarity >295 mmol/L were dehydrated [22]. It included impending dehydration (>295-300 mmol/L) and current dehydration (>300 mmol/L). Patients with serum-calculated osmolarity of 295 mmol/L or below were classified as normally hydrated.

**Outcomes**

MPI has originally been used to predict short- and long-term mortality [18,24-26], but in recent years it has also been used to identify frailty [9]. The MPI assessment includes clinical, cognitive, functional, nutritional, and social parameters, a total of 63 items in eight domains [18]. The MPI sum score is expressed as a number between 0 and 1 by aggregating the total scores of all eight domains. The patients are divided into three groups: Score 0 to 0.33 (MPI-1), from 0.34 to 0.66 (MPI-2), and from 0.67 to 1 (MPI-3), representing: None/low, moderate, and severe frailty [9,18].

Length of hospital stay was calculated from the date of admission to the date of discharge. All-cause 90-day mortality was calculated from the date of entry to the hospital to the date of death.

**Statistical analysis**

A sample size calculation was performed to ensure that the available number of patients from the Frailty database with sufficient blood measures was adequate. It was based on the study from Stookey et al. [27]. Overt hypertonicity measured as >300 mOsm/L was
found to differ between a group of older adults with a low frailty score (12.4%) compared with a high frailty score (40.7%) in older adults with no disabilities. With a power of 90%, at least 56 patients were needed in each group if we expected to find a similar association. However, as we did, Stookey et al. omitted mild hypertonicity in their definition of dehydration. Therefore, we added another 30 patients to each of the two groups of normal hydrated and dehydrated patients. When the number of at least 86 patients was reached consecutively in both groups, we stopped including more records from the geriatric quality database.

The characteristics between the two groups were compared. Age was compared by Student’s t-test, categorical variables by Pearson’s chi-squared test, and non-normal distributed with Wilcoxon Ranksum test.

A logistic regression model was used to test the association between dehydration (yes/no) and frailty, length of hospital stay, and 90-day mortality, respectively. Owing to the small number of patients in the frailty groups, we combined the MPI-1 and MPI-2 groups (low/moderate) and compared them with the MPI-3 group (severe). The estimates of the analysis are expressed as odds ratio (OR) with a 95% confidence interval (CI). Apart from the fluid values, we adjusted for the baseline characteristics in the tests that showed a p-value of less than 10% between groups. The regression model was controlled by computing the area under the receiver operating characteristics curve. All the analyses were performed using Stata version 17. P-values <0.05 were considered statistically significant, and those ranging from 0.05 to 0.10 were considered a tendency.

**Ethical considerations**

The study was a quality development project, and approval was obtained from the Head of the Department of Geriatrics to access the geriatric quality database and the patients’
electronic health records to collect additional information. Approval by The Central Denmark Region Committees on Health Research Ethics was not required according to the Danish Ethical Committee Law §14, subsection 2. The study was conducted according to the principles of the Declaration of Helsinki.

**Results**

During the study period, 376 patients were admitted with hip fractures and managed in the hospital. Of those, 162 were excluded following the criteria (Figure 1). The baseline characteristics are shown in Table 1. The mean age was 81.2 (± 7.6) years, and 69% of the patients were women. Of the patients included, 57% were living alone. Six percent were living in a nursing home. Around two-thirds of the patients had a normal cognitive status and used more than eight drugs. Approximately half of the patient was at moderate nutritional risk. The prevalence of preoperative dehydration was 40% (n=86). Compared with the normally hydrated patients before surgery, dehydrated patients showed a higher severity of comorbidities and nutritional risk (p≤0.05). Dehydrated patients had significantly higher concentrations of sodium, potassium, glucose, and urea (p<0.05). The two groups did not differ in age, sex, social living, cognitive status, and the number of drugs.

[Figure 1 near here]

[Table 1 near here]

Patients with preoperative dehydration had an increased probability of being categorized as severely frail at discharge when adjusted for sex (OR\textsubscript{adjusted} = 2.08; (95% CI: 1.11-3.90), p=0.02). Of patients categorized as severely frail at discharge, 51% were dehydrated at admission compared to 30% of the normally hydrated. More patients were admitted to the hospital for seven days or more with preoperative dehydration when adjusted for comorbidity, nutritional risk and sex (OR\textsubscript{adjusted} = 2.28; (95% CI: 1.29-
4.04), \( p=0.02 \). The median hospital days were 8 (IQR 7-10) in the dehydrated patients compared to 7.5 (IQR 6-9) in the normally hydrated. All-cause 90-day mortality did not differ between the two groups (OR_{\text{adjusted}} = 1.07 (95\%: 0.31-3.74); \( p=0.91 \)). Of the dehydrated patients, 7% died compared to 5% in the normal hydrated (Table 2).

[Table 2 near here]

[Figure 2 near here]

The control of the three logistic regression models showed an area under the curves between 0.63-0.71.

**Discussion**

**Interpretation**

In this observational study of older patients with hip fractures, we found that preoperative dehydration identified by serum-calculated osmolarity is associated with severe frailty at discharge and prolonged hospital stay.

In the present and previous observational studies, it is difficult to determine the direction of the relation between dehydration and frailty. Dehydration may be a risk factor for frailty, and frailty may contribute to dehydration. Our findings are in line with those of Stookey et al., who identified hypertonicity (>300 mOsm/L) as a marker of frailty in community-dwelling older adults [27]. They used incident disability as the outcome, defined as new difficulties based on the Activity of Daily Living (ADL) and instrumental-ADL, or Rosow-Breslau scale score as a marker of frailty. In comparison, Wojszel et al. used the Clinical Frailty Scale to assess frailty in patients in a geriatric ward and found no association with that instrument [28]. McCrow et al. found an association between dehydration and frailty, but only among cognitive well-functioning older people [29]. The study population in all the mentioned studies were the general geriatric population and did not specifically suffer a hip fracture. Potential reasons for
the lack of consensus in the existing literature could be the choices of study populations and the assessments used to evaluate dehydration and frailty.

Our study is the first to demonstrate the association between preoperative dehydration and prolonged length of hospital stay in hip fracture patients. Zanetti et al. conducted a similar observational study, finding an association between postoperative dehydration and length of hospital stay [30], indicating the importance of sufficient fluid management in the perioperative phase. However, we did not find any association between preoperative dehydration and short-term mortality, compared to a systematic review where an association between dehydration and long term-mortality was found [31]. A high MPI score is expected to be linked to increased short-term mortality. However, only 5-7% of the patients died within 90 days of follow-up, which would have required a larger sample to find an association. Furthermore, the MPI tool contains various information to explain an association with low-intake dehydration, such as low physical performance. Other possible explanations for this missing association might be the shorter follow-up period and the orthogeriatric management in our hospital, which is known to reduce adverse outcomes, including mortality [13-16]. Also, the smaller amount of nursing homes residents included could be an explanation. In the study of Zanetti et al., 19% of patients included were from nursing homes, compared to only 6% in ours [30]. Nursing home residents tend to be frailer and have an increased mortality rate compared to community-dwelling older adults [32,33].

Preoperative dehydration in our study population was frequent where 40% of the patients were classified as dehydrated. Adequate identification of dehydration as early as possible is essential due to its association with adverse outcomes [34,35]. Using Khajuria and Krahn’s equation [21], based on routine blood measures, is an easy and
reliable way to identify low-intake dehydration. Most older patients with dehydration will be identified with a sensitivity of 85% and a specificity of 59% [22]. Integrating serum-calculated osmolarity in the preoperative phase could drive interventions for correcting preoperative dehydration and prevent its adverse outcomes, such as falls [36] and further cognitive impairment in frail older persons [37]. This early identification of dehydration may contribute to more appropriate fluid therapy and individualised care plan, e.g., structured drinking intervention during hospitalisation. Frail older adults need more assistance to drink, overcome their fear of incontinence, and visit the toilet more frequently [38]. In early discharge planning and the interventions after discharge, low-intake dehydration must be handled. A study in nursing homes found that, of 188 residents, 20% were dehydrated, and a further 28% were in a state of impending dehydration [37]. This increases the risk of another trauma. Dehydration is the second most common cause of readmission to hospital for older adults [1], and may worsen the course of recovery from hip fracture surgery [39].

Strength and limitations
Our data set was complete, however, 37% of the population were excluded due to missing values on the routine blood test and frailty assessment. Instead, we could have used the method of missing imputation on these data to improve the external validity. Although fluid values were assessed at admission in the nursing home residents, bedside MPI screening was only performed in 6% of the residents as they were discharged after two median days and received follow-up visits by the geriatric team in the nursing home. From previous studies, we know that about 25% of our patients are nursing home residents. This means that our results are mainly based on community-dwelling older patients, which are not representative of the whole geriatric population. However, we found no indication of selection bias as data were initially collected for another purpose.
Due to the small number of patients in the MPI-1 group combined with the MPI-2 group [18], we chose to analyze osmolarity and frailty based on dichotomized values which might have been a poor practice since some information could have been lost. In the patients categorized as dehydrated, a direct measurement of serum osmolarity should have been performed to confirm the diagnosis [7,40]. Since this is a retrospective study, it has not been possible but should be recommended for future studies.

**Conclusion**

Preoperative dehydration identified by serum-calculated osmolarity is associated with severe frailty at discharge and prolonged hospital stay in older patients with hip fractures. Calculating osmolarity for identifying dehydration by routine laboratory screening at hospital admission may contribute to optimizing adequate fluid management. Our findings indicate that an individualized care plan during hospitalisation and immediately after discharge to prevent adverse outcomes needs to be elaborated in older patients with hip fractures.

**Acknowledgements**

The authors would like to thank the geriatric patients for their invaluable contributions to the bedside frailty assessment and the staff in the Department of Geriatrics for their outstanding involvement in performing the assessment.

**Declaration of interest statement**

The authors declare no conflicts of interest.

**Funding statement**

No funding was available.
Author contributions

Kenan Sabanovic performed conceptualization and writing of original draft.

Merete Gregersen performed conceptualization, data analysis, writing review and editing.

Else Marie Damsgaard performed conceptualization, writing review and editing.

References


**Figure 1** Flowchart of older patients with hip fracture selected from a quality database containing patients who were admitted to the Geriatric Department at Aarhus University Hospital due to acute illness.

**Figure 2** Distribution of patients with hip fracture assessed by Multidimensional Prognostic Index (MPI) as low or moderately frail (MPI-1 + MPI-2) versus severely frail (MPI-3) according to serum osmolarity. MPI-1: n=19, MPI-2: n=112, MPI-3: n=83.
Table 1. Baseline characteristics of 65+ years old patients with hip fracture divided in preoperative normal hydrated patients and dehydrated.

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>All patients N=214</th>
<th>Preoperative normal hydrated n=128</th>
<th>Preoperative dehydrated n=86</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean year (sd)</td>
<td>81.2 (7.6)</td>
<td>80.5 (8.1)</td>
<td>82.2 (6.8)</td>
<td>0.13</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>67 (31)</td>
<td>34 (27)</td>
<td>33 (38)</td>
<td>0.07</td>
</tr>
<tr>
<td>Female</td>
<td>147 (69)</td>
<td>94 (73)</td>
<td>53 (62)</td>
<td></td>
</tr>
<tr>
<td>Social living, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living with relatives</td>
<td>80 (37)</td>
<td>50 (39)</td>
<td>30 (35)</td>
<td>0.80</td>
</tr>
<tr>
<td>Institution</td>
<td>13 (6)</td>
<td>8 (6)</td>
<td>5 (6)</td>
<td></td>
</tr>
<tr>
<td>Living alone</td>
<td>121 (57)</td>
<td>70 (55)</td>
<td>51 (59)</td>
<td></td>
</tr>
<tr>
<td>Cognitive status1, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>158 (74)</td>
<td>100 (78)</td>
<td>58 (68)</td>
<td>0.21</td>
</tr>
<tr>
<td>Mild to moderate impaired</td>
<td>41 (19)</td>
<td>20 (16)</td>
<td>21 (24)</td>
<td></td>
</tr>
<tr>
<td>Severely impaired</td>
<td>15 (7)</td>
<td>8 (6)</td>
<td>7 (8)</td>
<td></td>
</tr>
<tr>
<td>Drugs, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-3</td>
<td>8 (4)</td>
<td>6 (5)</td>
<td>2 (2)</td>
<td></td>
</tr>
<tr>
<td>4-7</td>
<td>43 (20)</td>
<td>31 (24)</td>
<td>12 (14)</td>
<td></td>
</tr>
<tr>
<td>8+</td>
<td>163 (76)</td>
<td>91 (71)</td>
<td>72 (84)</td>
<td>0.10</td>
</tr>
<tr>
<td>Severity of comorbidities2, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>37 (17)</td>
<td>23 (18)</td>
<td>14 (16)</td>
<td>0.04</td>
</tr>
<tr>
<td>Moderate</td>
<td>111 (52)</td>
<td>74 (58)</td>
<td>37 (43)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>65 (31)</td>
<td>31 (24)</td>
<td>34 (40)</td>
<td></td>
</tr>
<tr>
<td>Nutritional risk3, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>13 (6)</td>
<td>12 (9)</td>
<td>1 (1)</td>
<td>0.05</td>
</tr>
<tr>
<td>Moderate</td>
<td>126 (59)</td>
<td>73 (57)</td>
<td>53 (62)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>75 (35)</td>
<td>43 (34)</td>
<td>32 (37)</td>
<td></td>
</tr>
<tr>
<td>Blood test at admission, mean (sd)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium, mmol/L</td>
<td>138 (4.3)</td>
<td>136 (4.54)</td>
<td>141 (2.45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Potassium, mmol/L</td>
<td>4.02 (0.48)</td>
<td>3.93 (0.40)</td>
<td>4.14 (0.57)</td>
<td>0.005</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>7.28 (2.38)</td>
<td>6.69 (1.32)</td>
<td>8.16 (3.22)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urea, mmol/L</td>
<td>6.91 (3.68)</td>
<td>5.38 (1.87)</td>
<td>9.19 (4.46)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

1 Cognitive status was assessed by Short Portable Mental Status Questionnaire
2 Comorbidity was assessed by Cumulative Illness Rating Scale – Geriatrics
3 Nutritional risk was assessed by Mini Nutritional Assessment – Short Form
Table 2. Preoperative dehydration in relation to frailty status, length of hospital stay, and mortality.

<table>
<thead>
<tr>
<th></th>
<th>Preoperative normal hydrated n=128</th>
<th>Preoperative dehydrated n=86</th>
<th>Crude Odds ratio (95% CI)</th>
<th>Adjusted* Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe frailty at discharge, n (%)</td>
<td>39 (30)</td>
<td>44 (51)</td>
<td>2.39 (1.36-4.21) p=0.003</td>
<td>2.08 (1.11-3.90) p=0.02</td>
</tr>
<tr>
<td>LOS of 7 days or more, n (%)</td>
<td>90 (70)</td>
<td>71 (83)</td>
<td>2.00 (1.02-3.92) p=0.04</td>
<td>2.28 (1.29-4.04) p=0.02</td>
</tr>
<tr>
<td>90-day mortality, n (%)</td>
<td>6 (5)</td>
<td>6 (7)</td>
<td>1.51 (0.47-4.86) p=0.49</td>
<td>1.07 (0.31-3.74) p=0.91</td>
</tr>
</tbody>
</table>

CI=Confidence Interval
LOS=Length of hospital stay
* Adjusted for sex, comorbidity severity and nutritional status. Frailty is only adjusted for sex since status on comorbidity and nutrition are included in the Multidimensional Prognostic Index.
Figure 1

65+ years old patients with hip fracture admitted to hospital between March 11, 2018 and May 31, 2020
N=376

Excluded:
- Missing frailty scores, n=16
- Diagnostic misclassification, n=16
- Malign HF, n=4
- Living in another municipality, n=4
- Missing blood test for osmolarity measurement, n=122

Included in the analysis
n=214

Figure 2

<table>
<thead>
<tr>
<th></th>
<th>Normal hydration</th>
<th>Dehydration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low/moderate frailty</td>
<td>80</td>
<td>40</td>
</tr>
<tr>
<td>Severe frailty</td>
<td>50</td>
<td>30</td>
</tr>
</tbody>
</table>

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