RESEARCH PAPER

Declining daily functioning as a prelude to a hip fracture in older persons—an individual patient data meta-analysis

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†TULIPS consortium: The TULIPS consortium includes the research groups of four population-based longitudinal studies on the very old. These studies and their principle investigators are the Leiden 85-plus Study (PI Prof. Dr. Jacobijn Gussekloo), the Newcastle 85+ Study (PI Louise Robinson), the Life and Living in Advanced Age in New Zealand (LiLACS NZ) Study (PI Prof. Dr. Ngaire Kerse) and the Tokyo Oldest Old Survey on Total Health (TOOTH; PI Prof. Dr. Yasumichi Arai).

Abstract

Background: Daily functioning is known to decline after a hip fracture, but studies of self-reported functioning before the fracture suggest this decline begins before the fracture.

Objective: Determine whether change in functioning in the year before a hip fracture in very old (80+) differs from change in those without a hip fracture.

Design: Two-stage individual patient data meta-analysis including data from the Towards Understanding Longitudinal International older People Studies (TULIPS)-consortium.

Setting: Four population-based longitudinal cohorts from the Netherlands, New Zealand and the UK.

Subjects: Participants aged 80+ years.

Methods: Participants were followed for 5 years, during which (instrumental) activities of daily living [(I)ADL] scores and incident hip fractures were registered at regular intervals. Z-scores of the last (I)ADL score and the change in (I)ADL in the year before a hip fracture were compared to the scores of controls, adjusted for age and sex.

Results: Of the 2,357 participants at baseline, the 161 who sustained a hip fracture during follow-up had a worse (I)ADL score before the fracture (0.40 standard deviations, 95% CI 0.19 to 0.61, \( P = 0.0002 \)) and a larger decline in (I)ADL in the year before fracture (−0.11 standard deviations, 95% CI −0.22 to 0.004, \( P = 0.06 \)) compared to those who did not sustain a hip fracture.

Conclusions: In the very old a decline in daily functioning already starts before a hip fracture. Therefore, a hip fracture is a sign of ongoing decline and what full recovery is should be seen in light of the pre-fracture decline.

Keywords: disability, hip fracture, function, older people
Older people who experience a hip fracture have worse daily functioning before the fracture. Treatment goals after a hip fracture should focus on optimising quality of life and stabilising further loss of function. A hip fracture does not mark the start of decline, but it is a sign of ongoing decline. The rate of decline in daily functioning leading up to the fracture is accelerated up to a year before the event.

Between September 1997 and September 1999, 705 subjects were included in the Leiden 85-plus Study. For 1,470 subjects (n = 1,470), information on functional status and other health outcomes was obtained from the GPs’ medical records. Of the 1,042 eligible subjects in the cohort, 849 subjects were unreachable and 358 subjects refused to participate. Of the 1,636 eligible subjects in 2010 (766 Māori and 870 non-Māori), 17 died before enrolment, 33 subjects were unreachable and 358 subjects refused to participate. Of the 1,042 eligible subjects in the cohort, 849 were included in this study because they had both a complete health assessment and a GP record review. At baseline and after 1.5, 3 and 5 years (starting at age 85), participants were visited at their place of residence by a research nurse for a structured face-to-face interview and (self-report) function tests. Information on the presence of known disease (including hip fracture) was obtained annually from general practitioners’ (GP) and elderly care physicians’ medical records. The study population has been described previously in more detail [16, 17].

Leiden 85-plus study

In the population-based longitudinal Leiden 85-plus Study, all inhabitants of the Lakes or Bay of Plenty District Health Board areas (New Zealand) of the 1920–1930 birth cohorts (Māori) or the 1925 birth cohort (non-Māori) were eligible for study participation. Of the 1,636 eligible subjects in 2010 (766 Māori and 870 non-Māori), 17 died before enrolment and 699 refused to participate. In total, 937 participants (421 Māori and 516 non-Māori) were included in the cohort. For 5 years (starting at age 85 for non-Māori and between age 80 to 90 for Māori), all participants were visited annually.
at their place of residence by a research nurse. Structured face-to-face interviews and (self-report) function tests were conducted. Information on the presence of known disease (including hip fracture) was obtained annually from GPs’ medical records and hospital data. The study population has been described previously in more detail [18, 19]. Throughout the rest of the manuscript the M¯aori and non-M¯aori cohorts will be reported separately, because of known health differences between these cohorts [18, 20].

Daily functioning
Participants’ daily functioning was measured with a self-report questionnaire including questions on basic activities of daily living (ADL) and instrumental activities of daily living (IADL) at each follow-up visit during the face-to-face interviews. ADL items in these combined questionnaires included amongst others bathing, toileting and transferring in and out of bed, while IADL items in the questionnaires included for example shopping and going up and down stairs (Appendix 1).

- In the Leiden 85-plus cohort, the 18-item Groningen Activities Restriction Scale (GARS) was used, which includes 11 ADL and seven IADL questions. Each question had four answer categories (i.e. (1) fully independent without problems; (2) fully independent, but with some difficulty; (3) fully independent, but with a lot of difficulty; (4) only with another person’s help). The total score ranged from 18 to 72, with a higher score indicating worse daily functioning.

- In the Newcastle 85+ cohort, a summed score of 12 ADL and five IADL questions (Summed Score) was used. Each question had four answer categories (i.e. (1) I have no difficulty doing this by myself; (2) I have some difficulty doing this by myself; (3) I can only do this by myself if I use an aid or appliance; (4) I am unable to do this by myself, I need someone else’s help). The first answer category (1) was coded as 0 ‘activity performed without difficulty’ and the other categories (2, 3 and 4) were coded as 1 ‘activity performed with difficulty’. This gave a total score ranging from 0 to 17, with a higher score indicating worse daily functioning.

- In the LiLACS NZ cohort, daily functioning was assessed with seven ADL and four IADL items derived from the Nottingham Extended Activities of Daily Living questionnaire (core NEADL). Each item had three answer categories (i.e. (0) not able at all; (1) able with help; (2) on my own with difficulty or on my own). The total score ranged from 0 to 22, with a lower score indicating worse daily functioning. To standardise the direction of the daily functioning scales, the individual core NEADL scores in the LiLACS NZ cohort were inverted (i.e. score\(_{\text{maximum}}^{\text{score}_{\text{individual}}})

For the analyses the daily functioning scales were standardised by subtracting in each cohort the sample mean of the baseline measurement from the individual score and dividing that by the sample’s standard deviation of the baseline measurement (i.e. standardised z-score = \(\frac{\text{score}_{\text{individual}} - \text{mean score}_{\text{sample baseline}}}{\text{SD}_{\text{sample baseline}}}\)). In case of a missing (I)ADL score, which occurred less than 20 times per measurement moment, that measurement was excluded from the analyses.

Participants
All studies obtained ethical approval [Medical Ethics Committee of the Leiden University Medical Center (1997); Newcastle and North Tyneside Local Research Committee One (Ref: 06/Q0905/2); national New Zealand Ministry of Health ethics Committee (NTX/09/09/088)] and all participants gave informed consent. An additional exclusion criterion for the present study was a hip fracture in the 12 months before the baseline visit.

Hip fractures
In all three studies, incident hip fractures during follow-up were extracted from the medical records from the GP (Leiden 85-plus and Newcastle 85+ cohorts) or the hospital records (LiLACS NZ cohort). In the LiLACS NZ cohort, the presence of a hip fracture was cross-checked with the Accident Compensation Corporation (ACC) records. All (proximal) femur fractures and intertrochanteric fractures were counted as a hip fracture. Only the first incident hip fracture during follow-up was counted as an event. In the Newcastle 85+ cohort and the LiLACS NZ cohort, the exact date of hip fracture during follow-up was also extracted from the GP or hospital records, respectively. In the Leiden 85-plus cohort, GP records were checked annually for incident hip fractures in the previous year, but no date of the hip fracture was registered. For the analyses, the date of hip fracture in the Leiden 85-plus cohort was set to the middle of the date of the visit at which the hip fracture was reported and the previous visit date (or to the date of death if there was no visit after the hip fracture). Only the two (I)ADL measurements before the fracture (t) were used (i.e. t – 1 and t – 2, with t = time of hip fracture). As a result, in the analyses on pre-fracture (I)ADL score and on change in pre-fracture (I)ADL score only participants with at least one (i.e. hip fracture at age 86 or older) and two (i.e. hip fracture at age 87 or older) measurements before the hip fracture were included, respectively.

Control subjects
All participants without a hip fracture were included as controls. Those without a hip fracture could potentially contribute five measurements (three in the Newcastle 85+ cohort). In univariate analysis of change in pre-fracture (I)ADL, an average yearly change was computed using all available measurements. In the other analyses, all measurements of those without a hip fracture were included separately.
Statistical analyses

A two-stage individual participant data (IPD) meta-analysis approach was used for all analyses. In the first stage, the change in (I)ADL prior to a hip fracture was compared to change in (I)ADL for subjects without a hip fracture. This analysis was performed in each cohort separately. In the second stage, the results from each of the cohorts were pooled using methods that are commonly used in meta-analysis (details are described below).

The first-stage (cohort level) analyses were performed using IBM SPSS Statistics version 27.0 (IBM, Armonk, NY, USA). The second-stage analyses (i.e. pooling of cohort results) were performed using Review Manager 5.4.1 (The Cochrane Collaboration, Copenhagen, Denmark).

Cohort level analyses

Categorical variables were presented as frequency with percentage of the total. Continuous variables were described as median with interquartile range (IQR). Data were analysed using linear regression [21].

Last pre-fracture (I)ADL measurement

The (I)ADL score in the year before a hip fracture (i.e. pre-fracture (I)ADL) was compared to the (I)ADL score of those without a hip fracture with a univariate linear regression model with the last of the (I)ADL measurements (i.e. t−1) as dependent and the presence of hip fracture (yes/no) as independent variable. To be able to correct for age and sex, the data were also analysed with a multivariate linear regression model, with the last of the (I)ADL measurements (i.e. t−1) as the dependent variable, and the presence of hip fracture (yes/no), age at t−1, and sex (male/female) as independent variables (Appendix 2). To take correlation between the measurements within subjects into account, we used non-parametric bootstrapping (1,000 bootstrap samples with replacement), stratified by hip fracture status and measurement moment.

Change in pre-fracture (I)ADL

With a univariate linear regression model, change in (I)ADL in the year before a hip fracture (i.e. pre-fracture delta (I)ADL = (I)ADL-1−(I)ADL−2) was compared to an average yearly change in those without a hip fracture (i.e. the last observed (I)ADL score minus the first observed (I)ADL score divided by the number of observed years: [(I)ADLlast−(I)ADL40]/t). The univariate model included the delta (I)ADL score as dependent and the presence of hip fracture (yes/no) as independent variable.

To be able to correct for age, sex and the last pre-fracture (I)ADL measurement, the data were also analysed with multivariate linear regression. The multivariate model assessed whether there was a difference in change in (I)ADL in the year before hip fracture even if there would be no difference in (I)ADL score in the year before hip fracture. The model included the first of the two (I)ADL measurements (i.e. t−2) as dependent, and the presence of hip fracture (yes/no), age at t−1, the last of the two (I)ADL measurements (i.e. t−1), and sex (male/female) as independent variables (Appendix 2). Again, bootstrap resampling was used to correct the standard error for recurrence of controls.

Pooled analyses

Standardised z-scores were pooled using a random-effects model with inverse variance weighting. In addition, results were presented using forest plots. Heterogeneity between cohorts was quantified using the I²-statistic. Because of a different timing of measurements in the Newcastle 85+ cohort, the scores at 1, 2 and 4 years follow-up were computed based on the available measurements by assuming a linear change between the measurements. These computed values were included in all pooled analyses.

Sensitivity analyses

The time between the last (pre-fracture) measurement and the hip fracture was included in the multivariate regression models on pre-fracture (I)ADL and pre-fracture change in (I)ADL for additional sensitivity analyses. To assess whether the assumption of a linear effect of age was correct, the analyses on pre-fracture (I)ADL and pre-fracture change in (I)ADL were repeated with age as a categorical factor in the multivariate regression models. Age categories were based on the age participants were supposed to have at the different measurement moments (e.g. 85 years at baseline, 86 years at 1-year follow-up, etc.).

Results

The combined cohort included 2,357 participants of which 161 had a hip fracture during the 5-year follow-up (Figure 1). Mean age was 85 years (range 79 to 91) and 39% was male (n = 930). The mean age of hip fracture during follow-up was 88 (range 84 to 91) (Table 1).

Inconsistency between cohorts due to heterogeneity was limited in all adjusted analyses (I² < 30%) and was therefore not considered important for the summarised values [22].

Last (I)ADL measurement before hip fracture

Participants had a worse (I)ADL score in the year before the fracture compared to those without a fracture. This difference was 0.45 (95% CI 0.21 to 0.68) standard deviations (P = 0.0002) before correction, and 0.40 (95% CI 0.19 to 0.61) standard deviations (P = 0.0002) after correction for age and sex (Figure 2 and Appendix 2). In the cohorts this corresponds with a difference of 5.7 points (95% CI 2.7 to 8.7) on the GARS scale, 1.9 points (95% CI 0.9 to 2.9) on the Summed Score and 1.9 points (95% CI 0.9 to 2.9) for Māori and 1.7 points (95% CI 0.8 to 2.6) for non-Māori on the NEADL core questions.
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**Figure 1.** Study participants with (HF) and without (non-HF) hip fracture in the four study cohorts. **Note 1.** Medical records were checked on hip fracture incidence in the previous year. Corresponding pre-fracture (I)ADL scores were also from the previous year(s). For example, for a participant with a hip fracture registered at 'medical records checked 3 years after baseline', the (I)ADL scores at 2 years and 1 year after baseline were used in the analyses. In the LiLACS NZ Study, interview data were available up to 5 years after baseline (just like the other cohorts), but medical records were checked up to 6 years after baseline. **Note 2.** For the Newcastle 85+ cohort, hypothetical scores at follow-up years 1, 2 and 4 were computed by assuming a linear change in (I)ADL between the available measurements (i.e. at 0, 1.5, 3 and 5 years). As a result, the pre-fracture scores for participants with a hip fracture reported at follow-up years 3 and 5 were absent, because imputed scores (at follow-up years 2 and 4) would be based on post-fracture measurements.

**Change in (I)ADL score year before hip fracture**

In all four cohorts, the mean (I)ADL score slightly increased over time in the total population. Compared to the average yearly change in (I)ADL in those without a hip fracture, participants with a hip fracture showed an additional change in (I)ADL score in the year before the fracture of 0.15 standard deviations per year (95% CI 0.02 to 0.28; \( P = 0.02 \)) (Appendix 2). After correction for age, sex and the last measurement before the fracture, this difference in change in (I)ADL score was −0.11 standard deviations per year (95% CI 0.004 to −0.22; \( P = 0.06 \)) (Figure 3 and Appendix 2). This corresponds to an additional change of −1.6 points (95% CI 0.06 to −3.1) on the GARS scale, −0.5 points (95% CI 0.02 to −1.1) on the Summed Score and −0.5 points (95% CI 0.02 to −1.0) for Māori and −0.5 points (95% CI 0.02 to −1.0) for non-Māori on the NEADL core questions.

**Sensitivity analyses**

Adding the time between the last (pre-fracture) measurement and the hip fracture to the multivariate regression models did not change the effect estimates substantially in either direction of effect or significance. The same applies for including age as a categorical instead of a linear factor in the models.

**Discussion**

This study shows that before a hip fracture older adults already had a worse (I)ADL score compared to subjects of the same age who did not get a hip fracture. Furthermore, a larger decline in (I)ADL was observed in the year before fracture compared to the normal decline observed at that age in those without a hip fracture.

Previous research mostly focused on the change in daily functioning after a hip fracture. There are some studies that used retrospective self-report to describe the pre-fracture (I)ADL score [10, 12, 23, 24]. Although these studies also found a worse score just before the fracture, the results were prone to (recall) bias and thus could not be reliably interpreted. In a longitudinal study by Ritchie et al. [14], the pre-fracture (I)ADL score of participants with an incident hip fracture during study follow-up was compared to the (I)ADL score of age, sex and race-matched controls. The results of this study were less prone to (recall) bias, but the functional status before the hip fracture was not accurately captured because of a time gap of up to 30 months between the pre-fracture (I)ADL measurement and the fracture. In this study, the last pre-fracture measurement was better able to reflect the functional status right before the hip fracture. Furthermore, this study went one step further by also assessing change in (I)ADL in the year before the fracture.
Table 1. Characteristics at baseline of participants with (HF) and without (nonHF) a hip fracture during follow-up in the four cohorts separately

| Cohort                  | Total | Leiden 85-plus | Newcastle 85+ | LiLACS NZ | Māori | Non-Māori |
|-------------------------|-------|---------------|---------------|-----------|-------|-----------|
|                         | HF    | nonHF         | HF            | nonHF     | HF    | nonHF     | HF         | nonHF     | HF            | nonHF         | HF          | nonHF           |
| N                       | 161   | 2,196         | 42            | 552       | 67    | 770       | 15         | 400       | 37            | 474           | 15          | 400             |

**Sociodemographic characteristics**

|                          | Total | Leiden 85-plus | Newcastle 85+ | LiLACS NZ | Māori | Non-Māori |
|--------------------------|-------|---------------|---------------|-----------|-------|-----------|
| Age, mean (range)        | 85 (81–87) | 85 (79–91) | 85 (84–86) | 85 (84–87) | 85 (84–86) | 85 (84–86) | 85 (84–86) | 85 (84–86) | 85 (84–86) |
| Male, n (%)              | 52 (32.3) | 878 (40.0)  | 10 (23.8) | 192 (34.8) | 22 (32.8) | 297 (38.6) | 8 (53.3) | 167 (41.8) | 12 (32.4) |
| Living situation, n (%)  | 18 (11.2) | 235 (10.7) | 7 (16.7) | 94 (17.0) | 6 (9.0) | 74 (9.6) | 2 (13.3) | 28 (7.0) | 3 (8.1) |
| Independent alone        | 86 (53.4) | 1,128 (51.4) | 19 (45.2) | 261 (47.3) | 39 (58.2) | 424 (55.1) | 7 (46.7) | 242 (60.5) | 21 (56.8) |
| Independent with partner | 51 (31.7) | 751 (34.2) | 16 (38.1) | 197 (35.7) | 22 (32.4) | 272 (35.3) | 5 (33.3) | 118 (29.5) | 22 (56.8) |

**Functional parameters**

|                          | Total | Leiden 85-plus | Newcastle 85+ | LiLACS NZ | Māori | Non-Māori |
|--------------------------|-------|---------------|---------------|-----------|-------|-----------|
| (I)ADL Questionnaire     |       |               |               |           |       |           |           |           |               |
| Median (IQR)             |       |               |               |           |       |           |           |           |               |
| Z-score, median (IQR)    |       |               |               |           |       |           |           |           |               |
| Mobility (yes), n (%)    |       |               |               |           |       |           |           |           |               |
| Indoors                  | 107 (66.5) | 1,250 (56.9) | 42 (100) | 516 (93.5) | 65 (97.0) | 734 (95.3) |           |           |               |
| Outdoors                 | 140 (87) | 1852 (84.3)  | 35 (83.3) | 460 (83.3) | 57 (85.1) | 620 (80.5) | 13 (86.7) | 352 (88.0) | 35 (94.6) |
| Stairs                   | 118 (73.3) | 1,546 (70.4) | 33 (78.6) | 444 (80.4) | 54 (80.8) | 640 (83.1) | 8 (53.3) | 170 (42.5) | 23 (62.2) |
| MMSE, median (IQR)       | 27 (24 to 29) | 27 (25 to 29) | 25.5 (19.75 to 28) | 26 (22 to 28) | 28 (25 to 28) | 27 (24 to 28) | 27 (24 to 28) | 27 (24 to 28) | 27 (24 to 28) |

**Hip fracture during follow-up**

|                          | Total | Leiden 85-plus | Newcastle 85+ | LiLACS NZ | Māori | Non-Māori |
|--------------------------|-------|---------------|---------------|-----------|-------|-----------|
| N (%) study population    | 161   | 2,196         | 42            | 552       | 67    | 770       | 15         | 400       | 37            | 474           | 15          | 400             |
| Age at hip fracture, mean (range) | 88 (84–91) | 87 (85–90)  | 88 (85–91) | 87 (84–91) | 89 (86–91) |

HF: Hip fracture; nonHF: No hip fracture (control); (I)ADL: (Instrumental) activities of daily living; MMSE: Mini-mental state examination; Missing (n): ~Leiden 85-plus: non-HF mobility indoors/outdoors/stairs 2, (I)ADL (z-score) 2; HF none. #Newcastle 85+: non-HF mobility outdoors 1, mobility stairs 2, (I)ADL (z-score) 8, MMSE 6; HF mobility outdoors 1, (I)ADL (z-score) 1. *LiLACS NZ Māori: non-HF living situation 12, mobility outdoors 6, mobility stairs 153, (I)ADL (z-score) 10, MMSE 143; HF living situation 1, mobility stairs 6, MMSE 6. &LiLACS NZ non-Māori: non-HF living situation 70, mobility outdoors 3, mobility stairs 108, (I)ADL (z-score) 5, MMSE 113; HF living situation 5, mobility stairs 6, MMSE 6. % Total study population: non-HF living situation 82, mobility indoors 876, mobility outdoors 12, mobility stairs 265, (I)ADL (z-score) 25, MMSE 262; HF living situation 6, mobility indoors 52, mobility outdoors 1, mobility stairs 12, (I)ADL (z-score) 1, MMSE 12.

Figure 2. Last (I)ADL measurement (in z-scores) before a hip fracture compared to very old without a hip fracture after correction for age and sex (multivariate).
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Figure 3. Change in (I)ADL (z-score) in year before a hip fracture compared to very old without a hip fracture after correction for age, sex and last measurement (multivariate).

Several differences between the cohorts included in the current IPD meta-analysis should be mentioned. In the Leiden 85-plus and the Newcastle 85+ cohorts, both a worse pre-fracture (I)ADL score and a larger decline in the year leading up to that worse function were observed. This means that the decline in daily functioning could be captured in the last year before the hip fracture in these cohorts. However, although both in the Māori and non-Māori LiLACS NZ cohorts a worse pre-fracture (I)ADL score was observed, the larger decline leading up to that worse score was not captured in the last pre-fracture year. This could suggest that in these cohorts, the decline in daily functioning already started earlier than the one year before the fracture assessed in this study.

Strengths and limitations

In this study, data from four unique population-based observational cohorts of community-dwelling older people aged 80 years and over were combined. Combining these cohorts allowed for analyses that would be impossible in the individual cohorts because of the high number of incident hip fractures needed to have sufficient power. Furthermore, the considerable follow-up time with extensive measurements of functional status at regular intervals gave the opportunity to assess pre-fracture functioning without having to rely on retrospective self-report and with the advantage to come close to the functional status right before the hip fracture. A limitation of this study is the subtle but relevant difference between the (I)ADL scales used in the Leiden 85-plus Study and Newcastle 85+ Study as compared to the (I)ADL scale used in the LiLACS NZ Study. The first two studies asked participants whether they ‘can do’ a certain activity, while the latter asked whether they ‘do do’ the activity [25]. The influence of this difference in wording on the direction and magnitude of effect in the four cohorts cannot be assessed. Another limitation that should be mentioned is the inclusion of multiple birth cohorts in this IPD meta-analysis. Several studies have shown differences in hip fracture incidence between birth cohorts over the last decades and thus the cohorts included in this study might be more heterogeneous than expected [26, 27]. The lower hip fracture rate in the Māori cohort observed in this study also suggests there is heterogeneity between the cohorts.

To conclude, older people who experience a hip fracture have worse daily functioning before the fracture and the rate of decline in the (I)ADL score leading up to the fracture is accelerated up to a year before the event. This means that a decline in daily functioning already starts before the hip fracture. It is important for clinicians to keep these findings in mind when determining the treatment goals for octogenarians after a hip fracture. If the decline already started before the fracture, expectations about a full functional recovery should possibly be more tailored. Furthermore, our findings suggest that a hip fracture could sometimes be more of a symptom of an underlying medical problem and therefore should prompt a clinician to screen for other (acute) medical problems at hand. A focus on optimising quality of life, stabilising further loss of function and a less stringent focus on full functional recovery might be more appropriate.

Supplementary Data: Supplementary data mentioned in the text are available to subscribers in Age and Ageing online.

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