ORIGINAL ARTICLE

Survival Analysis in Amputees Based on Physical Independence Grade Achievement

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Backgound: Survival implications of achieving different grades of physical independence after lower extremity amputation are unknown.

Objectives: To identify thresholds of physical independence achievement associated with improved 6-month survival and to identify and compare other risk factors after removing the influence of the grade achieved.

Design: Data were combined from 8 administrative databases. Grade was measured on the basis of 13 individual self-care and mobility activities measured at inpatient rehabilitation discharge.

Setting: Ninety-nine US Department of Veterans Affairs Medical Centers.

Patients: Retrospective longitudinal cohort study of 2616 veterans who underwent lower extremity amputation and subsequent inpatient rehabilitation between October 1, 2002, and September 30, 2004.

Main Outcome Measure: Cumulative 6-month survival after rehabilitation discharge.

Results: The 6-month survival rate (95% confidence interval [CI]) for those at grade 1 (total assistance) was 73.5% (70.5%-76.2%). The achievement of grade 2 (maximal assistance) led to the largest incremental improvement in prognosis with survival increasing to 91.1% (95% CI, 85.6%-94.5%). In amputees who remained at grade 1, the 30-day hazards ratio for survival compared with grade 6 (independent) was 43.9 (95% CI, 10.8-278.2), sharply decreasing with time. Whereas metastatic cancer and hemodialysis remained significantly associated with reduced survival (both $P \leq .001$), anatomical amputation level was not significant when rehabilitation discharge grade and other diagnostic conditions were considered.

Conclusions: Even a small improvement to grade 2 in the most severely impaired amputees resulted in better 6-month survival. Health care systems must plan appropriate interdisciplinary treatment strategies for both medical and functional issues after amputation.

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An estimated 100 000 transtibial or transfemoral amputations are performed annually in the United States,[1,2] more than half because of complications of diabetes mellitus.[3] Lower extremity amputation is associated with high mortality, high treatment costs,[4-9] and devastating functional consequences. After surgery, patients may receive rehabilitation in various settings. Although functional disability is strongly predictive of reduced survival in individuals with a variety of diagnoses in different settings,[10-14] the association between the degree of functional recovery achieved by rehabilitation discharge and longevity in amputees is unknown.

See Invited Critique at end of article

Studies addressing overall function in amputees generally apply composite summary scores of function such as the Functional Independence Measure (FIM), the Barthel Index, or the Sickness Impact Profile to assess individual ability to perform an array of activities.[15-18] These measures express severity by summing performance levels across many items, obscuring information about the specific activities patients have difficulty performing. Thus, 2 patients with the same score can have completely different types of disabilities. Stineman et al[19] developed the Physical Independence Grading System in an effort to express clinically meaningful physical function profiles of progressively increasing independence. Grades simultaneously express both the severity and types of limitations that individuals experience.

We used grades to study the 6-month survival implications of the physical func-

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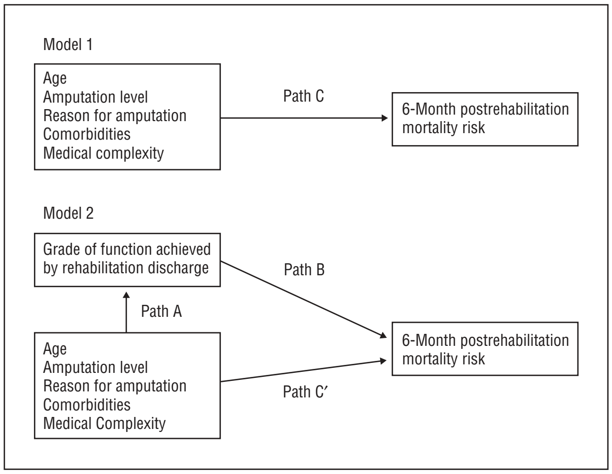

Figure 1. The hypothesized direct and indirect effects of demographic data and clinical characteristics on survival as operating through the grade of physical function achieved after surgical amputation of the lower limb. Path C (the ("Reduced" model 1) shows the total effect of demographic data and clinical characteristics on mortality before removing the mediating effect of physical grade. Path A (full model 2) shows the direct effect of demographic data and clinical characteristics on the grade of physical function achieved by rehabilitation discharge. Path B shows the direct effect of grade on mortality (without any indirect effect). Path C′ shows the direct effect of the demographic data and clinical characteristics on mortality. Paths A and B illustrate the assumption that certain demographic data and clinical characteristics are expected to influence mortality indirectly through the physical grade achieved, which then influences mortality directly. The paths (comparing A and B with C′) are used to show the independent effect (and singular importance) of the grade of physical independence achieved. The odds ratios associated with grade in this model show the independent or direct effects of grade after removing the effects of the other characteristics associated with mortality risk.

tional outcomes achieved by rehabilitation discharge in veterans after lower extremity amputation. We hypothesized that there would be thresholds, or grades of functional recovery, at which probabilities of 6-month survival would increase sharply and that the functional grades achieved would be significant predictors of mortality risk even after accounting for other risk factors.

METHODS

This retrospective longitudinal cohort study was approved by the institutional review boards of the University of Pennsylvania, Philadelphia; the Samuel S. Stratton Veterans Affairs Medical Center, Albany, New York; and the Kansas City Veterans Affairs Medical Center, Kansas City, Missouri.

DESCRIPTION OF DATABASES

Analyses included merging 8 national administrative databases from the Veterans Health Administration that track casemix and health care utilization of veterans. These include 4 inpatient data sets referred to as the Patient Treatment Files (main, bed section, surgery, and procedure),[20] 2 outpatient care files (visit and event),[21] the Beneficiary Identification Record Locator System death file,[22] and the Functional Status and Outcomes Database.[23] Our methods of data extraction have been described previously.[24-27]

STUDY POPULATION

Cases were identified with index surgical discharge dates between October 1, 2002, and September 30, 2004. Records of patients who had undergone transtibial, transfemoral, or hip disarticulation amputation were identified using *International Classification of Diseases, Ninth Revision, Clinical Modification* procedure codes 84.10, 84.13-84.19, and 84.91.[6] The study was intended to address prognosis of veterans with new amputations. Those with a record of transtibia, transfemoral, or hip disarticulation within the year preceding the surgical date were not included because they were considered as having revisions of their previous amputation. Patients who completed inpatient rehabilitation within 6 months of surgery captured by distinct admission and discharge dates in the Functional Status and Outcomes Database were included in this study. Rehabilitation discharge represented the baseline at which the patients' functional status was graded. Cumulative survival data were then tracked for 6 months.

There were 4727 patients admitted to 99 Veterans Affairs Medical Centers for new amputations, of whom 2805 (59.3%) met the inclusion criteria. After removing the records of 124 patients whose death date was the same as their rehabilitation discharge date (and, thus, had no valid discharge FIM assessment) and 65 patients who had missing function scores, our analyses included 2616 veteran amputees (93.3%).

OUTCOME

The study outcome was the length of time between discharge from inpatient rehabilitation and all-cause mortality to a censoring limit of 180 days after discharge from inpatient rehabilitation. The Patient Treatment Files were used to capture in-hospital deaths, and the Beneficiary Identification Record Locator System was examined to obtain information about deaths occurring elsewhere.

PHYSICAL GRADES

Physical independence grades[28] were assigned according to patient observed functional performances on the discharge FIM. The FIM is the standard tool used to assess patient functional status performance at discharge from inpatient rehabilitation. Mandated by the Center for Medicare and Medicaid Services and the Veterans Health Administration,[29] the FIM rates patient levels of independence (motor and cognitive) on a 7-point scale for 18 activities and has an acceptable degree of interrater reliability.[30-32] Physical grades are formed from the 13 motor FIM items, which combine self-care and mobility, that express severity of physical disability.[19,33]

Each physical grade defines a discrete empirically derived profile of function according to the most common or expected patterns of recovery across the motor FIM activities.[19,31-34] The 7 grades reflect the underlying order through which individuals with disabilities tend to recover physical functions, beginning with the most basic function (eating) and ending with the typically most difficult activities (stair climbing). The grades begin with total dependence (grade 1), progressing hierarchically to end with total independence in all activities (grade 7). Each intermediate grade describes a performance pattern across the 13 activities that the individual must meet or exceed. A pattern specifies the maximum amount and type of supportive care the individual will be expected to need for each activity.[28] Full instructions on how to determine patient scores and assign grades are available elsewhere.[28,35]

RISK FACTOR IDENTIFICATION

We organized risk factors according to 2 broad constructs: demographic data (age, sex, and marital status) and clinical characteristics (amputation level, reasons for amputation[contributing etiologies], comorbidity, cognitive status, and hospital treatment complexity).[36] Etiologies and comorbidities differentiated between diagnoses likely to have contributed directly to the amputation and concurrent conditions less likely to be related to the amputation. We captured procedures, the number of bed sections patients were treated in, and time between surgical amputation and rehabilitation discharge to gain a sense of the medical treatment complexity while hospitalized before or during rehabilitation.[26] A patient who receives care in many different bed sections or who undergoes multiple procedures would be considered to have high treatment complexity. A patient with a long period between the surgical amputation and rehabilitation discharge could have either medical complexity or delayed discharge because of social or other reasons.

STATISTICAL ANALYSES

Our purpose was to determine the degree to which the achievement of higher physical grades by rehabilitation discharge translated into improved survival during the 6 months after rehabilitation discharge. To demonstrate the incremental effect of grade on mortality over and above demographic data and other clinical characteristics, we estimated 2 multivariable regressions, each representing a subset of the different pathways shown in **Figure 1**. The first showed the predictive (total) effects of only demographic data and clinical characteristics on the likelihood of mortality (path C). The total effect of demographic and clinical characteristics includes both direct and indirect effects on mortality operating through grade.[37,38] Because it excludes the grade, this model is referred to as the reduced model.

The second model is considered the full model because the grades of physical independence achieved by rehabilitation discharge were added to the demographic data and clinical characteristics included in the first model. The coefficients associated with grade in this model provide an opportunity to test the independent capacity of grade as a predictor of mortality over and above the demographic data and clinical characteristics. Comparison of the coefficients in the 2 models enables estimation of the degree to which each demographic datum and clinical characteristic has direct or indirect effects on mortality. A substantial reduction in the associated odds ratio with the addition of grade implies a large indirect effect associated with the characteristic operating through grade.

For the second model, unadjusted and multivariable survival analyses were conducted using a series of Cox proportional hazards regressions.[39] The grades were described as mutually exclusive and exhaustive binary classes of dummy variables.

Age was expressed as 70 years or younger (reference), 71 to 85 years, and 86 years or older after showing a nonlinear association with mortality. Marital status included either married or not married. Amputation level included unilateral transtibial (reference), unilateral transfemoral, bilateral transtibial, and high bilateral. High bilateral level included bilateral transfemoral and those with unilateral transfemoral and unilateral transtibial amputations because of low prevalence of both. Reasons for amputation[24] were simplified into evidence and no evidence of trauma.[8] The 31-variable version of the Elixhauser measure expressed comorbidities.[16,17] *International Classification of Diseases, Ninth Revision, Clinical Modification* codes compiled from 3 months preceding the surgical hospitalization were included to express trauma and comorbidities. Procedures coded during the surgical hospitalization were included. Trauma, comorbidities, and procedures were coded as binary variables. Number of bed sections was expressed as a continuous variable. Time between surgery and rehabilitation discharge was structured to express the effects of 7-day increments by dividing the number of days by 7 before entry into the regression model. Cognitive FIM consisted of five 7-level items, with lower value scores indicating greater disabilities. Cognitive FIM was entered as a continuous measure and interpreted as the effect of a 1-level decrease in each of the 5 component items by dividing the score by 5.

The effects of grade and other factors on mortality were characterized by hazards ratios and associated 95% confidence intervals (95% CIs). Parameters of the Cox proportional hazards regression models were estimated with maximum likelihood methods using commercially available software (SAS PROC PHREG, version 9.0; SAS Institute, Inc, Cary, North Carolina). The time-varying nature of the associations between discharge grade and relative mortality was assessed using a nonproportional hazards model that included time by discharge grade interactions. The demographic data and clinical characteristics were defined the same way in the reduced and full models.

Survival analyses identified nonproportional hazards. Although group differences among hazards were greatest at discharge, attenuating over time, there was no statistically significant evidence that the hazards crossed. Therefore, logistic regression models for cumulative 6-month survival were used to assess overall predictive capacity as reflected in the logistic regression discrimination index.[40] The Hosmer-Lemeshow statistic was applied to determine model calibration of data to those models.[41]

RESULTS

Most veterans underwent unilateral transtibial (53.1%) or transfemoral (37.5%) amputation. Some veterans underwent bilateral transtibial (3.1%) or high bilateral (6.3%) amputation. Most of the sample were men (99.1%) and had evidence of peripheral vascular disease (87.7%), with a mean (range) age of 66.4 (33-107) years. Approximately 84.8% had diabetes mellitus, and 7.8% had renal failure of sufficient severity to require hemodialysis.

A large percentage of patients (35.9%) did not recover beyond the first grade of physical independence by rehabilitation discharge. The percentage of patients who achieved grades 2, 3, 4, 5, and 6 was 6.4%, 12.7%, 8.7%, 23.1%, and 13.2%, respectively. **Table 1** gives demographic data and clinical characteristics according to grade. Patients who achieved higher grades were typically younger, were unmarried, had undergone fewer procedures, and had less comorbidity.

The unadjusted cumulative 6-month survival rate was 87.2%, ranging from 73.5% for amputees who did not recover function beyond grade 1 to 98.0% for those who achieved grade 6 (**Table 2**). Significant nonproportionality among the hazards was observed ($P = .001$). Table 2 gives the adjusted and unadjusted attenuation of differences among grades over time and across grades. For example, comparing grades 1 to 6 at days 30, 90, and 120, the unadjusted mortality hazard ratios (95% CIs) were 43.9 (10.8-78.2), 12.5 (5.6-28.1), and 6.7 (3.0-14.9). In contrast, at day 180, these values were 1.9 (0.5-7.7). Adjusting for demographic data and clinical factors, the values for grade 1 compared with grade 6 were 17.0 (4.0-71.4), 5.2 (2.2-12.1), 2.8 (1.2-6.6), and 0.9 (0.2-3.6) at days 30, 90, 120, and 180, respectively.

Table 3 gives the odds ratios (95% CIs) for each demographic datum and clinical characteristic with and without adjustment for grade. Amputation level

Table 1. Baseline Clinical Characteristics According to Outcome Grade Achieved by Rehabilitation Discharge

	No. (%)					
	Grade[a]					
Demographic Data	1	2	3	4	5	6
Amputees	938 (35.9)	168 (6.4)	331 (12.7)	228 (8.7)	605 (23.1)	346 (13.2)
Age, y						
≤60	165 (17.6)[b]	56 (33.3)	120 (36.3)	81 (35.5)	300 (49.6)	205 (59.3)
61-70	207 (22.1)	44 (26.2)	96 (29.0)	62 (27.2)	154 (25.5)	91 (26.3)
71-85	510 (54.4)	63 (37.5)	113 (34.1)	80 (35.1)	148 (24.5)	50 (14.5)
≥86	56 (6.0)	5 (3.0)	2 (0.6)	5 (2.2)	3 (0.5)	0
Sex						
Male	926 (98.7)[c]	165 (98.2)	327 (98.8)	228 (100.0)	601 (99.3)	345 (99.7)
Female	12 (1.3)	3 (1.8)	4 (1.2)	0	4 (0.7)	1 (0.3)
Marital status						
Married	450 (48.0)[c]	74 (44.1)	154 (46.5)	111 (48.7)	278 (46.0)	133 (38.4)
Not married	488 (52.0)	94 (56.0)	177 (53.5)	117 (51.3)	327 (54.1)	213 (61.6)
Amputation level						
Unilateral transtibial	351 (37.4)[b]	95 (56.6)	200 (60.4)	130 (57.0)	356 (58.8)	256 (74.0)
Unilateral transfemoral	474 (50.5)	56 (33.3)	100 (30.2)	70 (30.7)	201 (33.2)	80 (23.1)
Bilateral transtibial	31 (3.3)	8 (4.8)	10 (3.0)	14 (6.1)	13 (2.2)	5 (1.5)
High bilateral	82 (8.7)	9 (5.4)	21 (6.3)	14 (6.1)	35 (5.8)	5 (1.5)
Reasons for amputation						
Chronic osteomyelitis	60 (6.4)[d]	16 (9.5)	16 (4.8)	16 (7.0)	49 (8.1)	43 (12.4)
Device infection	77 (8.2)[b]	24 (14.3)	37 (11.2)	25 (11.0)	91 (15.0)	47 (13.6)
Diabetes mellitus type 1	135 (14.4)	33 (19.6)	56 (16.9)	35 (15.4)	99 (16.4)	54 (15.6)
Diabetes mellitus type 2	625 (66.6)	114 (67.9)	241 (72.8)	159 (69.7)	422 (69.8)	227 (65.6)
Local significant infection	761 (81.1)[b]	134 (79.8)	267 (80.7)	176 (77.2)	438 (72.4)	237 (68.5)
Peripheral vascular disease	859 (91.6)[b]	150 (89.3)	294 (88.8)	198 (86.8)	527 (87.1)	266 (76.9)
Previous complication	72 (7.7)	12 (7.1)	45 (13.6)	18 (7.9)	75 (12.4)	24 (6.9)
Skin breakdown	639 (68.1)[d]	107 (63.7)	220 (66.5)	147 (64.5)	378 (62.5)	200 (57.8)
Systemic sepsis	109 (11.6)[d]	15 (8.9)	36 (10.9)	19 (8.3)	36 (6.0)	31 (9.0)
Trauma	130 (13.9)	23 (13.7)	41 (12.4)	26 (11.4)	85 (14.1)	64 (18.5)
Elixhauser comorbidities						
AIDS	3 (0.3)	0	3 (0.9)	2 (0.9)	5 (0.8)	1 (0.3)
Alcohol abuse	33 (3.5)[d]	7 (4.2)	27 (8.2)	13 (5.7)	47 (7.8)	25 (7.2)
Arrhythmias	215 (22.9)[b]	31 (18.5)	58 (17.5)	35 (15.4)	68 (11.2)	36 (10.4)
Chronic anemia from blood loss	20 (2.1)	3 (1.8)	8 (2.4)	5 (2.2)	11 (1.8)	1 (0.3)
Chronic pulmonary disease	204 (21.8)[d]	35 (20.8)	70 (21.2)	47 (20.6)	100 (16.5)	54 (15.6)
Coagulopathy	55 (5.9)[d]	8 (4.8)	12 (3.6)	11 (4.8)	27 (4.5)	6 (1.7)
Congestive heart failure	252 (26.9)[b]	45 (26.8)	76 (23.0)	62 (27.2)	115 (19.0)	47 (13.6)
Deficiency anemias	234 (25.0)[d]	30 (17.9)	79 (23.9)	57 (25.0)	120 (19.8)	63 (18.2)
Depression	85 (9.1)	13 (7.7)	33 (10.0)	25 (11.0)	56 (9.3)	35 (10.1)
Drug abuse	6 (0.6)[b]	2 (1.2)	12 (3.6)	6 (2.6)	19 (3.1)	21 (6.1)
Fluid and electrolyte disorders	233 (24.8)[b]	42 (25.0)	58 (17.5)	42 (18.4)	103 (17.0)	55 (15.9)
Hypertension	586 (62.5)[d]	97 (57.7)	220 (66.5)	154 (67.5)	410 (67.8)	235 (67.9)
Hypertension with complication	2 (0.2)	0	1 (0.3)	6 (2.6)	3 (0.5)	0
Hypothyroidism	34 (3.6)	11 (6.6)	13 (3.9)	7 (3.1)	19 (3.1)	5 (1.5)
Liver disease	21 (2.2)[d]	5 (3.0)	16 (4.8)	6 (2.6)	28 (4.6)	21 (6.1)
Lymphoma	8 (0.9)	3 (1.8)	0 (0.0)	1 (0.4)	3 (0.5)	3 (0.9)
Metastatic cancer	15 (1.6)	4 (2.4)	4 (1.2)	1 (0.4)	8 (1.3)	3 (0.9)
Other neurologic disorders	40 (4.3)[b]	2 (1.2)	4 (1.2)	5 (2.2)	11 (1.8)	1 (0.3)
Paralysis	56 (6.0)[b]	5 (3.0)	7 (2.1)	7 (3.1)	6 (1.0)	2 (0.6)
Peptic ulcer	7 (0.8)	5 (3.0)	5 (1.5)	3 (1.3)	9 (1.5)	3 (0.9)
Psychoses	73 (7.8)[c]	13 (7.7)	28 (8.5)	7 (3.1)	40 (6.6)	13 (3.8)
Pulmonary circulatory disease	9 (1.0)	1 (0.6)	6 (1.8)	2 (0.9)	5 (0.8)	3 (0.9)
Renal failure	199 (21.2)[b]	31 (18.5)	72 (21.8)	39 (17.1)	81 (13.4)	41 (11.9)
Rheumatoid arthritis	13 (1.4)	1 (0.6)	5 (1.5)	4 (1.8)	3 (0.5)	2 (0.6)
Solid tumor without metastasis	94 (10.0)[d]	14 (8.3)	26 (7.9)	11 (4.8)	42 (6.9)	21 (6.1)
Valvular disease	52 (5.5)	7 (4.2)	16 (4.8)	12 (5.3)	25 (4.1)	13 (3.8)
Weight loss	60 (6.4)[d]	9 (5.4)	11 (3.3)	9 (4.0)	22 (3.6)	11 (3.2)

(continued)

was not statistically significantly associated with mortality after adjusting for demographic data and other clinical characteristics; however, the overall effect of age was still related to 6-month mortality ($P=.002$).

Adjustment for demographic data and clinical characteristics diminished the mortality differences across the

Table 1. Baseline Clinical Characteristics According to Outcome Grade Achieved by Rehabilitation Discharge (continued)

	No. (%)					
	Grade[a]					
Demographic Data	1	2	3	4	5	6
Baseline medical complexity						
Medical acuity by procedures						
Active pulmonary disease	16 (1.7)[d]	0	2 (0.6)	3 (1.3)	2 (0.3)	1 (0.3)
Acute central nervous system disorder	90 (9.6)[b]	15 (8.9)	28 (8.5)	19 (8.3)	28 (4.6)	12 (3.5)
Ongoing cardiac disease	120 (12.8)	17 (10.1)	41 (12.4)	35 (15.4)	63 (10.4)	32 (9.3)
Ongoing wound problems	64 (6.8)[c]	12 (7.1)	22 (6.7)	10 (4.4)	27 (4.5)	14 (4.1)
Serious nutritional compromise	63 (6.7)[b]	3 (1.8)	7 (2.1)	2 (0.9)	3 (0.5)	3 (0.9)
Hemodialysis	95 (10.1)[b]	22 (13.1)	30 (9.1)	18 (7.9)	29 (4.8)	10 (2.9)
Substance abuse or mental health disorder	10 (1.1)	1 (0.6)	8 (2.4)	2 (0.9)	7 (1.2)	4 (1.2)
No. of bed sections						
Mean	2.5[c]	2.5	2.5	2.6	2.3	2.1
Range	1-18	1-9	1-14	1-11	1-14	1-11
Time from surgery to rehabilitation discharge, d						
Mean	28.1[b]	43.4	37.4	42.3	44.0	81.9
Range	1-176	1-176	1-180	2-178	1-180	1-180
Functional status						
Initial cognitive FIM score						
Mean	21.9[b]	29.3	31.3	31.0	33.1	34.2
Range	5-35	15-35	14-35	15-35	18-35	23-35

Abbreviation: FIM, Functional Independence Measure.
Numbers in parentheses are percentages of column totals for sex, marital status, living location before hospitalization, amputation level, and total bed sections.
[a] See the "Physical Grades" subsection of the "Methods" section for a detailed explanation.
[b] $P < .001$.
[c] $P < .05$.
[d] $P < .01$.

Table 2. Time-Varying Nature of Relationship Between Physical Grade at Rehabilitation Discharge and Mortality Risk Up to 6 Months After Discharge

	Days After Discharge, Hazards Ratios (95% Confidence Intervals)			
Grade[a]	30	90	120	180
1				
Unadjusted	43.9 (10.8-78.2)	12.5 (5.6-28.1)	6.7 (3.0-14.9)	1.9 (0.5-7.7)
Adjusted	17.0 (4.0-71.4)	5.2 (2.2-12.1)	2.8 (1.2-6.6)	0.9 (0.2-3.6)
2				
Unadjusted	8.9 (1.9-42.4)	4.8 (1.9-12.4)	3.5 (1.3-9.6)	1.9 (0.3-10.6)
Adjusted	4.5 (0.9-21.6)	2.4 (0.9-6.3)	1.8 (0.6-4.9)	0.9 (0.2-5.4)
3				
Unadjusted	11.4 (2.6-49.2)	3.1 (1.2-7.9)	1.6 (0.6-4.6)	0.4 (0.1-2.6)
Adjusted	7.4 (1.7-32.2)	2.0 (0.8-5.2)	1.0 (0.4-3.0)	0.3 (0.0-1.7)
4				
Unadjusted	3.8 (0.7-20.0)	2.1 (0.7-5.8)	1.6 (0.5-4.7)	0.9 (0.1-5.8)
Adjusted	2.4 (0.4-12.8)	1.3 (0.5-3.7)	1.0 (0.3-3.0)	0.5 (0.1-3.7)
5				
Unadjusted	4.6 (1.1-20.4)	2.7 (1.2-6.5)	2.1 (0.9-5.0)	1.2 (0.3-5.6)
Adjusted	3.7 (0.8-16.3)	2.2 (0.9-5.2)	1.7 (0.7-4.0)	1.0 (0.2-4.5)

[a] See the "Physical Grades" subsection of the "Methods" section for a detailed explanation.

grades; however; overall, the effect of grade on survival remained highly statistically significant ($P < .001$). According to the full model, there was still a nearly 7-fold increase in risk of dying within 6 months in individuals at grade 1 compared with those at grade 6 (odds ratio [95% CI], 6.8 [2.9-15.7]). Age was no longer statistically significantly associated with mortality after grade adjustment ($P > .05$). For every 5-point decline in the 5-variable cognitive FIM score, there was an approximately 20% increase in risk of dying within 6 months of inpatient rehabilitation discharge (1.2 [1.1–1.3]), controlling for all other factors. Known metastases were associated with a greater than 9-fold increased risk of death, and pulmonary circulation problems were associated with a greater than 3-fold increased risk of death. Need for hemodialysis, valvular disease, or anemia from blood loss were associated with a greater than 2-fold increased risk. Amputees with a history of depression, congestive heart failure, or chronic lung

Table 3. Multivariate ORs for Cumulative Risk of 6-Month Mortality

	OR (95% CI)[a]	
	Clinical Characteristics	
Variable	Adjusted for Demographic Data	Adjusted for Demographic Data and Clinical Characteristics
Functional grade (reference, grade 6)[b]		
1	...	6.8 (2.9-15.7)[c]
2	...	2.4 (0.9-6.3)
3	...	2.4 (1.0-6.0)[d]
4	...	1.2 (0.4-3.3)
5	...	2.2 (0.9-4.9)
Demographic data	...	
Age (reference, age ≤60), y	...	
61-70	1.3 (0.9-1.9)	1.1 (0.7-1.6)
71-85	1.7 (1.2-2.4)[e]	1.3 (0.9-1.9)
≥86	2.9 (1.5-5.5)[e]	2.2 (1.1-4.1)[d]
Sex (reference, female)		
Male	1.7 (0.4-6.4)	1.6 (0.4-6.1)
Marital status (reference, not married)		
Married	1.1 (0.8-1.4)	1.1 (0.8-1.4)
Amputation level (reference, unilateral transtibial)		
Unilateral transfemoral	1.4 (1.1-1.9)[d]	1.2 (0.9-1.6)
Bilateral transtibial	1.1 (0.5-2.4)	0.9 (0.4-2.1)
High bilateral	1.1 (0.7-1.9)	0.9 (0.5-1.5)
Contributing etiology		
Trauma	1.5 (1.1-2.1)[d]	1.4 (1.0-2.0)[d]
Elixhauser comorbidities		
Congestive heart failure	1.5 (1.1-2.0)[e]	1.4 (1.1-1.9)[d]
Chronic anemia from blood loss	2.7 (1.3-5.5)[e]	2.7 (1.3-5.7)[e]
Chronic pulmonary disease	1.4 (1.1-1.9)[d]	1.5 (1.1-2.0)[e]
Depression	1.9 (1.3-2.8)[e]	1.8 (1.2-2.8)[e]
Metastatic cancer	9.4 (4.5-19.6)[b]	9.7 (4.5-20.8)[c]
Other neurologic disorders	0.5 (0.2-1.2)	0.5 (0.2-1.2)
Paralysis	0.8 (0.3-1.7)	0.5 (0.2-1.2)
Psychoses	0.7 (0.4-1.1)	0.6 (0.4-1.1)
Pulmonary circulatory disease	3.4 (1.3-8.7)[e]	3.9 (1.5-10.2)[e]
Valvular disease	2.3 (1.4-3.7)[e]	2.4 (1.5-4.0)[c]
Weight loss	1.8 (0.8-2.3)	1.4 (0.8-2.4)
Baseline medical complexity		
Medical acuity by procedures		
Active pulmonary disease	5.2 (2.1-13.1)[e]	4.2 (1.6-10.9)[e]
Acute central nervous system disorder	1.8 (1.2-2.7)[e]	1.9 (1.3-2.8)[e]
Hemodialysis	2.8 (1.9-4.1)[c]	2.3 (1.6-3.5)[c]
Substance abuse or mental health disorder	1.8 (0.7-4.8)	2.1 (0.8-5.6)
Time from surgery to rehabilitation discharge, d	1.1 (1.0-1.1)[e]	1.0 (0.9-1.0)[e]
Functional status		
Initial cognitive FIM score	1.4 (1.3-1.5)[c]	1.2 (1.1-1.3)[c]

Abbreviations: CI, confidence interval; ellipses, not estimated; FIM, Functional Independence Measure; OR, odds ratio.
[a]Survival analysis showed nonproportional hazards. Consequently, odds ratios and 95% confidence intervals were reported for clinical covariates.
[b]See the "Physical Grades" subsection of the "Methods" section for a detailed explanation.
[c]$P < .001$.
[d]$P < .05$.
[e]$P < .01$.

disease were at approximately 84%, 42%, and 48% increased risk over and above the grade achieved.

Figure 2 shows survival curves from the full model. This characterizes lack of progression beyond grade 1 as being associated with a markedly poorer prognosis for 6-month survival compared with even minimal recovery to grade 2. Improvements in prognoses beyond grade 2 occurred but to a much smaller degree. The C statistic of the reduced model was 0.80 for mortality on demographic data and clinical characteristics (a 26-variable model). In the full model, combining grade with demographic data and clinical characteristics, the C statistic was 0.82 (a 31-variable model). The Hosmer-Lemeshow goodness-of-fit tests yielded $P > .05$, indicating appropriate model calibration.

COMMENT

Results document a single threshold at the second grade of physical independence compared with the first grade at which the relative probability of 6-month survival increases sharply in veterans after lower extremity amputation. There were much smaller incremental benefits as-

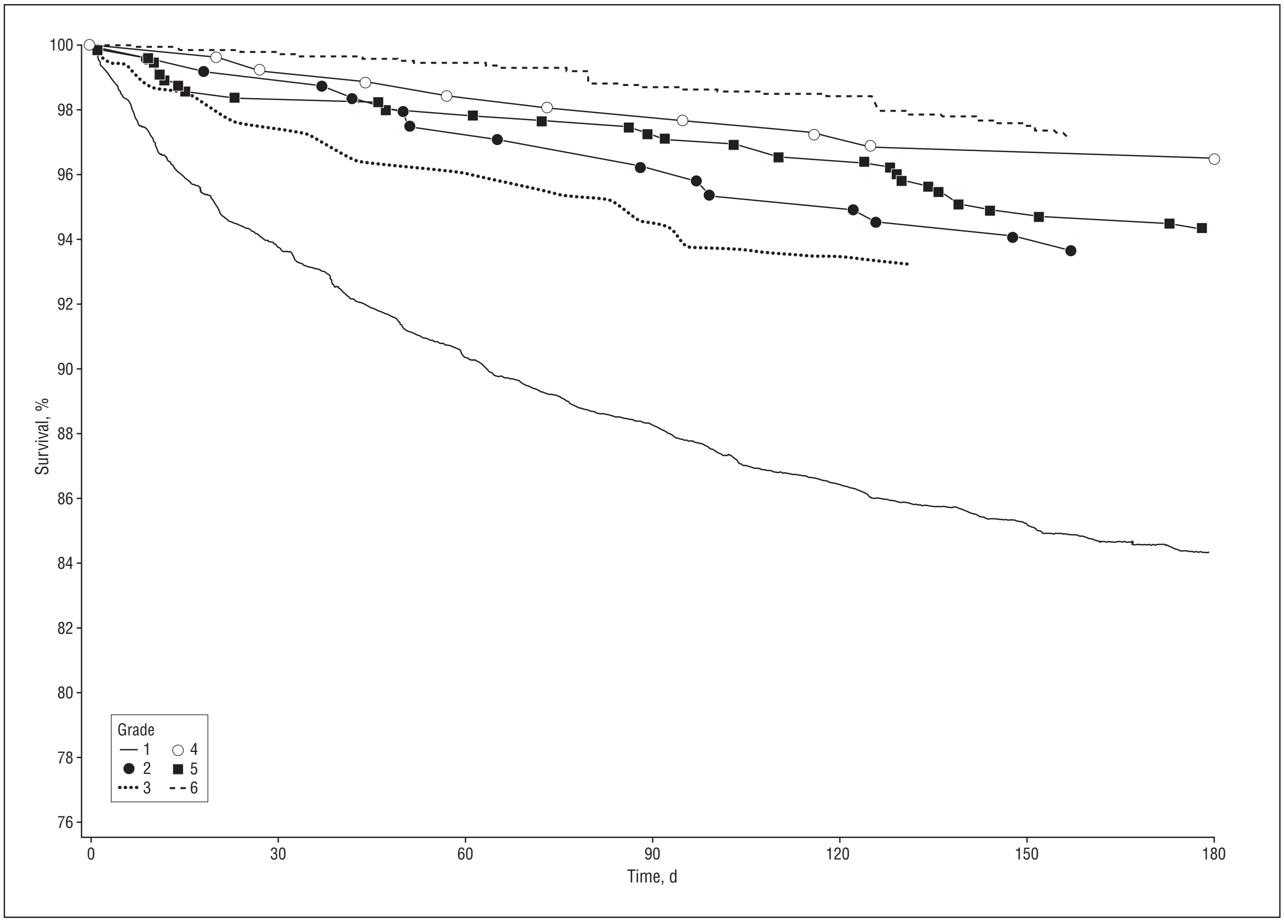

Figure 2. Adjusted survival by grade. See the "Physical Grades" subsection of the "Methods" section for a detailed explanation.

sociated with improving 1 grade beyond that point. Thus, the effects of improvement seem to have a far greater survival benefit at the lower than the higher levels of function. The achievement of grade 2 and above compared with grade 1 continued to differentiate amputees by lower and higher mortality risk even after adjusting for the other demographic data and clinical characteristics. Just more than 25% of veterans at grade 1 died within 6 months of completing inpatient rehabilitation compared with less than 10% of those who achieved grade 2.

Because grade 2 seems to be an important threshold, it is valuable to compare the functional characteristics of these patients with those at grade 1. Patients at grade 2 are beginning to be able to participate in self-care. They require no more than moderate assistance to eat, groom, manage bowel functions, transfer from bed to chair, and transfer from chair to toilet. In contrast, patients at grade 1 have almost no ability to participate purposively in any of these activities; thus, they are the group with the heaviest custodial care need. Functional grade remained a clinically and statistically significant predictor of death even after removing the effects of demographic data and other types of clinical characteristics. This supports our hypothesis that the grade achieved independently affects survival.

Findings begin to disentangle the complex influence of diagnoses and functional information on survival and provide insight into causal mechanisms. The full model estimates the singular importance of grade. Even after removing the risks associated with demographic data and clinical characteristics, patients who remained at grade 1 after surgical amputation were almost 7 times more likely to die within 6 months of completing rehabilitation compared with those at grade 6. The grade achieved provides prognostic information over and above other types of clinical information and is consistent with other studies showing the independent effects of function on mortality risk.[42-45]

Findings also provide insight into the causal mechanisms through which amputation level, associated clinical characteristics, and grade combine to influence 6-month mortality. Analyses confirmed that clinical characteristics have varying direct and indirect effects on risk of dying. The full model with grade present compared with the reduced model shows that although advanced age, high amputation level, metastatic cancer, and hemodialysis are associated with greater mortality,[6,24,44,46-48] some of these factors primarily influence 6-month mortality indirectly. The effect of advanced age and amputation level seem to have little direct or independent effect on grade. Advanced age is highly associated with morbidity and logically retards the ability to regain function, which in turn affects mortality. Moreover, without a knee joint, individuals who have undergone transfemoral compared with transtibial amputation are less likely to recover physical function. Thus, it seems that the indirect effects of age and amputation level on functional recovery are influencing mortality more than the direct effects of these variables. In contrast, certain comorbidities have a predominant direct influence. Patients receiving hemodialysis had a 2.8-fold increased likelihood of death, which changed only slightly after removing the influence of grade. A history of metastatic cancer was associated with more than 9-fold unadjusted and adjusted increased likelihood of death, showing the strongest direct effect of all conditions with virtually no indirect effect.

The study has several limitations. Findings cannot necessarily be generalized to all amputees, only to those who undergo surgery and subsequent inpatient rehabilitation in the Veterans Health Administration. However, this study would be impossible in the private sector because certain data elements are not available. Race/ethnicity was not included because of large amounts of missing data. Because the data were from an aged veteran population, findings may be more relevant to men than to women. Although functional outcomes achieved by rehabilitation discharge seem to have a strong influence on survival, this design provides no information about the degree to which the grades were caused by rehabilitation.

To our knowledge, this is the first time discrete grades of physical independence have been used to study how the level and type of physical recovery achieved in a specific diagnostic group translates into cumulative survival over time. We hope that introduction of these distinct grades of physical function will provide a major stimulus for advances in studying the effects of treatment and the implications of disability. The magnitude and variability in risk among individuals at grade 1 highlights both the high levels of vulnerability and clinical heterogeneity among amputees who recover little function, which implies the need to study patients at grade 1 more closely.

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