■ *Research paper*

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Identifying Risk Factors for Falls after Lower Limb Amputation: A Comparison of Regression Models

Abstract. We analysed the data on 876 patients after lower limb amputation who were admitted to inpatient rehabilitation at the University Rehabilitation Institute in Ljubljana from 2015 to 2017. Upon admission, they were asked about falls at home and/or in the acute hospital since the amputation. The data on comorbidities was also recorded. Six months after discharge, the patients were asked about falls in their home environment. In addition, a test group took part in a short education during inpatient rehabilitation about fall prevention. We applied tobit, negative binomial, logistic, Poisson, zero-inflated Poisson and proportional odds regression models to assess the effect of potential fall risk factors. All regression models were fitted with main effects only. The models for falls during inpatient rehabilitation were adjusted for the length of hospital stay (either as offset variable or as predictor). Different regression models with different assumptions led to similar conclusions. A short-term effect of the education program was observed. Unilateral amputation, age, female sex, falls before admission to inpatient rehabilitation and stroke and/or myocardial infarction proved to be the main risk factors for falls at various stages after lower limb amputation.

Key words: fall risk; inpatient rehabilitation; statistical models; Slovenia.

Ugotavljanje dejavnikov tveganja za padce po amputaciji spodnjega uda: primerjava regresijskih modelov

Povzetek. Analizirali smo podatke 876 pacientov, sprejetih na bolnišnično rehabilitacijo na Univerzitetnem rehabilitacijskem inštitutu Republike Slovenije Soča v letih od 2015 do 2017. Ob sprejemu so odgovorili na vprašanja o padcih po amputaciji doma in v akutni bolnišnici. Zajeti so bili tudi podatki o sočasnih boleznih. Šest mesecev po odpustu so pacienti poročali o padcih doma v tem obdobju. Med bolnišnično rehabilitacijo je del pacientov sodeloval v kratkem izobraževanju o preprečevanju padcev. Za ugotavljanje morebitnih dejavnikov tveganja za padce smo podatke analizirali z različnimi regresijskimi modeli (tobit, negativni binomski, logistični, Poissonov, Poissonov s presežkom ničel, sorazmernih obetov). V vse regresijske modele smo vključili zgolj glavne učinke. V modelih za padce v času bolnišnične rehabilitacije smo upoštevali čas hospitalizacije (kot privzeto vrednost ali napovedni dejavnik). Različni regresijski modeli z različnimi predpostavkami so vodili do podobnih sklepov. Opazili smo kratkotrajen učinek izobraževalnega programa. Enostranska amputacija, starost, ženski spol, padci pred sprejemom na bolnišnično rehabilitacijo ter možganska kap in/ali srčni infarkt so se pokazali kot glavni dejavniki tveganja za padce v različnih obdobjih po amputaciji spodnjega uda.

Ključne besede: tveganje za padce; bolnišnična rehabilitacija; statistični modeli; Slovenija.

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Introduction

From the body function perspective,[1] amputation has got severe impact on a patient's static and dynamic balance and changes the centre of gravity,[2] thereby increasing risk of falling compared with able-bodied individuals, as well as other clinical populations during all stages of recovery.[3,4] One in five patients with lower limb amputation will likely experience at least one fall during inpatient rehabilitation, with 18 % sustaining an injury.[5] Each stage of recovery is associated with different fall risk factors.[4] Some risk factors that increase the incidence of falls are the same as in the general population of older adults (lower limb muscle weakness, increasing age, comorbidities, and number of prescription medications), and some are unique to the adults with lower limb amputation (dysvascular aetiology of the amputation, transtibial level of amputation in the postoperative period and transfemoral level post-rehabilitation, and reduced sense of vibration).[6]

We conducted a retrospective analysis of a comprehensive dataset, applying various regression models in order to assess the effect of potential fall risk factors for falls and test whether a short inpatient education program reduced fall risk. This way, we wanted to verify and expand upon the results of initial univariate analyses.[7]

Methods

The study included 876 patients after lower limb amputation who were admitted to inpatient rehabilitation at our institute between 2015 and 2017. Upon admission, they were asked about falls at home and/or in the acute hospital since the amputation, and those data were recorded for 861 patients. The data on comorbidities was also recorded upon admission. Falls during rehabilitation were routinely recorded in detail. In 2016, a test group (127 patients) took part in a 30-minute education during inpatient rehabilitation about fall prevention. Six months after discharge, all the patients were called (157 replied) and asked about falls in their home environment.

As an outcome in quantitative medical research, falls are a typical example of count data. If the association of such an outcome with several potential risk factors is explored, regression models should be applied.[8] A mathematical presentation of the relevant models would far exceed the scope of this paper, so below we only provide references to textbooks on each of those models that are suitable for applied researchers.

If only presence or absence of falls (i. e., one or more vs. none) is considered, a logistic regression[9] model is suitable. However, falls can also be conceptualised as a result of a latent process, so that they actually occur only if a certain threshold (so-called hurdle) is exceeded. In statistical terms, the number of falls therefore represents left-censored data, for which several regression models have been developed.[10] We applied the simplest and most widely used among them, the tobit model, in which the same set of variables, with the same coefficients, determines the probability of truncation as well as the expected value of the observed dependent variable.[10]

To model the number of falls in a given period as a count variable, negative binomial regression,[11] Poisson regression[12,13] and zero-inflated Poisson (ZIP) regression[12] were applied. The fit of negative binomial and Poisson distribution to the observed number of falls was tested using chi-squared test.

In addition, the proportional odds regression model[12,13] was applied, in which the number of falls was treated as an ordinal variable. Like the negative binomial, Poisson and ZIP model, this model belongs to the family of generalised linear models,[13] where the overall feasibility of the model (i. e., superiority to the null model) was assessed using Wald or likelihood-ratio (LR) test. Additionally, test of parallel lines (PL) was used to probe the assumption of the proportional odds model that the null hypothesis states that the location parameters (i. e., slope coefficients) are the same across response categories.

All regression models listed above were fitted with main effects only (i. e., without interaction terms). The models for falls during inpatient rehabilitation were adjusted for the length of hospital stay.

- It was used as offset variable in the logistic model for falling at least once and the Poisson and negative binomial model for the number of falls. The number of hospital days was logarithmised because of a highly right-skewed distribution.
- The number of hospital days was used as a predictor in the tobit and proportional odds model.

Microsoft® Excel 2016 (Microsoft Corp., Redmond, WA, USA) software was used for distribution fitting and visualisation, whereby negative binomial distribution was fitted using the built-in Solver add-in.[14] IBM SPSS Statistics 28 (IBM Corp., Armonk, NY, USA) software was used for regression modelling, which called R[15] software package *AER*[16] for tobit regression and *pscl*[17] package for ZIP regression.

Results

The results of distribution fitting are shown in Figure 1 and summarised in Table 1. Negative binomial distribution proved to be a better fit to the observed data than Poisson distribution. Compared to the latter, the excess of zeroes in the observed data (representing patients who did not fall) was evident, and the mean was much smaller than the variance (remember that they are equal in the Poisson distribution).[18] All three observed distribution differed statistically significantly from Poisson distribution, but only the distribution of the number of falls before admission to inpatient rehabilitation differed statistically significantly from negative binomial distribution.

The regression models for falls before, during and after inpatient rehabilitation are summarised in Table 1, 2 and 3, respectively. The models that are not listed for a given outcome could not be fitted because the maximum-likelihood algorithm did not converge. The results can be summarised as follows:

- Unilateral amputation was associated with increased fall risk before and after inpatient rehabilitation as compared to bilateral amputation.
- Age increased fall risk before and during inpatient rehabilitation.
- Having previously survived stroke and/or myocardial infarction greatly increased fall risk during inpatient rehabilitation.
- Having fallen before admission was possibly a risk factor for falls during inpatient rehabilitation, and very likely after discharge at home.
- Women were at higher risk of falling during inpatient rehabilitation then men.
- The education program did not reduce the risk of falling at least once during inpatient rehabilitation, but it did reduce the number of falls per hospital day. However, the possible effect waned after discharge at home.

Table 1 Summary of fitting theoretical distributions to the observed distributions of number of falls.

Number of falls	Before admission	During rehabilitation	After discharge
Sample size	861	876	157
Mean	0.67	0.15	0.83
Variance	2.09	0.22	2.82
Negative binomial			
no. of successes	0.48	0.26	0.26
prob. of success	0.42	0.63	0.24
GOF *p*	0.005	0.299	0.059
Poisson GOF *p*	< 0.001	< 0.001	< 0.001

Legend: GOF – goodness-of-fit test.

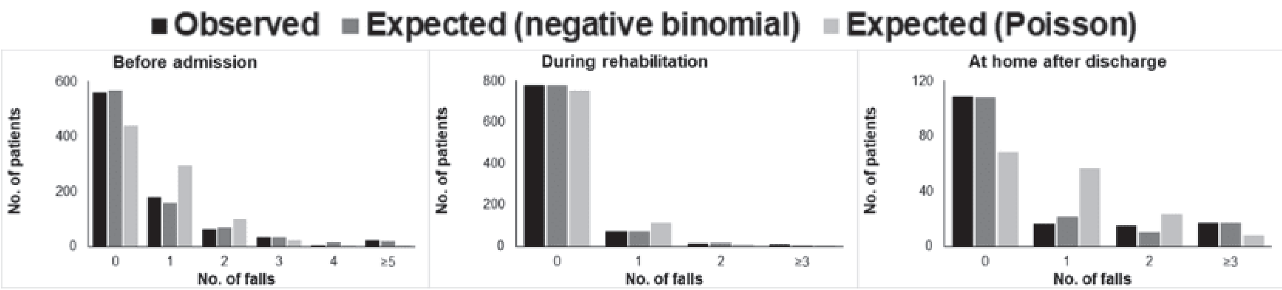

Figure 1 Observed distributions of the number of falls before admission, during inpatient rehabilitation and at home after discharge with best-fitting theoretic (negative binomial and Poisson) distributions.

Table 2 Summary of regression models for predicting the number of falls before admission to inpatient rehabilitation.

Regression model	ZIP			Negative binomial			Tobit			Ordinal logistic		
Model fit (test)	NA			<0.001 (LR)			0.002 (Wald)			0.002(LR); 0.585(PL)		
Predictor	*b*	(SE)	*p*	*b*	(SE)	*p*	*b*	(SE)	*p*	*b*	*(SE)*	*p*
Sex (Female vs. Male)	-0.025	(0.120)	0.838	0.040	(0.146)	0.782	0.111	(0.276)	0.687	0.092	(0.153)	0.548
Age (years)	**0.010**	**(0.005)**	**0.050**	0.008	(0.005)	0.123	0.012	(0.011)	0.266	0.006	(0.006)	0.301
Amputation (uni- vs. bilateral)	**0.945**	**(0.323)**	**0.003**	**0.915**	**(0.209)**	**<0.001**	**1.463**	**(0.401)**	**<0.001**	**0.787**	**(0.231)**	**<0.001**

Legend: ZIP – zero-inflated Poisson; NA – not applicable; *b* – regression coefficient; SE – standard error of the estimate of *b*; LR – likelihood-ratio; PL – parallel lines; predictors and parameter estimates with $p < 0.05$ are typeset in boldface (only for easier interpretation, not as a reliable indication of statistical significance).

Table 3 Summary of regression models for predicting the number of falls during inpatient rehabilitation.

Regression model	Poisson			Negative binomial			Tobit			Ordinal logistic			Logistic		
Model fit (test)	<0.001 (LR)			<0.001 (LR)			0.015 (Wald)			<0.001(LR); <0.001(PL)			<0.001 (LR)		
Predictor	*b*	(SE)	*p*	*b*	(SE)	*p*	*b*	(SE)	*p*	*b*	(SE)	*p*	*b*	*(SE)*	*p*
Sex (Female vs. Male)	**0.450**	**(0.186)**	**0.016**	**0.461**	**(0.208)**	0.026	0.358	(0.297)	0.228	0.242	(0.240)	0.314	0.023	(0.256)	0.930
Age (years)	**0.031**	**(0.009)**	**<0.001**	**0.031**	**(0.010)**	**0.001**	**0.039**	**(0.014)**	**0.005**	**0.037**	**(0.012)**	**0.001**	**0.030**	**(0.012)**	**0.010**
Admission (re- vs. first)	-0.062	(0.215)	0.774	-0.066	(0.238)	0.783	0.343	(0.337)	0.310	0.377	(0.281)	0.179	**0.602**	**(0.290)**	**0.038**
Amputation (uni- vs. bilateral)	0.009	(0.275)	0.974	0.028	(0.302)	0.926	0.123	(0.418)	0.769	0.179	(0.349)	0.607	0.488	(0.367)	0.184
Falls before rehab. (yes vs. no)	0.202	(0.182)	0.266	0.226	(0.202)	0.262	**0.536**	**(0.288)**	**0.062**	**0.416**	**(0.229)**	**0.069**	**0.613**	**(0.242)**	**0.011**
Educational program (yes vs. no)	**-0.578**	**(0.289)**	**0.045**	**-0.637**	**(0.313)**	**0.042**	-0.558	(0.429)	0.192	-0.453	(0.349)	0.194	0.030	(0.356)	0.934
Assoc. hypertension (yes vs. no)	-0.150	(0.274)	0.585	-0.162	(0.306)	0.597	-0.05	(0.426)	0.906	0.020	(0.359)	0.956	0.295	(0.386)	0.446
Assoc. hyperlipidemia (yes vs. no)	0.102	(0.187)	0.583	0.132	(0.207)	0.523	0.223	(0.291)	0.443	0.171	(0.234)	0.465	0.266	(0.248)	0.284
Assoc. CVI or MI (yes vs. no)	**0.603**	**(0.183)**	**0.001**	**0.615**	**(0.205)**	**0.003**	**0.743**	**(0.298)**	**0.012**	**0.599**	**(0.232)**	**0.010**	**0.522**	**(0.246)**	**0.034**
Associated DM (yes vs. no)	0.134	(0.190)	0.479	0.143	(0.211)	0.499	0.241	(0.295)	0.414	0.255	(0.240)	0.289	0.334	(0.257)	0.195
Amputation (uni- vs. bilateral)	NA	NA	NA	NA	NA	NA	0.159	(0.189)	0.400	0.144	(0.155)	0.352	NA	NA	NA

Legend: NA – not applicable; *b* – regression coefficient; SE – standard error of the estimate of *b*; LR – likelihood-ratio; PL – parallel lines; the results from the models that are not feasible because of not being statistically significantly better than the null model and/or because of a violated key assumption are typeset in grey; predictors and parameter estimates with $p < 0.05$ (or $p \approx 0.05$) are typeset in boldface (only for easier interpretation, not as a reliable indication of statistical significance).

Table 4 Summary of regression models for predicting the number of falls at home after discharge from inpatient rehabilitation.

Regression model	Negative binomial			Tobit			Ordinal logistic			Logistic		
Model fit (test)	0.001 (LR)			0.199 (Wald)			0.144(LR); <0.001(PL)			0.142 (LR)		
Predictor	*b*	(SE)	*p*	*b*	(SE)	*p*	*b*	(SE)	*p*	*b*	*(SE)*	*p*
Sex (Female vs. Male)	-0.039	(0.276)	0.886	-0.251	(0.833)	0.763	-0.162	(0.380)	0.669	-0.242	(0.393)	0.537
Age (years)	-0.015	(0.011)	0.171	-0.021	(0.034)	0.533	-0.005	(0.015)	0.753	0.006	(0.016)	0.700
Amputation (uni- vs. bilateral)	**2.542**	**(1.063)**	**0.017**	**4.263**	**(2.064)**	**0.039**	**2.017**	**(1.095)**	**0.066**	**1.983**	**(1.091)**	**0.069**
Falls before rehabilitation (yes vs. no)	**0.670**	**(0.264)**	**0.011**	**1.790**	**(0.796)**	**0.024**	**0.797**	**(0.356)**	**0.025**	**0.815**	**(0.367)**	**0.026**
Educational program (yes vs. no)	-0.233	(0.284)	0.412	-0.830	(0.835)	0.320	-0.365	(0.374)	0.329	-0.421	(0.388)	0.278
Associated hypertension (yes vs. no)	-0.161	(0.358)	0.653	0.033	-1.135	0.977	-0.063	(0.498)	0.900	0.075	(0.530)	0.887
Associated hyperlipidemia (yes vs. no)	0.017	(0.283)	0.953	-0.210	(0.849)	0.804	-0.027	(0.387)	0.944	-0.069	(0.399)	0.862
Associated CVI or MI (yes vs. no)	-0.280	(0.322)	0.385	-0.550	(0.931)	0.555	-0.231	(0.420)	0.582	-0.178	(0.429)	0.678
Associated DM (yes vs. no)	0.082	(0.267)	0.760	-0.373	(0.804)	0.643	-0.165	(0.365)	0.651	-0.255	(0.377)	0.498

Legend: *b* – regression coefficient; SE – standard error of the estimate of *b*; LR – likelihood-ratio; PL – parallel lines; the results from the models that are not feasible because of not being statistically significantly better than the null model and/or because of a violated key assumption are typeset in grey; predictors and parameter estimates with $p < 0.05$ (or $p \approx 0.05$) are typeset in boldface (only for easier interpretation, not as a reliable indication of statistical significance).

Discussion

Some of the planned regression models could not be fitted, but those that were fitted, including those that were not feasible in principle because of lack of overall statistical significance or violated key assumption, led to essentially equivalent conclusions.

Like previous researchers,[4] we found that risk factors for falls differ between different stages of recovery. Unilateral amputation was associated with increased fall risk before and after inpatient rehabilitation as compared to bilateral amputation. Age increased fall risk before and during inpatient rehabilitation, as already described in a systematic review.[4] Having previously survived stroke and/or myocardial infarction greatly increased fall risk during inpatient rehabilitation. Having fallen before admission to inpatient rehabilitation was possibly a risk factor for falls during inpatient rehabilitation, and very likely after discharge to home environment. In addition, women were at higher risk of falling during inpatient rehabilitation then men, which has not been observed in previous studies.[3,4] The education program did not appear to reduce the risk of falling at least once during the stay in our hospital, but it did appear to reduce the number of falls per hospital day. However, the possible effect disappeared in the home environment.

Limitations

Although the dataset was large and comprehensive, our analysis and hence its conclusions are subject to several limitations. Firstly, although a variety of regression models were fitted, some were not tried, such as sample-selection models,[10] or the zero-inflated negative binomial model. Secondly, only main effects of the studied variables were entered into the models, though the assumption of no interactions was not very realistic. Thirdly, the patients who took part in the education program were not selected at random, but rather constituted a convenience sample. Their potential differences from other patients were adjusted for in the regression models, but propensity scoring[19] (or some other approach to causal inference in observational studies) was not attempted. Finally, the proportion of patients whose data on falls before admission can be considered as negligible,[20] but the potential selection bias for the patients whose data on falls at home after discharge from inpatient rehabilitation is evident, so the conclusions about them are much less reliable.

Conclusion

Different regression models with different assumptions led to very similar conclusions. Some models could not be fitted (did not converge), some were not statistically significantly better than the null model. Nevertheless, an often-quoted maxim in statistics is that all models are wrong, but some models are useful.[21] Bearing this in mind, age, stroke and/or myocardial infarction, falls before admission to inpatient rehabilitation, unilateral lower-limb amputation, and female sex were identified as the main risk factors for falls at various stages after lower limb amputation. A short-term effect of the education program was observed. A pragmatic approach combining several seemingly competing statistical approaches proved to be useful for obtaining clinically applicable insights.

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