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ORIGINAL ARTICLE

Changes in Cognitive Function From Presurgery to 4 Months Postsurgery in Individuals Undergoing Dysvascular Amputation

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Abstract

Objective: To describe cognition among individuals with new amputations at 3 time points: presurgical, 6 weeks postamputation, and 4 months postamputation.

Design: Prospective cohort.

Setting: Medical centers.

Participants: Referred sample Veterans who were primarily men (N=80) experiencing their first lower extremity amputation as a result of complications of diabetes mellitus or peripheral arterial disease. Patients were screened for the absence of gross cognitive impairment using the Short Portable Mental Status Questionnaire (SPMSQ). Of those 87 individuals who were eligible, 64% enrolled; 29 were enrolled presurgically and have cognitive data for all 3 time points, and 58 were enrolled postamputation. Eighty of the 87 individuals enrolled by 6 weeks remained enrolled at 4 months.

Interventions: Not applicable.

Main Outcome Measures: Demographic and general health information, general mental status (SPMSQ), and 4 brief, well-established neuropsychological measures.

Results: Most mean neuropsychological test scores fell in the low average or average range. For most participants, overall cognitive status improved from pre- to postsurgery and then remained stable between 6 weeks and 4 months. There were significant improvements between pre- and postsurgical test scores in verbal learning and memory, and these remained unchanged between 6 weeks and 4 months. Better 4 month cognitive performance was associated with higher perceived general health.

Conclusions: Overall cognitive performance is poorest presurgically. Though there is improvement between pre- and postamputation, cognition appears generally stable between 6 weeks and 4 months.

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Diabetes mellitus (DM) and peripheral arterial disease (PAD) account for 82% of lower limb amputations in the United States.[1] These chronic diseases are frequently comorbid, with at least 20% of individuals with PAD also having DM[2] and roughly 25% of individuals with DM also having PAD.[3,4] Among those with lower limb amputation, upward of 48% are diagnosed with DM, and 94% are diagnosed with PAD.[5]

Both PAD and DM can impact cognitive function,[6,7] causing decreases in processing speed, verbal memory, and cognitive flexibility. This has implications for rehabilitation because stronger

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attention, working memory and visual-constructional skills are associated with successful prosthetic fitting,[8-10] restoring mobility,[8,11-13] and greater independence with activities of daily living.[14,15] Additionally, prevalence of dementia among those with amputations due to dysvascular disease is higher than among amputees without PAD[16,17] (estimates range from 5% to 49%) and is associated with poorer overall rehabilitation outcomes.[18,19]

In addition to the underlying disease processes, new amputees may experience postoperative cognitive dysfunction (POCD) or a decline in cognitive performance from pre- to postsurgery related to anesthesia and the surgical intervention. POCD is common 1 week after surgery[20] and can persist for as long as 3 months. Late POCD, present beyond 3 months, is more likely to be present among older individuals or those with preexisting cognitive impairment[20-23] and continues to be present in about 1% of older adults at 1 to 2 year follow-up.[24] Other superimposed acute factors may create or exacerbate cognitive deficits around the time of amputation surgery. Anxiety and depressive symptoms, which are prevalent among new amputees[25] have been associated with decreased cognitive performance,[26,27] as has pain,[28,29] which is reported in 85% of new amputees.[30] The presence of even minor infection has also been shown to impact cognitive performance.[31] A variety of common medications, such as narcotic pain medications, can interfere with cognitive performance as well.[32]

Of 3 pertinent studies, all suggest that dysvascular amputees have impairment in several cognitive domains compared with case-matched controls or population norms.[10,15,33] Of these, only 1 study is prospective.[15] None of these studies evaluate or describe presurgical cognition.[34] This is notable because cognitive status may factor into presurgical rehabilitation decisions (ie, level of amputation).

The overarching objective of this study is to describe cognition from presurgery to 4 months postamputation in individuals undergoing first lower limb amputation. First, we assess whether there are changes in an aggregate measure of cognition over time. Second, we assess variation in specific cognitive domains. Third, we assess if there are subgroups of participants for whom overall cognitive status is more vulnerable to change around amputation.

Methods

Study design

This study is part of a larger multisite prospective cohort study of individuals undergoing major lower extremity amputation surgery because of PAD or DM at 2 Veterans Affairs medical centers, a university hospital, and a level I trauma center. For this study, participants were assessed via in-person interview presurgically and via in-person or telephone interview at 6 weeks and 4 months postsurgically. Participants who were not available presurgically were enrolled at 6 weeks. This study was conducted in accordance with the procedures approved by the human subjects review boards at each study site.

List of abbreviations:

DM	**diabetes mellitus**
MDE	**major depressive episode**
PAD	**peripheral arterial disease**
POCD	**postoperative cognitive dysfunction**
SPMSQ	**Short Portable Mental Status Questionnaire**

Participants

Subjects were considered eligible if they were age ≥18 years; they were awaiting (or underwent in the last 6wk) a first major lower extremity amputation, defined as transmetatarsal level or higher; and the primary cause of amputation was DM or PAD. Subjects were excluded if they had cognitive or language impairment that would preclude consent or participation, defined by >4 errors on the Short Portable Mental Status Questionnaire (SPMSQ),[35] or if they were nonambulatory prior to admission to the hospital for reasons unrelated to impairment of the extremity awaiting amputation, or if the planned amputation was bilateral. Of 239 individuals screened between 2005 and 2008, 136 (57%) met study criteria, and 87 (64%) enrolled (29 presurgically and 58 at 6wk). The primary reason for exclusion was prior amputation (n=34, 38%); these individuals may also have had dementia or failure of the SPMSQ, but this was not assessed once a candidate was excluded for other reasons. An additional 23 (22%) participants were excluded solely because of dementia or failure of the SPMSQ. Five (5.8%) participants died, and 2 (2.3%) were lost to follow-up; 80 (92%) participants remained enrolled at 4 month follow-up (table 1).

Measures

Cognitive tests were administered within the week prior to amputation surgery for 29 subjects. The same battery was administered to 87 subjects at 6 weeks and 80 subjects at 4 months (table 2). There were no significant differences in neuropsychological test scores between those who were enrolled presurgically and those who were enrolled postamputation at either time point, and there were not significant health and demographic difference between the 2 groups.

Two rehabilitation psychologists trained research staff to administer the tests and supervised initially to ensure competent administration. Tests were scored by a trained psychometrist and then rescored by a postdoctoral neuropsychology fellow. When scores were discrepant, a project investigator (R.M.W.) reviewed the scores to ascertain accuracy. Standardized z scores were computed using available norms that adjust for sex, age, and in the case of digit span, education also (see table 2). In all cases, a z score of 0 indicates function at the 50th percentile, whereas positive/greater z scores indicate better cognitive performance, and negative/lower z scores indicate poorer function. Scores can be interpreted as follows: average range ($-.67 \geq z \geq .67$, 25th−75th percentile), low average range ($-.66 \geq z \geq -1.33$, 9th−24th percentile), borderline ($-1.32 \geq z \geq -2.01$, 2nd−8th percentile), and impaired ($-2 \geq z$, <2nd percentile).[36]

Neuropsychological tests

Participants completed the 10-item SPMSQ at each time point. Several subtests of the Repeatable Battery for the Assessment of Neuropsychological Status[37] were administered to assess executive function (semantic fluency), auditory-verbal learning (list learning), and verbal memory (list recall). The Repeatable Battery for the Assessment of Neuropsychological Status offers alternative forms to minimize practice effects. Form A was used at the presurgical and 4-month assessments, whereas form B was used for the 6-week administration. Participants completed the digit span