# 4

# Is accurate prediction of gait in nonambulatory stroke patients possible within 72 hours poststroke? The EPOS study

JM Veerbeek
EEH van Wegen
BC Harmeling-van der Wel
G Kwakkel
EPOS Investigators

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## ABSTRACT

**Background** Early prognosis, adequate goal setting, and referral are important for stroke management.

**Objective** To investigate if independent gait 6 months poststroke can be accurately predicted within the first 72 hours poststroke, based on simple clinical bedside tests. Reassessment on days 5 and 9 was used to check whether accuracy changed over time.

**Methods** In 154 first-ever ischemic stroke patients unable to walk independently, 19 demographic and clinical variables were assessed within 72 hours and again on days 5 and 9 poststroke. Multivariable logistic modeling was applied to identify early prognostic factors for regaining independent gait, defined as ≥4 points on the Functional Ambulation Categories (FAC).

**Results** Multivariable modeling showed that patients with an independent sitting balance (Trunk Control Test – sitting; 30 seconds) and strength in the hemiparetic leg (Motricity Index leg; e.g. visible contraction for all 3 items, or movement against resistance but weaker for 1 item) on day 2 poststroke had a 98% probability of achieving independent gait at 6 months. Absence of these features in the first 72 hours was associated with a probability of 27%, declining to 10% by day 9.

**Conclusions** Accurate prediction of independent gait performance can be made soon after stroke, using 2 simple bedside tests: "sitting balance" and "strength of the hemiparetic leg." This knowledge is useful for making early clinical decisions regarding treatment goals and discharge planning at hospital stroke units.

## INTRODUCTION

Regaining independent gait is considered a primary goal in stroke rehabilitation.[1] A number of prospective cohort studies have shown that approximately 60%[2,3] to 80%[4,5] of stroke patients are able to walk independently at 6 months poststroke. Early accurate prediction of the outcome in terms of independent gait poststroke is paramount for stroke management, in order to (1) facilitate an early start of proper discharge planning; (2) inform clients and their relatives properly; (3) set realistic multidisciplinary therapeutic goals;[6] and (4) anticipate possible consequences such as home adjustments and the need for community support.[7] A number of prognostic studies suggest that age,[8-10] severity of sensory and motor dysfunction of the paretic leg.[9,11] homonymous hemianopsia,[9,11] incontinence for micturation,[8,10] sitting balance,[10,12-14] initial disability in activities of daily living and ambulation,[2,10,12] level of consciousness on admission,[8] and the number of days between stroke onset and first assessment[15] are independently associated with gait outcomes 6 months after stroke.[12]

Unfortunately, it is difficult to compare results of these prognostic studies, due to differences in patient characteristics, the candidate determinants selected for regression modeling, measurement instruments used and definitions of gait, as well as poststroke timing of physical assessments, ranging from 7[10] to 14 days.[11,12] It is particularly the moment when clinical determinants are measured after a stroke that influences the accuracy of prediction, since early spontaneous neurological recovery as a function of time is an important confounder in understanding prognostic models.[3,16] This finding suggests that determinants such as continence, sitting balance, and severity of hemiplegia should be measured preferably at a fixed moment after stroke and not at nonfixed moments such as the time of admission to a stroke rehabilitation ward.[16,17]

The first aim of the present study was to investigate if independent gait at 6 months poststroke can be accurately predicted within the first 72 hours after stroke, in order to optimize early goal setting and referral policy in hospital stroke units. The second objective was to investigate the effects of early reassessment on days 5 and 9 on the accuracy of predicting outcomes in term of regaining independent gait at 6 months poststroke.

# MATERIALS AND METHODS

## Design and procedures

The EPOS study (acronym for Early Prediction of functional Outcome after Stroke) is a prospective cohort study with an intensive repeated-measurements design during the first 2 weeks poststroke. Patients were recruited from 9 hospital stroke units in the Netherlands. Assessments were performed within 72 hours and on days 5 and 9 poststroke. The main pragmatic reasons for (re)testing every 3 days were that daily testing would intervene in the usual rehabilitation program for included patients at (sub)acute stroke units, whereas previous studies have shown that the added value of day-to-day change is limited. Considering the nonlinear recovery pattern observed early poststroke as well as the early discharge policy of patients with stroke from hospital stroke units to other care facilities, we restricted to reassessment of the candidate determinants up till day 9 poststroke. Final outcome was measured at 6 months poststroke. All assessments were performed by trained physical therapists from each participating stroke unit, and patients received physical therapy treatment according to the Clinical Practice Guideline for physical therapy in patients with stroke.[18] The EPOS study was approved by the ethics committees of the participating hospitals.

## Subjects

Stroke was defined according to the World Health Organization criteria.[19] The Bamford classification was used to record the size and site of the infarct, based on clinical features.[20] Patients were included when they met the following criteria: (1) having suffered an ischemic first-ever anterior circulation stroke; (2) suffering from hemiparesis within 72 hours poststroke, even after application of recombinant Tissue Plasminogen Activator; (3) no disabling medical history (i.e. a premorbid Barthel Index score ≥19); (4) aged 18 years or older; (5) no severe deficits of communication, memory, or understanding; (6) being unable to walk independently (i.e. Functional Ambulation Categories [FAC] <4) within 72 hours; and (8) giving written informed consent to participate.

## Dependent variable

The outcome variable was independent gait, measured by the FAC. The FAC is a reliable and valid tool to classify the level of physical support needed by patients to ambulate safely after a stroke, and comprises six levels (0–5), ranging from ”nonfunctional ambulation” (0) to “ambulate independently, on level and non-level surfaces including stairs and inclines” (5).[21-23] For the present study, the FAC score was dichotomized into 0 (dependent gait, FAC <4) and 1 (independent gait, FAC ≥4).[22,23]

## Independent variables

The 19 variables used to develop a prediction model included gender, age, body mass index, social support, comorbidity (Cumulative Illness Rating Scale[24]), hemisphere of stroke, days between stroke onset and first assessment, type of stroke (Bamford classification[20]), urinary incontinence (Barthel Index[25] item 1), sitting balance (Trunk Control Test item 3 [TCT-s][26,27]; i.e. sitting unsupported for 30 seconds), muscle strength of the upper (Motricity Index [MI] arm[26,28]) and lower paretic limb (MI leg), synergism of the upper (Fugl-Meyer Assessment [FMA] arm[29]) and lower extremity (FMA leg), and 5 neurological functions: consciousness at onset (National Institutes of Health Stroke Scale [NIHSS][30] item 1A; no/yes), extinction or inattention (NIHSS item 11; yes/no), hemianopsia (NIHSS item 3; yes/no), conjugate deviation (NIHSS item 2; yes/no), and sensory loss (NIHSS item 8; yes/no).

## Data analysis



Only subjects with completed baseline and 6 months assessments were included in statistical analysis. Baseline demographics, stroke characteristics, and severity of impairments caused by the stroke were recorded. Candidate determinants were preferably dichotomized (0/1) on the basis of clinical grounds. Otherwise, the optimal cut-off point for each determinant was established by applying a receiver-operating characteristic analysis. Sensitivity/1-specificity and area under the curve for each cut-off score were used to estimate the optimal dichotomization for each individual variable. In case of missing values for days 5 or 9, the last value was carried forward.

Subsequently, bivariable logistic regression analysis was applied to calculate odds ratios (OR) with 95% confidence intervals (95% CI) for each individual variable to identify statistically significant determinants related to the dichotomized FAC score at 6 months. To prevent omission bias, determinants with a liberal significance level of $p \leq 0.10$ were selected for further analysis. Collinearity diagnostics ($r_s$) were used to prevent spurious relationships in the multivariable regression model. If the correlation coefficient ($r_s$) was ≥0.70, only one of these determinants was selected for further use in the multivariable analysis.

The retained determinants were used for forward stepwise multivariable logistic regression analysis. These analyses were tested two-tailed using critical p-values for entry and removal of ≤0.05 and ≥0.10, respectively. The probabilities of developing independent gait at 6 months poststroke were calculated from the multivariable model using the constants and regression coefficients of the included determinants in the following equation:

$P=1/(1+(\exp^{[-(\beta 0 + \beta 1X1 + \beta 2X2 + \beta 3X3 + \ldots + \beta nXn)]}))$

Finally, 2-way contingency tables were used to calculate sensitivity, specificity, and positive predictive value (PPV) and negative predicted value (NPV), including their 95% CIs, for the derived model within 72 hours and on days 5 and 9 poststroke. Statistics were performed using SPSS version 15.

# RESULTS

Between February 2007 and November 2009, 221 patients were recruited. Thirty-five patients were lost to follow-up, for reasons including death (N=21), withdrawal (N=3), recurrent stroke (N=5), or other reasons such as migration (N=2). Another 32 were excluded from the analysis because they achieved independent gait within 72 hours. Hence, a total of 154 patients were available for further analysis. Patient demographics and associated stroke characteristics are shown in Table 4.1. At 6 months poststroke 122 patients (79%) were able to walk independently (FAC≥4).

## Bivariable association between dependent variable and independent variables

Table 4.2 shows ORs and their 95% CIs for independent gait at 6 months, as determined by bi-variable logistic regression analysis for the assessment within 72 hours after stroke onset. Of 19 candidate variables, 15 were significantly related to the return of independent gait at 6 months poststroke. Collinearity diagnostics revealed a high level of association between MI leg score and FMA leg score ($r_s$=0.81, p=0.01). The MI arm score was strongly associated with FMA arm score ($r_s$=0.84, p=0.01). MI leg and arm scores were selected for regression modeling, based on clinical applicability (i.e. MI takes less time to administer than the motor part of FMA).

## Multivariable modeling

Table 4.3 shows the variables included in the prediction model and the probabilities of achieving independent gait 6 months poststroke. Testing all 15 significant candidate determinants simultaneously in a multivariable regression analysis resulted in a final model including two significant variables: TCT-s and MI leg score. Based on regression coefficients and constants, the maximum probability of achieving independent gait was estimated at 98% if the patients had a maximum TCT-s score of 25 (i.e. independent sitting for 30 seconds) and an MI leg score of ≥25 (i.e.

**Table 4.1** Characteristics of patients measured within 72 hours poststroke

| Patient characteristics | Total |
|---|---|
| N | 154 |
| Gender, male/female | 61/93 |
| Mean (SD) age, years | 67.54 (14.15) |
| Mean (SD) BMI | 25.87 (4.46) |
| Social support, no/yes | 60/93[a] |
| Hemisphere of stroke, right/left | 87/67 |
| rTPA, yes/no | 44/110 |
| Conscious at onset, no/yes | 28/126 |
| Mean (SD) time between stroke onset and | |
| First assessment, days | 2.24 (1.32) |
| Second assessment, days | 5.52 (1.38) |
| Third assessment, days | 9.00 (1.84) |
| Type of stroke (Bamford) | |
| LACI | 64 |
| PACI | 57 |
| TACI | 33 |
| Inattention or extinction, yes/no | 75/79 |
| Impairments of vision | |
| Hemianopsia, yes/no | 52/102 |
| Conjugate deviation, yes/no | 45/109 |
| Sensory loss, yes/no | 97/57 |
| Comorbidity, yes/no[b] | 129/25 |
| Sitting balance, no/yes | 49/104[a] |
| MI leg (0–100)[c] | 44.50 (9–69.75) |
| MI arm (0–100)[c] | 33 (33–65) |
| FMA leg (0–34)[c] | 17 (6.75–25.25) |
| FMA arm (0–66)[c] | 12 (4–43.25) |
| TCT (0–100)[c] | 62 (25–87) |
| BBS (0–56)[c] | 5 (1–23) |
| FAC (0–5)[c] | 0 (0–2) |
| BI (0–20)[c] | 6 (2–10) |
| BI urinary incontinence, yes/no[d] | 85/67[a] |

[a]Missing value(s).
[b]Cumulative Illness Rating Scale (yes>0, no=0).
[c]Median values (interquartile ranges).
[d]yes≤1, no=2.
BBS, Berg Balance Scale; BI, Barthel Index; BMI, Body Mass Index; FAC, Functional Ambulation Categories; FMA arm, Fugl-Meyer Assessment upper extremity; FMA leg, Fugl-Meyer Assessment lower extremity; LACI, Lacunar Anterior Circulation Infarcts; MI arm, Motricity Index upper extremity; MI leg, Motricity Index lower extremity; PACI, Partial Anterior Circulation Infarcts; rTPA, recombinant Tissue Plasminogen Activator; SD, Standard Deviation; TACI, Total Anterior Circulation Infarcts; TCT, Trunk Control Test.

4

**Table 4.2** Impairments and disabilities within 72 hours associated with independent gait 6 months poststroke as determined by bivariable logistic regression analysis (N=154)

| Determinant | Odds Ratio | 95% CI | P |
|---|---|---|---|
| Gender (male/female)[a] | 0.89 | 0.40–2.00 | 0.784 |
| Age (0≥70; 1=<70)[a] | 2.20 | 0.96–5.03 | 0.062 |
| BMI (0=overweight; 1=normal and underweight)[b] | 0.77 | 0.33–1.78 | 0.767 |
| Social support (0=no; 1=yes)[a] | 2.23 | 1.00–4.96 | 0.049 |
| Comorbidity (0=yes; 1=no)[c] | 7.60 | 0.99–58.43 | 0.052 |
| Hemisphere of stroke (right/left)[a] | 1.93 | 0.84–2.42 | 0.120 |
| Consciousness at onset (0≥1; 1=0)[a,d] | 4.88 | 2.01–11.87 | 0.000 |
| Days between stroke onset and first assessment | 1.07 | 0.76–1.52 | 0.690 |
| Type of stroke (0=TACI/PACI; 1=LACI)[a] | 6.77 | 2.24–20.48 | 0.001 |
| Extinction or inattention (0≥1; 1=0)[a,d] | 5.14 | 2.07–12.81 | 0.000 |
| Hemianopsia (0≥1; 1=0)[b,d] | 5.60 | 2.43–12.93 | 0.000 |
| Conjugate deviation (0≥1; 1=0)[a,d] | 5.40 | 2.36–12.35 | 0.000 |
| Sensory loss (0≥1; 1=0)[a,d] | 26.30 | 3.48–198.86 | 0.002 |
| BI irinary incontinence (0≤1; 1=2)[a,d] | 36.00 | 4.76–272.53 | 0.001 |
| TCT-s (0<25; 1=25)[b] | 33.33 | 10.57–105.11 | 0.000 |
| MI leg (0<25; 1≥25)[b] | 20.84 | 7.63–56.91 | 0.000 |
| MI arm (0<11; 1≥11)[b] | 9.24 | 3.66–23.36 | 0.000 |
| FMA leg (0<10; 1≥10)[b] | 16.00 | 5.96–42.97 | 0.000 |
| FMA arm (0<10; 1≥10)[b] | 30.75 | 7.00–135.14 | 0.000 |

[a]Cut-off points are based on clinical grounds.
[b]Cut-off points are based on analyses of receiver-operating characteristic curves.
[c]Cumulative Illness Rating Scale (yes>0; no=0).
[d]Item of the National Institutes of Health Stroke Scale.
BI, Barthel Index; BMI, Body Mass Index; CI, Confidence Interval; FMA arm, Fugl-Meyer Assessment upper extremity; FMA leg, Fugl-Meyer Assessment lower extremity; LACI, Lacunar Anterior Circulation Infarcts; MI arm, Motricity Index upper extremity; MI leg, Motricity Index lower extremity; PACI, Partial Anterior Circulation Infarcts; TACI, Total Anterior Circulation Infarcts; TCT-s, Trunk Control Test sitting balance.

visible contraction but no movement for all 3 test items, or movement against resistance but weaker than the nonparetic side for one item) within 72 hours poststroke, whereas a probability of 27% was found for patients who did not reach this level within 72 hours after stroke onset. An analysis of the time dependency of these probabilities for the former group, showed that probabilities had remained about the same on days 5 and 9, whereas in the latter group, the probability of achieving independent gait was reduced to 23% on day 5 and 10% on day 9.

The sensitivity of the model ranged from 0.93 (95% CI, 0.86–0.96) on day 2 to 0.94 (95% CI, 0.87–0.97) on day 9, while specificity ranged from 0.63 (95% CI, 0.43–0.78) on day 5 to 0.83 (95% CI, 0.64–0.93) at day 9. The PPV changed from 0.93 (95% CI, 0.85–0.96) on day 2 to 0.96 (95% CI, 0.90–0.98) on day 9, whereas the NPV changed from 0.63 (95% CI, 0.57–0.82) on day 5 to 0.75 (95% CI, 0.56–0.88) on day 9.

**Table 4.3** Probabilities of achieving independent gait 6 months poststroke (N=154)

| | FAC ≥4 at 6 months | | | | | | |
|---|---|---|---|---|---|---|---|
| Determinants | TCT-s | MI leg | True negatives N | False negatives N | False positives N | True positives N | Probability |
| Cut-off | 25 | ≥ 25 | | | | | |
| Model <72 hours | $P=1/(1+(EXP^{(-0.982 + 2.691*TCT\text{-}s + 2.083*MI\ leg)}))$ | | | | | | |
| | + | + | 24 | 9 | 8 | 112 | 0.98 |
| | + | - | | | | | 0.85 |
| | - | + | | | | | 0.75 |
| | - | - | | | | | 0.27 |
| Model day 5 | $P=1/(1+(EXP^{(-1.236 + 2.815*TCT\text{-}s + 1.609*MI\ leg)}))$ | | | | | | |
| | + | + | 20 | 7 | 12 | 115 | 0.96 |
| | + | - | | | | | 0.83 |
| | - | + | | | | | 0.59 |
| | - | - | | | | | 0.23 |
| Model day 9 | $P=1/(1+(EXP^{(-2.226 + 3.629*TCT\text{-}s + 1.854*MI\ leg)}))$ | | | | | | |
| | + | + | 24 | 5 | 8 | 117 | 0.96 |
| | + | - | | | | | 0.80 |
| | - | + | | | | | 0.40 |
| | - | - | | | | | 0.10 |

FAC, Functional Ambulation Categories; MI leg, Motricity Index lower extremity; TCT-s, Trunk Control Test sitting balance.



## DISCUSSION

To the best of our knowledge, this was the first study to investigate prospectively the accuracy of predicting independent gait within 72 hours after onset in nonambulatory stroke patients. The present study showed that accurate prediction within 72 hours is attainable at hospital stroke units by means of 2 simple bedside tests: sitting balance and muscle strength of the paretic leg. Those nonambulatory patients who regained their sitting balance as assessed by the TCT-s and developed some voluntary movement of the hip, knee, and/or ankle as assessed by the MI leg score (≥25 points) within the first 72 hours poststroke had about a 98% chance of regaining independent gait within 6 months. In contrast, those patients who were unable to sit independently for 30 seconds and were hardly able to contract the muscles of the paretic lower limb within 72 hours had a probability of about 27% of achieving independent gait. Early reassessment of sitting balance and lower limb strength on days 5 and 9 showed that if sitting ability and lower limb strength failed to recover, the probability of regaining independent gait declined to 23% on day 5 and 10% on day 9 poststroke.

The aforementioned findings allow valid prediction of independent gait after stroke and are important for clinicians to improve their discharge policy at hospital stroke units and to support the standardization of care processes in clinical pathways after stroke. These findings on the early prediction of poststroke outcome are important, since it takes advantage of a decreased length of stay at a hospital stroke unit and could help tailor rehabilitation interventions.

Comparing our findings with those of other prognostic studies is difficult because of the lack of prognosis studies investigating the accuracy of prediction within 72 hours. However, a number of prognosis studies have shown that muscle strength of the hemiparetic leg[9,11] and sitting balance,[10,13] when measured in the second to fourth week after stroke, are significantly associated with improvement of walking ability[3] and achieving independent gait[12,14,17] at 6 months. Obviously, the early control of sitting balance as a prerequisite for regaining standing balance and gait is an important factor for the final outcome at 6 months.[14,17] The importance of balance control for gait is also supported by a study by Kollen and colleagues,[3] who showed that improvement in standing balance was the most important variable associated with improvement of gait performance as measured with the FAC.

Since the proportion of false positives (≈7%) was clearly smaller than the proportion of false negatives (≈27%) within 2 days, the present study suggests that our model is generally somewhat pessimistic and illustrates that some patients with an initially poor sitting balance and a severe paresis of the hemiparetic limb will nevertheless regain independent gait.[12] The increasing accuracy of prediction over time may reflect underlying intrinsic neurological mechanisms such as elevation of diaschisis after stroke.[16,31] This elevation is generally completed within the time window used in this study,[31] making it virtually impossible to improve the accuracy of prediction based on the 2 variables of our model. For example, our model does not take into account the ability or inability of patients to use compensatory strategies. This is supported by a number of recent longitudinally conducted studies showing that gait recovery is closely related to learning to use compensatory movement strategies.[3,32,33] For instance, patients learn to keep their balance by shifting their center of gravity to the nonparetic side,[33] while significant change in motor control on the paretic side is almost lacking.[32] Obviously, patients learn to cope with existing neurological deficits.[32]

Future studies should not only investigate the optimal timing of clinical assessments at hospital stroke units, but also try to gain insight into recovery profiles in the early poststroke period.[34] For this purpose, prospective cohort studies should use an intensive repeated-measurement design, allowing clinicians to increase their understanding of the longitudinal relationships between early changes in body functions, like coordination, compensation strategies, and improved gait performance, preferably by including kinematic and electromyography measures. Simultaneously, neuroimaging techniques such as functional magnetic resonance imaging should be added to increase our knowledge about the neurophysiological mechanisms that accompany gait recovery.

The present study was subject to some limitations, such as being restricted to first-ever anterior circulation strokes and the lack of cross-validation of the derived prediction model in an independent sample of stroke patients. In addition, the influence of some cognitive and emotional disabilities such as depression[35] and anxiety on recovery were not addressed in the present study, even though they could negatively influence independent gait. Finally, although recovery of walking function mainly occurs within 6 months poststroke,[2,36] about 10% of the patients still show functional changes after these 6 months.[37] Hence, we cannot exclude that patients who are nonambulatory within the first 6 months may still be dependent in this chronic phase poststroke.[37,38]

In conclusion, the 2 simple bedside tests of "sitting balance" and "strength of the paretic leg" allow early and accurate prediction within 2 days poststroke of the recovery of walking ability after 6 months for nonambulatory patients who score positive on both tests. Patients with a poor prognosis should be reassessed with these 2 tests on day 9 to improve the accuracy of prediction.



## EPOS Investigators

*Executive committee:* G. Kwakkel (PhD), principal investigator, Department of Rehabilitation Medicine, VU University Medical Center, Amsterdam; and co-principal investigator B.C. Harmeling-van der Wel, Department of Rehabilitation Medicine, Erasmus MC, Rotterdam. *Steering committee and data management:* J.M. Veerbeek and R. Nijland, Department of Rehabilitation Medicine, VU University Medical Center, Amsterdam. *Monitoring board:* M.A. van der Beek, UMC Utrecht; W.A.M. Cornelissen, AMC Amsterdam; A.A.G. Goos, Franciscus Hospital, Roosendaal; C.S. Steeg, UMC Sint Radboud, Nijmegen; J.M. Timmermans, LUMC, Leiden; R. Tichelaar, Amphia Hospital, Breda.

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