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Association of depressive disorders and dementia with mortality among older people with hip fracture

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Abstract

Background Hip fracture (HF) is a significant cause of mortality among older people. Almost half of the patients with HF have dementia, which increases the mortality risk further. Cognitive impairment is associated with depressive disorders (DDs) and both dementia and DDs are independent risk factors for poor outcome after HF. However, most studies that evaluate mortality risk after HF separate these conditions.

Aims To investigate whether dementia with depressive disorders (DDwD) affects the mortality risk at 12, 24, and 36 months after HF among older people.

Methods Patients with acute HF ($n=404$) were included in this retrospective analysis of two randomized controlled trials performed in orthopedic and geriatric departments. Depressive symptoms were assessed using the Geriatric Depression Scale and cognitive function was assessed using the Mini-Mental State Examination. A consultant geriatrician made final depressive disorder and dementia diagnoses using the Diagnostic and Statistical Manual of Mental Disorders criteria, with support from assessments and medical records. The 12-, 24- and 36-month mortality after HF was analyzed using logistic regression models adjusted for covariates.

Results In analyses adjusted for age, sex, comorbidity, pre-fracture walking ability, and fracture type, patients with DDwD had increased mortality risks at 12 [odds ratio (OR) 4.67, 95% confidence interval (CI) 1.75–12.51], 24 (OR 3.61, 95% CI 1.71–7.60), and 36 (OR 4.53, 95% CI 2.24–9.14) months. Similar results were obtained for patients with dementia, but not depressive disorders, alone.

Conclusion DDwD is an important risk factor for increased mortality at 12, 24, and 36 months after HF among older people. Routinely assessments after HF for cognitive- and depressive disorders could identify patients at risk for increased mortality, and enable early interventions.

Trial registration RCT2: International Standard Randomized Controlled Trial Number Register, trial registration number: ISRCTN15738119.

Keywords Dementia, Depressive disorders, Hip fracture, Mortality, Older people

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Introduction

The hip fracture (HF) incidence increases with age, and HF is a significant cause of mortality among older (aged < 60 years) people [1, 2]. The mortality risk increases shortly after HF, and persists for 10 years [3, 4]; predictors are high American Society of Anesthesiologists scores, pre-fracture mobility, and dementia [5, 6].

Almost half of patients sustaining HFs have dementia [6–8] and increased short- and long-term mortality [9, 10]. Cognitive impairment/dementia is associated with depressive disorders (DDs) [11, 12], which are more common among patients sustaining HF than in the general population [13, 14]. Older patients with DDs have an increased fall risk [15] and greater comorbidity burden [16]. Patients with DDs, in addition to comorbidity, have an increased 1-year mortality risk [17]. However, knowledge of DDs' effect on mortality among patients sustaining HFs is limited.

DDs and dementia are independent predictors of poor outcomes and increased mortality risk after HF [18]. However, most studies that evaluate mortality risk after HF have separated these conditions, and to our knowledge, only one small study, has explored whether dementia with depressive disorders (DDwD) affects long-term mortality after HF surgery, which revealed a significantly increased 12-month mortality risk [19]. The present study has the aim to investigate whether DDwD affects the mortality risk at 12, 24, and 36 months after HF among older people.

Method

Study design and participants

Data used in this secondary analysis of 404 patients with acute HFs were from two randomized controlled trials (RCT1 and RCT2). Both RCT were performed in the orthopedic- and the geriatric departments of Umeå University Hospital, Sweden. RCT1 included 199 patients with femoral-neck fractures enrolled in May 2000-December 2002 [20]; RCT2 included 205 patients with femoral-neck and trochanteric-region fractures enrolled in May 2008-June 2011 [21]. Inclusion criteria for both studies were age ≥ 70 years and Umeå municipality residence. Exclusion criteria for RCT1 were severe rheumatoid arthritis/hip osteoarthritis, pathological/hospital-acquired HF, renal failure, and bedridden before the fracture occurred. Those for RCT2 were hospital-acquired/pathological HF. Both RCTs included patients with cognitive impairment or dementia.

Randomized controlled trials

Participants in both RCTs were randomized consecutively to intervention and control groups. In RCT1, participants in the intervention group received postoperative care according to a multifactorial rehabilitation program in a specialist orthopedic geriatric unit. Multidisciplinary teams performed comprehensive geriatric assessment, management, and rehabilitation to prevent, detect and treat early postoperative complications. Control participants received conventional postoperative care in a specialist orthopedic [20].

In RCT2, all patients received postoperative care in the geriatric orthopedic department according to the multifactorial rehabilitation program (now the standard of care, based on RCT1 results). The intervention focus was early discharge, with rehabilitation in patients' homes supported by an interdisciplinary geriatrics team [21]. As no difference in survival was detected in either RCT, data from all participants were analyzed together.

Randomization, recruitment, and intervention contents have been described previously [20, 21]. Participants in both RCTs received written and oral information, and they or their next of kin provided consent. Participants and/or next of kin were informed that they could withdraw at any time with no repercussion. The RCTs were approved by the Regional Ethical Review Board in Umeå, Sweden (Dnr 00–137 and Dnr 08-053 M), and amendments for this study was approved by the Swedish Ethical Review Authority (Dnr 2021–00,024 and Dnr 2021–00,681). All methods were performed in accordance to the Declaration of Helsinki.

Data collection

At baseline, research assistants (nurses, physiotherapists, and occupational therapists) collected medical, functional, and social data from the patients, their relatives, and/or medical charts. In RCT1 and RCT 2, assessments were performed at 3–5 days postoperatively. Dates of death were collected from medical records.

Participants' pre-fracture indoor walking ability was assessed [scale, 1 (no functional ability/need for two people's assistance)–7 (normal function)] [22]. Walking device use was registered. Pre-fracture independence in personal and instrumental activity of daily living (ADL) was assessed using the Katz ADL index [23]. Patients' vision (ability to read 5-mm block letters with/without glasses) and hearing (ability to hear normal speech with/without hearing aids for 1 m) were assessed.

Outcome measurements

The outcome was 12-, 24- and 36-month mortality following HF surgery. DDs diagnoses were based on current antidepressant treatment and Geriatric Depression Scale (GDS-15) scores (scores ≥ 5 indicate significant depressive symptoms) [24]. In addition, fluctuations of clinical state were observed and registered by the Organic Brain Syndrome scale (OBS scale) [25]. The GDS-15 has good

sensitivity and specificity, even among very old people with low Mini Mental State Examination (MMSE) scores, for DDs detection according to the Diagnostic and Statistical Manual of Mental Disorders – Text revision (4.th ed.; DSM-IV-TR) [26, 27]. Cognitive function was assessed using the MMSE, (scores 0–30, scores ≤ 23 indicate significant cognitive impairment) [28].

At the end of the RCTs, a consultant geriatrician (YG), blinded to group allocation and not employed at the wards, set all diagnoses. The consultant geriatrician used all possible information from patient's medical record (diagnoses, complications, and other important documentations), patient's prescribed drugs and assessments performed in these RCTs (including the MMSE, GDS-15, Philadelphia Geriatric Center Morale Scale (PGCMS) [29, 30], Katz ADL index, OBS Scale), as well as vision and hearing tests, to determine whether participants fulfilled the DMS-IV-TR criteria for DDs and dementia.

Statistics

Baseline characteristics were compared between surviving and deceased participants at 36 months after HF. Pearson's chi-square test and Fisher's exact test were used to analyze categorical variables. Normally and non-normally distributed data were compared between groups using the independent-sample t and Mann–Whitney U test, respectively.

To identify independent factors predicting 36-month post-HF mortality; correlations between baseline variables were tested using Pearson's and Spearman's coefficients (< 0.6 for all covariates) [31]. Univariate analysis was performed to examine unadjusted associations of potential risk factors with HF and increased mortality risk. Variables with $p \leq 0.10$ (t or chi-squared test) were subjected to multivariable logistic regression using the forward stepwise conditional method [32]. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to identify factors associated with 12-, 24-, and 36-month mortality. Adjusted analysis was used to obtain ORs for depressive disorders with dementia (DDwD).

Statistical analyses were conducted with SPSS (version 25; IBM Corporation, Armonk, NY, USA). $P < 0.05$ was considered to indicate significance.

Results

Patients and descriptive

The sample comprised 404 patients [295 (73.0%) women, mean age 82.6 ± 6.5 years]. Most (87.5%) participants walked independently before HF. More participants who died than survived within 36 months had the comorbidities examined. Vision and hearing impairment frequencies did not differ significantly between groups. At baseline, 153 (38.5%) patients had DDs and 167 (41.3%) had dementia; 94 (23.3%) patients had DDwD. Fifty-nine (15.0%) had DDs without dementia and 72 (18.0%) had dementia without DDs. One patient with dementia could not perform assessment for DDs, and is missing (Table 1). DDs correlated weakly to moderately with dementia ($r = 0.31$).

Mortality

The overall 36-month mortality rate was 41.6%; it was significantly higher among older patients, nursing home residents, and patients with pre-fracture personal ADL dependence. Significant differences between deceased and surviving participants were observed for the comorbidities examined (Table 1). Mortality was equivalent between participants in RCT1 and RCT2, and between intervention and control groups (data not shown).

Half of the patients who had died at 36 months had DDs (50.3%) or dementia (56.0%) preoperatively. Fifty-nine (35.8%) patients with DDwD,14.5% of those with DDs alone, and 20.6% of those with dementia alone died within 36 months.

The mortality risk among patients with dementia alone was increased at 12 (OR 4.05, 95% CI 1.52–10.79), 24 (OR 2.87, 95% CI 1.38–5.98), and 36 (OR 2.55, 95% CI 1.30–4.99) months. No significant increase was observed for those with DDs alone. Patients with DDwD had increased mortality risk at 12 (OR 4.67, 95% CI 1.75–12.51), 24 (OR 3.61, 95% CI 1.71–7.60), and 36 (OR 4.53, 95% CI 2.24–9.14) months (Table 2).

Discussion

The main finding in our study was that DDwD were significantly associated with increased 12-, 24- and 36-month mortality risk following HF. In addition, patients with dementia, without DDs, also had increased mortality risk at all three follow ups.

The mortality risk is the highest the first year after hip fracture, which is also supported in by Katsoulis et al.'s [3]. Factors that contribute most to the increased mortality risk the first year are co-morbidities and numerous postoperative complications, such as infections, cardiac- and pulmonary complications [9]. The mortality risk will persist to be high even on a long-term, were the underlying excess risk remains more unclear [3]. DDwD increases short- and long-term mortality risks [33, 34]. Our findings are supported by Bellelli et al.'s [19], report of an increased 12-month mortality risk following HF among patients with DDwD, but their sample was small and from a rehabilitation unit, and thus not representative of all people sustaining HFs.

DDs are significantly more common among patients with dementia than among cognitively intact individuals

Table 1 Study population characteristics and comparison of the 404 patients deceased or survived within 36 months after hip fracture. Continuous variables are presented with mean and standard deviation

	Total No. 404	Deceased 36 months No. 168	Survivors 36 months No. 236	*P*-value
Age	82.6 (±6.5)	83.8 (±6.5)	81.7 (±6.4)	**0.002**
Sex				
Female	295 (73.0%)	113 (67.3%)	182 (77.1%)	**0.037**
Living in nursing home	136 (33.7%)	76 (55.9%)	60 (44.1%)	**<0.001**
Not having a partner	293 (72.5%)	129 (76.8%)	164 (69.5%)	0.132
Independent in walking indoors before fracture	350 (87.5%)	135 (82.3%)	215 (91.1%)	**0.014**
Independent in P-ADL before fracture	173 (43.3%)	40 (24.4%)	133 (56.4%)	**<0.001**
Normal vision	231 (61.8%)	90 (60.4%)	141 (62.7%)	0.740
Normal hearing	299 (76.5%)	119 (73.9%)	180 (78.3%)	0.381
Pulmonary disease	58 (14.5%)	34 (20.7%)	24 (10.3%)	**0.006**
Cerebrovascular disease	94 (23.5%)	48 (28.9%)	45 (19.7%)	**0.042**
Cardiovascular disease	215 (53.9%)	108 (65.1%)	107 (45.9%)	**<0.001**
Cancer (current)	41 (10.3%)	29 (17.7%)	12 (5.1%)	**<0.001**
Diabetes	72 (17.9%)	38 (22.8%)	34 (14.5%)	**0.045**
Depression pre fracture	154 (38.5%)	83 (50.3%)	71 (30.2%)	**<0.001**
Depression, but not dementia	60 (15.0%)	24 (14.5%)	36 (15.3%)	0.943
Dementia pre fracture[a]	167 (41.3%)	94 (56.0%)	73 (30.9%)	**<0.001**
Dementia, but not depression	72 (18.0%)	34 (20.6%)	38 (16.2%)	0.315
Dementia and depression	94 (23.5%)	59 (35.8%)	35 (14.9%)	**<0.001**
Fermoral neck fracture	329 (81.6%)	140 (83.3%)	189 (80.4%)	0.540
Undisplaced/minimally displaced (B1)	88 (21.8%)	40 (45.5%)	48 (54.5%)	
Basicervical (B2)	14 (3.5%)	10(71.4%)	4 (28.6%)	
Displaced (B3)	226 (56.3%)	90 (39.6%)	137 (60.4%)	
Intertrochanteric fracture	74 (18.4%)	28 (16.7%)	46 (19.6%	
Trochanteric (A1-A2.1)	38 (9.4%)	11 (28.9%)	27 (71.1%)	
Trochanteric (A2.2-A2.3)	21 (5.2%)	10 (47.6%)	11 (52.5%)	
Trochanteric (A3)	15 (3.7%)	7 (46.7%)	8 (53.3%)	

[a] Diagnostic assessment for depressive disorder was not performed in one patient with dementia

P-ADL Personal activities of daily living

[12]. DDs in older people are often underdiagnosed, undertreated, or untreated [35] possibly due to their complexity and similarity to other cognitive and psychiatric diseases. DDs may be a risk factor, prodromal symptom, or a consequence of dementia [36]. Older people have different pathophysiology and clinical presentation of DDs, compared to younger patients [37]. Further, several factors, such as biological- and psychosocial mechanisms, can contribute and be the cause of DDs among older people [38, 39], requiring a focus on addressing underlying causes.

Findings from younger populations with DDs may not be applicable to older populations, in which drug treatment alone has limited effects [40], especially among those with dementia [41, 42]. Combined psychosocial/drug interventions may yield better outcomes for patients with dementia [43–45]. The assessment and treatment of underlying risk factors (e.g. malnutrition and drug-side effects) is also important. Thus, the identification of alternative treatments or prevention of DDs in this population is important.

DDs influence functional outcome negatively after HF [46–48], which may be contributed by difficulties in goal-setting, planning, and rehabilitation-initiation [49]. Patients with dementia alone, and combined with DDs, are provided less rehabilitation, which can partly be influenced by the attitudes of the clinical staff [50]. However, patients with dementia benefit similarly, to those without dementia, from rehabilitation in a specialized geriatric ward after HF [51].

Table 2 Multivariable logistic regression of mortality risk at 12-, 24- and 36 months after a hip fracture with the combination of depressive disorders and dementia

Variable	12 months		24 months		36 months	
	OR	CI	OR	CI	OR	CI
Age	**1.08**	**1.03–1.14***	**1.07**	**1.02–1.10***	**1.05**	**1.01–1.09***
Sex						
Female	1.0	ref	1.0	ref	1.0	ref
Male	1.29	0.63–2.62	1.70	0.98–2.96	1.33	0.78–2-26
Resident						
Own home	1.0	ref	1.0	ref	1.0	ref
Nursing home	1.15	0.53–2.51	1.22	0.65–2.29	1.04	0.56–1.92
Walking ability indoor						
Independent	1.0	ref	1.0	ref	1.0	Ref
Dependent	2.32	0.99–5.38	1.46	0.70–3.07	1.27	0.60–2.69
Type of fracture						
Cervical	1.0	ref	1.0	ref	1.0	ref
Trochanteric	1.05	0.44–2.47	0.68	0.34–1.38	0.98	0.53–1.80
Pulmonary disease	1.49	0.60–3.67	**2.19**	**1.10–4.39***	**2.60**	**1.33–5.03***
Cerebrovascular disease	1.16	0.56–2.38	1.19	0.62–2.01	1.44	0.83–2.47
Cardiovascular disease	0.98	0.51–1.91	1.30	0.77–2.20	1.57	0.98–2.53
Diabetes	1.58	0.73–3.41	0.85	0.44–1.66	1.74	0.96–3.16
Cancer (current)	2.52	0.97–6.58	**4.23**	**1.92–9.33***	**6.57**	**2.83–15.29***
Depression, but not dementia	2.38	0.82–6.90	1.47	0.68–3.22	1.33	0.65–2.70
Dementia, but not depression	**4.05**	**1.52–10.79***	**2.87**	**1.38–5.98***	**2.55**	**1.30–4.99***
Depression and dementia	**4.67**	**1.75–12.51***	**3.61**	**1.71–7.60***	**4.53**	**2.24–9.14***

CI Confidence interval, *OR* Odds ratio

* Statistically significant $p < 0.05$

The identification of DDs in older people after HF surgery enables early intervention and minimize negative impacts on recovery and mortality. Clinical staff should provide early screening, especially for patients with dementia, to detect these disorders and provide adequate treatment, if indicated.

Limitations of this study include the use of old data from two RCTs and the operative treatment has changed since these studies were performed [52, 53]. However, the post-HF mortality rate has not changed in the past 25 years [2]. Other confounders, such as time-to-surgery [54], time to standing up after surgery [55] and socioeconomic status [56] could be potential factors that might contribute to increased mortality risk, but data were not available in the present study. A study strength derives from the same comprehensive assessment using validated scales, inclusion criteria, and methods in both RCTs. In addition, the same consultant geriatrician made all DDs and dementia diagnoses using the DSM-IV TR criteria, reducing the misclassification risk. For these reasons, the merging of data from the two RCTs to acquire a larger sample was possible.

Conclusion

This study showed that patients with baseline DDwD have increased mortality risks at 12, 24, and 36 months after HF. Routinely assessments after HF for cognitive- and depressive disorders could identify patients at risk for increased mortality, and enable early interventions.

Abbreviations

ADL	Activity of daily living
CIs	Confidence intervals
DDs	Depressive disorders
DDwD	Dementia with depressive disorders
DSM-IV TR	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
GDS-15	Geriatric Depression Scale
HF	Hip fracture
MMSE	Mini Mental state examination
OBS scale	The Organic Brain Syndrome scale
OR	Odds ratio
PGCMS	Philadelphia Geriatric Center Morale Scale
RCT	Randomized controlled trial

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Authors' contributions
EO analyzed, interpreted the patient data and was a major contributor in writing the manuscript. YG analyzed all assessments, documentations, registered diagnosis and complications from patients' medical records. The same consultant analyzed all assessment data and documentation to determine whether participants fulfilled the DSM-IV criteria for DDs and dementia. BO collected the data in both RCTs. All authors contributed to the study concept and design, interpretation of data, read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Participants in both RCTs received written and oral information, and they or their next of kin was consulted to provide written informed consent on their behalf. Participants and/or next of kin were informed that they could withdraw at any time with no repercussion. The RCTs were approved by the Regional Ethical Review Board in Umeå, Sweden (Dnr 00–137 and Dnr 08-053 M), and amendments for this study was approved by the Swedish Ethical Review Authority (Dnr 2021–00024 and Dnr 2021–00681). All methods were performed in accordance to the Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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