The long term consequences of stroke

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Chapter 4

Post stroke depression, a long term problem for stroke survivors

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Erratum:
In the Abstract, the Results, and the Discussion sections of this article, it was stated that "Male sex and being born abroad was statistically significantly associated with a high HADS depression score, adjusted for age, sex and stroke severity." This phrase contains a seemingly contradictory statement. The authors suggest rephrasing this statement in those sections as follows to avoid confusion:

Abstract:
Male sex and being born abroad was statistically significantly associated with a high HADS depression score, adjusted for age, sex and stroke severity (where appropriate).

Results:
A HADS depression score ≥ 8 at follow up was associated with male sex (0.46; CI 0.22 – 0.93; adjusted for age and Barthel Index at discharge) and with being born abroad (OR 2.70; CI 1.31 – 5.53; adjusted for age, sex and Barthel Index at discharge); less patients in the depression group drank alcohol (Table 3)

Table 3:
Asterix at age, sex and Barthel at discharge indicating:
* with adjustment for the other two confounding factors

Abstract

Objectives: To ascertain the prevalence of depressive mood and its determinants in the chronic phase after stroke.

Design: 576 consecutive patients were invited to participate 2-5 years after hospitalization for a first-ever stroke. Stroke characteristics at hospitalization were collected retrospectively from medical records. Patients and their caregivers completed questionnaires on depression (Hospital Anxiety and Depression Scale; HADS), socio-demographic characteristics, healthcare usage, daily activities, Quality of Life and caregiver strain. Patients with HADS depression scores <8 were compared to patients with HADS depression scores ≥8 by means of univariate logistic regression analyses, adjusted for age, sex and Barthel Index at discharge.

Results: 207 patients (36%) returned the questionnaires. After a mean follow-up of 36.3 months, 67 patients (34%) had a HADS depression score ≥8. Male sex and being born abroad was statistically significantly associated with a high HADS depression score, adjusted for age, sex and stroke severity. Depressed patients had higher anxiety levels, a more avoidant coping style, less daily activities and a lower Quality of Life; their caregivers experienced a higher burden.

Conclusion: In the chronic phase after stroke, a considerable proportion of patients has depressive symptoms. This appears to be related to sex, country of origin, anxiety, coping style, daily activities, Quality of Life and caregivers' strain. Future research should focus on causal relationships, and opportunities for treatment.

Keywords: stroke; depression; outcome assessment; humans; disability evaluation; social participation.

Introduction

Post stroke depression (PSD) is a common sequel of stroke, warranting the need for appropriate identification, education and treatment not only in the acute hospital phase but also in later stages. However, research on the longer term after stroke in a hospital based population is scanty.

A recent systematic review on depression post stroke including 23 studies showed that approximately one-third of survivors at any time up to five years after stroke are affected;[1] in this systematic review physical disability in the acute and later phases of stroke and stroke severity were consistently associated with depression. The follow up period of the hospital based studies in this review was only up to one year post stroke.

Another systematic review on this topic demonstrated that the prevalence of depression is stable across studies assessing patients at different time points in different areas of the world.[2] Across 43 studies, 29 studies used validated scales, 2 studies used a validated question as a definition of PSD, and 12 studies used DSM IV criteria; However, only two studies were based on a hospital population and had a follow up time of more than one year.[3, 4] Major predictors of depression were found to be: disability, depression pre-stroke, cognitive impairment, stroke severity and anxiety; On the other hand, depression was also found to be a predictor of lower quality of life, higher mortality and disability after stroke.

Depressive symptoms in the acute or subacute phase after stroke are associated with persistence of depression after 12 months.[5, 6, 7] To what extent socio-demographic factors (age, sex, educational level) contribute to PSD risk on the longer term is still out for debate.[6]

Depression is often poorly recognized and receives suboptimal treatment in primary care.[8] This is important, as chronic stroke patients usually do not receive intensive therapy anymore one year after stroke.

Several interventions have been reported to be effective in PSD. In an uncontrolled study cognitive behavioral therapy led to lower depression scores, compared with baseline.[9] A meta-analysis in stroke patients provided evidence for the positive effects of exercise on depression.[10] In addition, antidepressive medication seems to have an effect on PSD superior to placebo.[11]

Given the large impact of depression in patients after stroke, and the opportunities for treatment, identification of patients at risk, even in the later phases, is important. As literature on PSD in the chronic phase of hospital based populations is scarce, the aim of this study was to determine the prevalence of depressive mood in this specific population. Secondly, it aimed to determine which patient and stroke characteristics and measures of their current health status are associated with depressive mood. These results can guide professionals in order to identify and advise patients adequately along the line of therapy, and to make evidence-based decisions in treatment options.

Methods

Study design

This study was executed in 2012 at the Haaglanden Medical Center (HMC), a large teaching hospital in The Hague, The Netherlands. It has a comprehensive stroke department with vascular neurologists, neuro-interventionalists and vascular neurosurgeons.

Data were collected by means of patient reported outcome measures. Additional medical information was extracted retrospectively from the participants' medical records. The study was judged to fall outside the remit of the Medical Research Involving Human Subjects Act by the Medical Ethics Review Committee South West Netherlands, and a written exemption from ethical approval was obtained. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2013 (https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/); accessed April 7, 2017). Written informed consent was obtained from all patients participating in the study. This study conforms to all STROBE guidelines and reports the required information accordingly (see Supplementary Checklist).

Patients

All patients hospitalized for a stroke between January 2008 and December 2010 were identified from the hospital registries. From patients who had been hospitalized for a stroke more than once during the study period, only the first admission was taken into account. The following inclusion criteria were used: a. first ever ischaemic or haemorrhagic stroke; b. age

18 years or older at the time of hospitalization. Exclusion criteria were: a. other diagnosis such as traumatic brain injury, cerebral neoplasms or transient ischaemic attack (TIA); b. medical condition not allowing participation (patients in a vegetative state); c. insufficient Dutch language skills.

Subsequently, of all potentially eligible patients the hospital and town council registries were checked to identify any deceased patients.

Patients were invited by the treating physician to participate by means of a letter and an information leaflet. Participation concerned the completion of a questionnaire about their current health status and of a questionnaire by their spouse or other caregiver, if applicable. They were asked to return the questionnaires and a signed informed consent form using a pre-stamped envelope. Patients were instructed to take their time, and were encouraged to complete the questionnaires. In case of no response patients were contacted by telephone by a research nurse.

Assessment methods

Stroke-related determinants

Of all patients who agreed to participate in the present study, data were collected from the medical records about the type of stroke (hemorrhagic/ischaemic), lateralization (left hemisphere / right hemisphere / vertebrobasilar), thrombolysis treatment (rtPA), functioning after admission to and at discharge from hospital (Barthel Index;[12] score range 0 to 20) and duration of hospital stay (Length of Hospitalization – LOS).

Socio-demographic determinants

The survey comprised questions on the following socio-demographic determinants: life style characteristics (smoking Y/N, alcohol Y/N), educational level (Low: up to and including lower technical and vocational training; medium: up to and including secondary technical and vocational training; and high: up to and including higher technical and vocational training and university), living alone or not (social situation), and being born in the Netherlands or not (ethnicity).

Measures of current health status

The outcomes with respect to psychological and physical functioning concerned the following aspects:

- Anxiety and depression were measured by means of a Dutch version of the Hospital Anxiety and Depression Scale (HADS) which contains two 7-item scales, one for anxiety and one for depression, both with a score range of 0–21.[13] A higher score means higher level of depression or anxiety. A HADS-D score of 8 points or higher is used as a cut off point for clinically relevant depressive symptoms.[13]

- Coping was measured using the CopeEasy (Coping Orientations to Problems Experienced), a self-reported questionnaire comprising 32 items, with an ordinal scale from 1 to 4.[14, 15] It describes the extent to which three different types of coping strategies are used by patients to deal with their situation: Active, Avoiding and Seeking Support. Higher scores mean the patient uses this coping strategy more.

- The FAI (Frenchay Activity Index) describes the level of activities and participation. This inventory scores the frequency of 15 activities on a 4 point scale (range 0-3, never – frequently). The maximum score is 45 points and represents the highest level of functioning.[16]

- Caregiver strain was measured using the Caregiver strain index (CSI): This questionnaire consists of 13 items to assess the subjective care load of the caregiver, range from 0 to 13; higher means more caregiver strain. A score of seven or more indicates a high level of strain. [17, 18]

Healthcare usage was estimated by the number and type of physicians visited in the last six months (none or 1 physician; 2 or more physicians).

Health related quality of life

The SF-36 is a generic instrument with 36 items covering eight domains (physical function, role physical, bodily pain, general health, vitality, social function, role emotional, and mental health). The SF-36 subscale scores range from 0 to 100, with a higher score indicating better health status. From these, a physical and a mental summary scale can be computed.

Scoring of the summary scales is undertaken by weighting and summing the original eight dimensions. These weights are gained from factor analysis of data from a general population. The SF-36 has been translated and validated by Aaronson et al into a Dutch version.[19]

Patients described their general health status using the EuroQol classification system (EQ5D), consisting of 5 questions on mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.[20] From the EQ5D classification system, the EQ5D utility index was calculated. The five 3-point Likert questions of the EQ5D yield a summary score ranging from –0.329 (no health) to 1 (full health).

Analysis

A missing or incomplete answer on a question was considered as a missing value. If an individual patient did not meet the questionnaire-specific rules regarding the maximum number of missing values to calculate the total or subscale scores, the total numbers do not add up to 207 subjects.

Comparisons of age, sex, Barthel Index on admission, Barthel at discharge and discharge destination between patients who completed the questionnaires versus those who were eligible but did not participate were done by unpaired T-tests or Chi-Square tests.

Descriptive statistics were used for the stroke-related and patient characteristics, the measures of current health status and caregiver strain (mean (SD) or median (inter quartile range; IQR) dependent on their distribution).

We dichotomized the population according to their score on the HADS depression (HADS < 8, or HADS ≥ 8).[13] The group with higher depression scores was compared with the group with lower depression scores by means of univariate logistic regression analysis, with adjustment for age, sex and Barthel at discharge as confounders. Independent variables were categorized into patient characteristics (educational level, social situation, ethnicity), stroke characteristics (type and localization of stroke, length of hospitalization, Barthel Index at admission and discharge, discharge destination) and measures of current health status and caregiver strain (HADS-Anxiety, CopeEasy, FAI, SF-36, EQ5D, CSI and healthcare usage). Results were reported as odds ratios (OR) with 95 % confidence interval (CI). For the EQ5D we multiplied the outcome by 10 in this analysis (EQ5D-decile), to have a meaningful OR of a

raise of 0.1 point in the EQ5D. Analysis of interaction effects was conducted for sex and age in relation to patient characteristics, stroke characteristics and patient reported outcomes by means of additional logistic regression analysis.

Statistical analyses were performed using IBM SPSS Statistics, version 22. For all analyses, p≤0.05 (2-tailed) was considered the criterion for statistical significance.

Results

A total of 576 patients met the inclusion criteria of the study, of whom 207 (36%) gave informed consent and returned the questionnaires. There were no significant differences between responders and non-responders with respect to sex, age, Barthel Index on admission or discharge destination (Figure 1). The Barthel Index at discharge was higher for the responders compared to the non-responders (T-test, p = 0.01). The difference is less than 1.85 which is considered as the Minimal Clinically Important Difference (http://www.rehabmeasures.org/Lists/RehabMeasures/DispForm.aspx?ID=916).

Patient and stroke-related determinants (Table 1)

The mean age of the responders was 63.8 years (SD 14.2) at time of stroke, 60.4% were male. The median duration of hospital stay was 7 days (IQR 7). During admission the median Barthel Index improved from 14 (IQR 11) to 19 (IQR 8) at discharge, with 77 of 174 (44.3%) reaching the maximal Barthel score (20 points) at discharge. The majority of the patients was discharged to their homes (53.6%); others were transferred to another hospital, a rehabilitation clinic or a nursing home. 161 of 204 patients were born in the Netherlands (78.9%). Of the 43 patients born abroad 4 were European of origin, the others were born in Africa, Middle East or Indonesia.

181 patients (87.4%) had had an ischaemic stroke. The stroke location was predominantly supratentorial (164 patients, 79.2%), whereas 43 (20.8%) were cerebellar- or stem lesions. One patient had bilateral cerebral lesions.

The mean time of follow up was 36.3 months (SD 9.9; range 21 to 57 months). At follow up 29 of 205 patients (14.1%) were currently smoking and 90 of 205 patients (43.9%) used alcohol. Most patients were living with a partner (135 of 204 patients, 66.2%).

58 patients (29.4%) had seen 2 or more physicians in the last 6 months.

Current health status

In Table 2 the results of the measures concerning the patients' current health status and the caregiver strain are presented. Of the patients 38 (22.2%) had a FAI score lower than 15, indicating a serious level of dependence.

Risk of depression

Of 196 patients who completed the HADS, 67 (34.2%) had a score of 8 or higher on the depression scale of the HADS, which is an indication of clinically relevant depressive symptoms. In both groups 9 patients had visited a psychiatrist in the last 6 months. Male sex (0.46; CI 0.22 – 0.93) and being born abroad (OR 2.70; CI 1.31 – 5.53) was associated with a HADS depression score ≥ 8 at follow up, adjusted for age, sex and Barthel Index at discharge; less patients in the depression group drank alcohol (Table 3).

In Table 4 the current health status of patients and their caregiver strain in relation to depression are presented. The subgroup with depression score ≥ 8 were compared to patients with depression score < 8, adjusted for age, sex and Barthel Index at discharge. Patients with higher depression scores showed higher anxiety scores and lower outcomes on daily activities (FAI, OR 0.90; CI 0.87 – 0.94). They were significantly more avoidant in their coping (OR 8.26; CI 3.92 – 17.41). The Quality of Life was substantially lower (EQ5D-decile, OR 0.38; CI 0.28-0.51; PCS, OR 0.91; CI 0.88 – 0.94; MCS, OR 0.85; CI 0.81 – 0.89). Their caregivers showed higher strain levels (OR 1.28; CI 1.14 – 1.43).

According to the interaction analysis of age and sex on outcome measures no interaction was observed except for two relations: the relation between the FAI and depression was influenced by age; the relation between the EQ5D and depression was influenced by sex.

Discussion

In this hospital-based cohort of 207 subjects 2-5 years after stroke, one third was at risk for a depression. This subgroup showed a lower level of activities, was more avoidant in their coping, and had a lower quality of life; their caregivers experienced more strain. Being born abroad and male sex were related to higher depression scores.

The stroke severity in this cohort was comparable to other hospital based studies as can be concluded from the Barthel Index on admission to the hospital (median 14 points), and at discharge (Barthel Index of 19 or above in 50%). At follow up 22.2% were seriously limited in their activities (FAI < 15 points). These determinants are in line with other hospital based stroke studies.[7, 21]

In a meta-analysis the prevalence of PSD was 29% after follow up of more than 1 year, and 30% in hospital based studies.[2] Two hospital based studies had a follow up of more than 1 year, they used different instruments to identify PSD. Robinson et al used the DSM IV, resulting in 42% of the patients with a minor or major depression.[3] Gesztelyi et al used the Becks Depression Inventory;[4] 26% scored 10 point or more as an indicator of a mild depression or worse. In a recent prospective study with follow up of 1 year 27% of the stroke patients scored ≥ 8 on the depression scale of the HADS.[7]

In recent literature the risk of depression was found to be related to the initial severity of the stroke.[1, 2, 6, 7] In the present study the Barthel Index at discharge, as a proxy variable for stroke severity, was used as a covariate in the logistic regression in order to evaluate the risk of depression irrespective of the neurological deficit.

Male participants scored significantly higher on the HADS depression subscale in this study. In the literature, the relation between sex and depression in stroke patients is not consistent. Being female was a negative predictor for the EQ5D in one study.[22] In another study, male gender was an additional predictor for post-stroke depressive symptoms 3 years after stroke.[23] Kootker et al found no influence of gender on depression.[7] Age and gender did not predict depression in six out of the seven studies in a meta-analysis.[2]

The results show that ethnicity is a predictive factor for the development of depressive symptoms, being born abroad is related to higher depression scores on the HADS. Other

studies consistently report an elevated burden of stroke in some race/ethnic groups, e.g. Hispanics and Blacks compared with Whites.[24] Latino stroke survivors have a significantly higher prevalence of depression compared to their non-Latino counterparts.[25] The reason for the influence of ethnicity is unknown; social, environmental and genetic factors can be involved.

Stroke localization was not related to depression in this study. In a systematic review only 1 study reported a significant association between PSD and stroke location;[6] subcortical and ACA lesions were independent risk factors for PSD. The study of Kootker et al suggested a small contribution of a lesion in the PCA as a risk factor for PSD. [7] In another recently published study, PSD was not related to lesion location.[26]

Inactivity, defined as a low score on the FAI, and depression are closely related in literature.[27] We confirmed the close relationship between lower outcomes on the FAI and mood disturbances (HADS-D ≥ 8). This relation was not influenced by the initial stroke severity, age or sex, as these factors were used as covariates in the analysis.

An avoidant coping strategy was related to higher depression scores in this study. In a hospital based study, avoidance was the independent factor most closely related to post stroke depression 3 months after stroke.[26] Avoidant responses may be more effective for managing short-term threats, but for long-term threats problem-solving coping may manage stress more effectively.[28] Stroke patients who prefer an accommodative coping strategy, accepting the consequences of an event, show fewer symptoms of depression;[29] this accommodative coping strategy corresponds largely to a less avoidant coping style.

The burden of caregivers was comparable to the results of previous studies on this subject, although the follow up was shorter, 6 months and 12 months respectively.[21, 30] As expected from this literature, the CSI was strongly related to depressive symptoms of the patients.

Due to the cross sectional design causal relations cannot be inferred. Another limitation of the study was that data on comorbidity, on the current treatment of depression and on cognitive deficits were not available. Furthermore, survey studies may be subject to response bias, therefore interpretation of the results must be done with care. Nevertheless, responders and non-responders were comparable with respect to age, sex, Barthel on admission

and discharge destination. Notably, the characteristics of responders in the current study population were comparable with other stroke populations.

In conclusion, the present study found that depression is a relatively common problem even in the chronic phase after stroke, and is strongly related to coping style, Quality of Life, activities in daily life and participation. Caregivers of depressed patients experience a large burden. A higher risk of a depression in the chronic phase after stroke is observed in male patients and in patients from abroad.

The cross-sectional design of the study does not allow conclusions on potential targets for interventions, as it is not possible to make causal inferences. Research on causal relationships is essential, however for that purpose a prospective study design is needed.

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Figure 1. Characteristics of responders and non-responders.

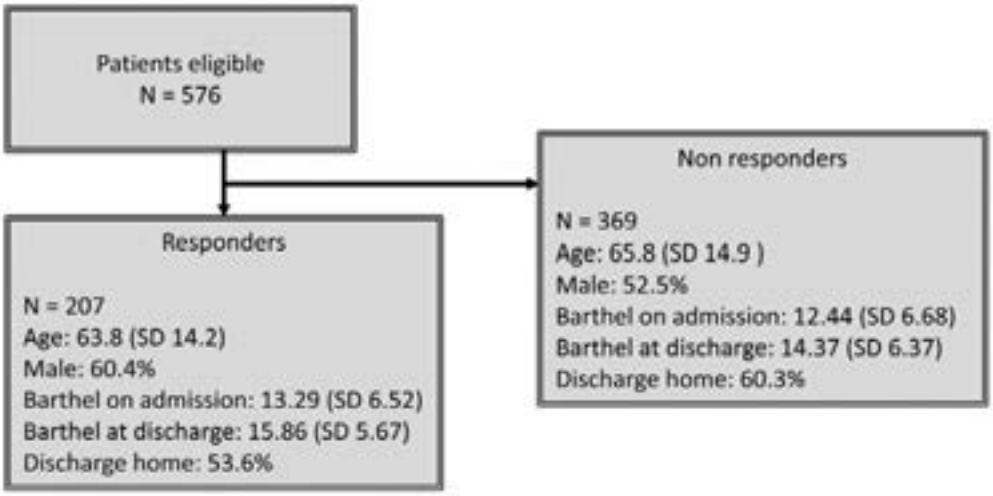

Table 1. Patient characteristics and stroke characteristics.

		Responders, N = 207
Patients' characteristics		
Mean age at stroke, years (SD)		63.8 (14.2)
Sex (%) Male/ Female		125 (60.4) / 82 (39.6)
Follow up		
- 2-3 years (%)		93 (45)
- 3-4 years (%)		63 (30)
- 4-5 years (%)		51 (25)
Mean duration of follow-up; Months (SD)		36.3 (9.9)
Educational level, number (%):	- Low	72 (36.2)
	- Middle	72 (36.2)
	- High	55 (27.6)
Social situation, living together (%)		
Yes / No		135 (66.2) / 69 (33.8)
Born in the Netherlands (%)		
Yes / No		161 (79) / 43 (21)
Smoking (%)		
Yes / No		28 (14) / 168 (86)
Alcohol (%)		
Yes / No		87 (44) / 109 (56)
Stroke Characteristics		
Type of stroke:	- ischaemic number (%)	181 (87.4)
	- hemorrhagic (%)	26 (12.6)
Lesion; Number (%)		
	- Left hemisphere	97 (46.9)
	- Right hemisphere	66 (31.9)
	- Bilateral	1 (0.5)
	- Vertebrobasilar	43 (20.8)
Thrombolysis (%)		49 (23.7) / 156 (76.3)
Yes / No		
Length of hospital stay, days; median (IQR)		7 (7)
Barthel Index (0-20; worst – best); Median (IQR)		
Admission / Discharge		14 (11) / 19 (8)
Discharge (%):		
Home / other institution		98 (53.6) / 85 (46.4)

Abbreviations: SD = standard deviation, IQR = interquartile range

Table 2. Current health status of stroke patients and caregiver strain.

Outcome	**Mean (SD)**
HADS	
Score 0-21; best-worst	
- Anxiety	5.41 (4.71)
- Depression	5.57 (4.93)
Cope Easy	
Score 1-4; less-more	
- Active coping	2.01 (0.75)
- Avoidant coping	1.67 (0.59)
- Seeking support	1.87 (0.66)
FAI	
Score 0-45: worst-best	23.19 (10.82)
SF 36	
- PCS	41.49 (13.57)
- MCS	46.44 (12.53)
EQ5D	0.73 (0.25)
CSI total score	
Score 0-13; worst-best	4.46 (3.71)
Healthcare usage:	
- 0 or 1 physician (%)	139 (70.6)
- 2 or more physicians (%)	58 (29.4)

Abbreviations: SD = standard deviation, HADS = Hospital Anxiety and Depression Questionnaire, FAI = Frenchay Activity Index, SF-36 = Short Form 36 Health Survey, PCS = physical component summery scale, MCS = mental component summery scale, EQ5D = EuroQol, CSI = caregiver strain index

Table 3. Depression in relation to patient and stroke related characteristics. Univariate logistic regression (OR (95% CI)), adjusted for Barthel at discharge, age and sex.

Patient characteristics	N	HADS-d < 8	N	HADS-d ≥8	OR (95% CI)	p level
Mean age at stroke, years	129	64.7	67	61.9	0.99 (0.96 – 1.01)	0.253
Sex, Male/Female	129	72/57	67	47/20	0.46 (0.22 – 0.93)	0.032
Educational level low/middle/ high	125	42/45/38	66	27/24/15	*	0.076
Social situation living together/alone	128	82/46	67	47/20	1.17 (0.56 – 2.47)	0.673
Born Netherlands/abroad	128	109/19	67	45/22	2.86 (1.29 – 6.31)	0.010
Smoking Yes/No	129	15/114	67	13/54	0.68 (0.27 – 1.72)	0.412
Alcohol Yes/No	129	65/64	67	22/45	2.31 (1.12 – 4.74)	0.023
Stroke characteristics						
Stroke location Left/Right/vertebrobasilar	128	58/41/29	67	31/23/13	*	0.693
Stroke type Ischaemic/hemorrhagic	129	114/15	67	56/11	1.14 (0.43 – 3.04)	0.789
Thrombolysis Yes/No	128	33/95	67	14/53	2.19 (0.91 – 5.26)	0.079
Barthel on admission mean (SD)	112	13.6 (6.5)	53	12.4 (6.7)	0.98 (0.91 – 1.06)	0.579
Barthel at discharge mean (SD)	112	16.2 (5.7)	53	15.0 (5.9)	0.96 (0.91 – 1.02)	0.174
Length of hospital stay mean (SD)	129	7.8 (5.9)	67	10.5 (11.3)	1.05 (0.99 – 1.10)	0.102
Discharge destination Home/other	114	64/50	60	29/31	0.86 (0.35 – 2.15)	0.754

*Abbreviations: SD = standard deviation. * in these 3-category variable the OR value is less informative.*

Table 4. Depression in relation to measures of health status and caregiver strain, adjusted for Barthel (discharge), age and sex; univariate logistic regression (OR (CI 95%)).

	N	HADS-d < 8	N	HADS-d ≥8	OR (95%)	p level
HADS anxiety						
Score 0-21; best-worst	195	3.1		9.9	1.82 (1.50 – 2.20)	<0.001
Cope Easy (SD)						
Score 1-4; less-more						
- Active coping	165	2.0 (0.8)		2.1 (0.7)	1.13 (0.68 – 1.89)	0.653
- Avoidant coping	172	1.5 (0.5)		2.1 (0.6)	8.33 (3.66 – 18,93)	<0.001
- Seeking support	176	1.8 (0.7)		2.0 (0.6)	1.38 (0.76 – 2.52)	0.294
FAI (SD)						
Score 0-45: worst-best	171	26.5 (9.1)		17.6 (11.6)	0.90 (0.86 – 0.95)	<0.001
SF 36 (SD)						
- PCS	186	46.3 (12.9)		33.1 (10.8)	0.91 (0.87 – 0.94)	<0.001
- MCS	186	52.8 (7.9)		35.6 (11.0)	0.86 (0.82 – 0.90)	<0.001
EQ5D (SD)	195	0.85 (0.14)		0.52 (0.27)	0.33 (0.23 – 0.48) ‡	<0.001
CSI total score (SD)						
Score 0-13; worst-best	133	3.2 (3.1)		6.3 (3.8)	1.30 (1.13 – 1.49)	<0.001
Health care usage	123		65		2.20 (1.14 – 4.25)	0.062
- 0 or 1 physician		94		39		
- 2 or more physicians		29		26		

Abbreviations: SD = standard deviation, OR = Odd's Ratio, HADS = Hospital Anxiety and Depression Questionnaire, FAI = Frenchay Activity Index, SF-36 = Short Form 36 Health Survey, PCS = physical component summery scale, MCS = mental component summery scale, EQ5D = EuroQol, CSI = caregiver strain index.

‡ The OR of the EQ5D refers to a change in a decile of the score (0.1 points)