Comparison of the Functional Outcomes of Lower Limb Amputees with or without End-Stage Renal Disease

Atzmon Tsur MD[1,3], Nael Shakeer MD[1] and Ronit Geron MD[2,3]

Departments of [1]Rehabilitation and [2]Nephrology, Galilee Medical Center, Nahariya, Israel
[3]Bar Ilan University Faculty of Medicine in the Galilee, Safed, Israel

ABSTRACT: **Background:** The potential for full rehabilitation following amputation among end-stage renal disease patients is poor.
Objectives: To evaluate the functional outcomes and survival among amputees treated with hemodialysis at the end of the rehabilitation procedure.
Methods: We recruited 46 patients after lower limb amputation. Of these individuals, 19 (41.3%) were treated with dialysis and 27 (58.7%) were non-dialysis-dependent patients (NDDP). Both groups were divided into three sub-groups according to their independence with regard to activities of daily living (ADL) and their ability to walk with a prosthesis.
Results: The survival of lower limb amputees treated with dialysis was shorter compared to NDDP. Survival after amputation among the NDDP who were fully or partially independent in ADL and with regard to mobility, was longer compared to the non-mobile amputees as with the patients treated with dialysis.
Conclusions: Survival was significantly longer in lower limb amputees NDDP and shorter in patients who did not achieve a certain level of functioning. The level of functioning among amputees who were not treated by dialysis was higher than those who received dialysis.

IMAJ 2019; 21: 585–588

KEY WORDS: amputees, non-dialysis-dependent patients (NDDP), dialysis, end-stage renal disease (ESRD)

The number of patients who present with end-stage renal disease (ESRD) treated by dialysis is continuously increasing and their rate of death is higher than the general population [1]. In these patients, there is a high frequency of background diseases such as diabetes mellitus, ischemic heart disease, arterial hypertension, peripheral vascular disease (PVD), and polyneuropathy [1,2].

Patients treated with dialysis have a higher frequency of arteriosclerotic disease and intensive cardiovascular morbidity and mortality. PVD is one of the main causes that negatively influence survival of the patients treated with dialysis [3-5].

Non-traumatic lower limb amputation (LLA) is a serious complication of both diabetic neuropathy and PVD. Many people with ESRD present with advanced progression of these diseases and are at an extremely high risk for LLA. Diabetes is the strongest risk factor for amputation in dialysis patients, starting as soon as the dialysis therapy is initiated [6]. The progression of diabetes to ESRD is associated with the progression of multiple other complications of diabetes, including neuropathy and PVD [8]. Loss of protective sensation puts patients at risk for neuropathic ulceration from repetitive stress or minor trauma [9,10]. Primary major amputation may be the treatment of choice in patients with forefoot or heel gangrene, or in patients with uncontrolled deep-seated infection of the foot [11,12,13].

Of the patients who present with ESRD, 5% can develop severe ischemia in the lower limbs, especially among those treated by dialysis [11]. According to Orimoto et al. [12], the annual frequency of ischemic necrosis in the limbs due to arteriosclerosis is 0.14/1000 in patients who are diagnosed with diabetes mellitus without renal involvement, 7.1/1000 in non-diabetic patients with dialysis, and 41.4/1000 in diabetic patients treated with dialysis. ESRD represents a vasculopathic state with atherosclerotic cardiovascular disease remaining the major contributor to their high morbidity [7,13]. Due to the aging population and increasing prevalence of diabetes mellitus, lower extremity PVD has become common in ESRD patients, leading to an increase in the need for amputation in this population [11,14]. Limb amputation is usually a last resort, when conservative measures and/or revascularization have failed or when the patient is not a candidate for revascularization. Dialysis patients have high rates of non-traumatic LLA resulting from various causes, compared to the general population [14,15]. Among ESRD patients receiving dialysis, the incidence of amputation is about 10 times higher than in the general diabetic population [15].

The purpose of this study was to evaluate the functional outcomes and survival at the end of the rehabilitation procedure, among the amputees with ESRD who were treated by dialysis, compared to non-dialysis-dependent patients (NDDP) amputees.

PATIENTS AND METHODS

The study was approved by the institutional ethics committee in agreement with the Helsinki Declaration. This 4-year retrospective study (2010–2013) examined the medical charts of patients who underwent either a below-knee or above-knee amputation, and were admitted for in-hospital prosthetic rehabilitation at the Galilee Medical Center, Nahariya, Israel. The study compared the population of lower-limb amputees treated by dialysis (research group) with the NDDP (control group). The

following parameters were recorded for each patient: age, gender, familial status, religion, type of dialysis, length of dialysis treatment before the amputation, reason mostly responsible for LLA, length of rehabilitation period given in the hospital, and the cause of death if relevant.

The in-hospital rehabilitation procedure of lower-limb amputees included two stages. The first occurred several days after the amputation surgery, and the second was a few months later, after receiving the first-time prosthesis. Both stages lasted from 2 to 4 weeks.

Forty-six patients, 35 men and 11 women, underwent LLA. Of these, 19 (41.3 %), with an average age of 62.6 ± 11.6 years, were treated by dialysis and 27 (58.7%), with an average age of 57.9 ± 11.5 years, were not. The reasons for LLA in patients treated by dialysis were diabetes mellitus (n=14), and PVD (n=5). The reasons for lower-limb amputation in patients not treated by dialysis were diabetes mellitus (n=19), PVD (n=5), and trauma (n=3). Among the 19 patients in dialysis treatment, 16 (84.2%) were treated by hemodialysis and 3 (15.8%) by peritoneal dialysis. Eleven patients underwent below-knee amputations and 8 above-knee amputations. Among the 27 patients not treated by dialysis, 16 underwent below-knee amputations and 11 had above-knee amputations. The duration of dialysis before lower-limb amputation in the research group was 25.0 ± 14.2 months. Three amputees were excluded from the study due to complications after surgery that prevented them from receiving a prosthesis.

Both the research and control groups were divided into three sub-groups according to their functional ability at the end of the second stage of the rehabilitation treatment [16]:

- *Sub-group 1:* Patients who achieved independence in their activities of daily living (ADL), were able to walk on a flat surface with or without an assistive device, could walk up and down stairs, and could assemble the prosthesis by themselves
- *Sub-group. 2:* Patients who achieved only partial independence in their ADL and were able to walk on a flat surface, but expressed difficulty in using stairs and needed assistance to assemble the prosthesis
- *Sub-group 3:* Patients who were not able to walk with the prosthesis at the end of the in-hospital rehabilitation period

STATISTICAL ANALYSIS

Statistical analyses were performed using IBM Statistical Package for the Social Sciences statistics software, version 19 (SPSS, IBM Corp, Armonk, NY, USA). Qualitative data were described by frequencies and percentages. Quantitative data were described by mean and standard deviation, median, and range.

Comparison of quantity characteristics between the groups were performed by ANOVA, Kruskal–Wallis test, independent sample *t*- test, and Wilcoxon rank sum test.

The decision of which test to use was determined according to the size of the groups and the shape of the data distribution. To compare qualitative data, Chi-square test or Fisher's exact test was used. The choice between those tests was according to pre-assumptions of these tests.

Kaplan–Meier analysis was performed to evaluate the survival function and log rank (Mantel–Cox) was used to compare the survival function between the groups. A P value < 0.05 was considered statistically significant

RESULTS

The duration of rehabilitation following amputation (first step) and after receiving the prosthesis (second step), the length of survival after amputation, and the level of functioning after rehabilitation, are shown in Table 1. The level of functioning among amputees who were not treated by dialysis was higher than those who received dialysis (P = 0.037).

The 3-year survival rate of dialysis patients after LLA surgery was shorter (46.5%) compared to patients not treated with dialysis (46.5% vs. 83.5%, respectively, P = 0.018) [Figure 1].

The survival after the amputation among non-dialysis patients who belonged to sub-groups 1 or 2, was significantly longer compared to the amputees who belonged to sub-group 3 (P = 0.011) [Figure 2]. The length of survival after amputation was 51.4 ± 3.4 months in sub-group 1, 43.8 ± 3.0 months in sub-group 2, and 18.0 ± 7.9 months in sub-group 3.

Among the dialysis patients in sub-group 1, the odds of survival and the length of life one year after amputation were

Table 1. Duration of rehabilitation, survival, and level of functioning of the amputees

Duration, survival, and functioning		In dialysis N=19	Non-dialysis dependent N =27	*P* 2-sided
Duration of rehabilitation after amputation, in days	mean	24.1 ± 7.7	23.1 ± 14.2	0.231**
	median	21.0	20.0	
	range	13–42	12–82	
Duration of rehabilitation after receiving of prosthesis, in days	mean	16.5 ± 7.8	16.7 ± 6.2	0.932*
	median	18.0	17.0	
	range	0–28	0–28	
Survival after amputation, in months	mean	20.1 ± 15.5	25.8 ± 14.5	0.216**
	median	17.1	23.1	
	range	2–50	3–55	
Level of functioning after discharge from rehabilitation department	Independent	5 26.3%	11 40.7%	0.037**
	Partially independent	5 26.3%	13 48.1%	
	Completely assisted	9 47.4%	3	

*Student's *t*-test

**Wilcoxon rank sum test

Figure 1. Overall survival after amputation of patients treated or not treated by dialysis (log rank test, $P = 0.018$)

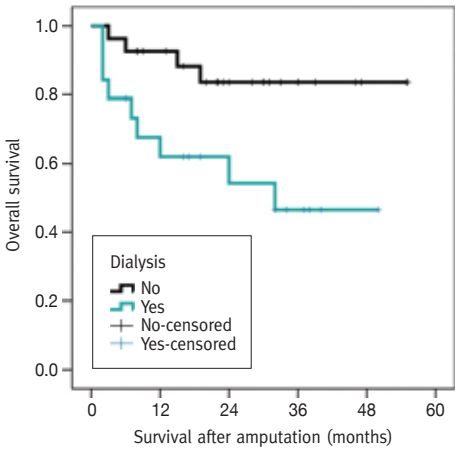


Figure 2. Overall survival after amputation in patients who were not treated by dialysis, according the level of functioning in the three sub-groups (log rank test, $P = 0.011$)

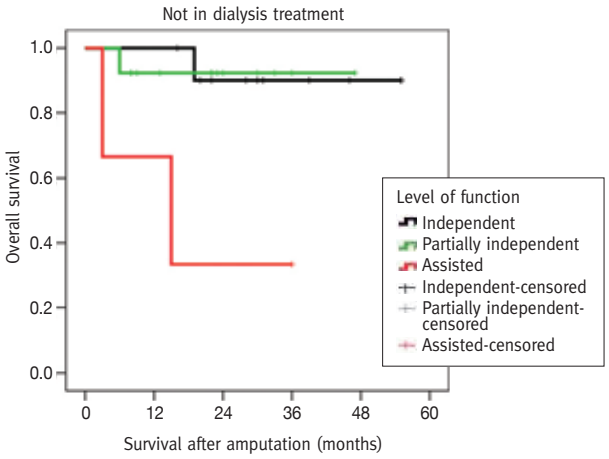
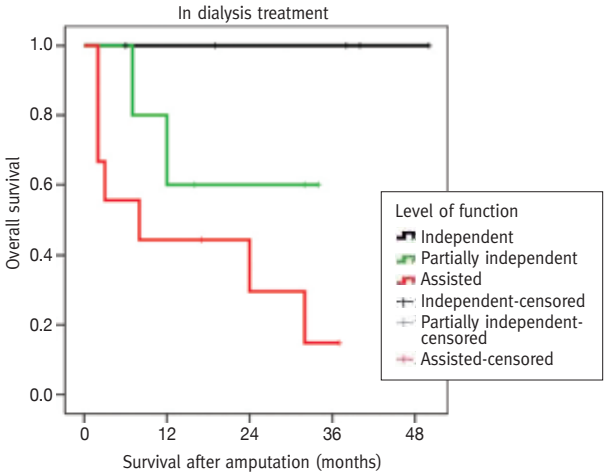


Figure 3. Overall survival after amputation in patients treated by dialysis, according the level of functioning in the three sub-groups (log rank test, $P = 0.034$)



higher (100%) than in sub-group 2 (60%) and much higher than in sub-group 3 (44%), ($P = 0.034$) [Figure 3].

DISCUSSION

In this study, rehabilitation outcomes and survival in a cohort of amputees who underwent two stages of rehabilitation as in-patients were examined. Inpatient rehabilitation improved functional status, and length of stay were important predictors of functional gain [17,18]. Patients with poor functional capacity at admission may have longer length of stay because of unstable medical conditions resulting in higher care needs. Younger amputees tend to have greater functional recovery, initiate prosthesis use, maintain ambulation with prosthesis, and have improved survival [19,20]; however, in our study, age was not found to have a significant effect on functional gain. Rehabilitation in amputees with limb loss due to ESRD, before and after fitting of prosthesis, is generally more difficult than in those who do not have severe chronic kidney disease. The dialysis treatment weakens the patients for several hours and prevents them from effort-making during physical therapy. Stump dimensions are different before and after the dialysis,which may prevent the patients from succeeding in assembling the prosthesis [16].

The lower survival of 50% among all the ESRD patients one year after amputation is not surprising in view of the overall morbidity and mortality among this group [21]. In ESRD, a co-morbid illness may have a greater effect on the individual patient's outcome than renal disease. Chae et al. [2] enrolled 456 patients on hemodialysis. Diabetes with complications was the most common co-morbidity. Congestive heart failure, coronary artery disease, cerebrovascular accident, and mild liver disease were less common co-morbidities. The potential for full rehabilitation following amputation is poor in ESRD patients compared with other amputees, and the loss of independence may necessitate institutional care [15].

Patients with prior amputation displayed considerably higher mortality than patients who did not undergo previous amputation [14]. Patients on dialysis who had undergone amputation had a 10-year mortality rate that was three times greater than in NDDP who required amputation [22]. Patients with ESRD had increased hospital mortality rates and decreased long-term survival rates after amputation compared with non-ESRD patients [23]. Our research showed that 54% of the patients treated by dialysis survived 2 years, and 47% survived 3 years after amputation, while 84% of the patients not treated

by dialysis survived 2 and even 3 years after amputation. These data conform approximately with published results [22,23].

The short survival rate found in patients not treated by dialysis who were discharged from the rehabilitation department still needing assistance (sub-group 3), is explained by their immobility. Among the patients treated by dialysis, survival was shorter in those who were discharged from rehabilitation either as partially independent (sub-group 2) or as needing assistance (sub-group 3). Functional gain such as "initiate prosthetic use" and "maintain ambulation with the prosthesis" are predictors of long-term survival [18].

Patients receiving inpatient-based rehabilitation had better survival compared to patients receiving community rehabilitation, having a multi-disciplinary team to provide holistic care in place [17], and needing early rehabilitation after amputation improves functional outcome [24].

The mean duration of the dialysis conducted before amputation was 25 months. The age of the patients in dialysis treatment was higher compared to those who did not receive this kind of treatment. There was no significant difference in the two groups regarding the duration of rehabilitation before and after fitting the prosthesis.

This study has several limitations. The most important one involves missing data of risk factors that can influence the rehabilitation outcomes such as neuropathy, retinopathy, severity of vascular disease, and heart disease. Another limitation was the inability to know the motivation of the patients to use their prosthesis as well as the existence of eventual cognitive disorders, anxiety, and depressive symptoms.

Singh and Prasad [25] found that initial prosthetic limb-fitting was an independent predictor of mortality. It is always possible that encouraging patients by prosthesis fitting results in better mobility and health. Non-fitted patients may find it harder to execute their activity of daily living and to achieve independence in mobility.

CONCLUSIONS

The level of functioning after discharge from rehabilitation department was higher among amputees who were not dialysis dependent. The findings of this research have several implications for rehabilitation care services. Survival was significantly higher in LLA non-dialysis dependent. The level of mobility and the independence in the activity of daily living among patients with chronic kidney disease treated or not treated with dialysis, had significant influence on the survival of those patients.

The study suggests encouraging amputees with ESRD and treated by dialysis to use a prosthesis and to engage in the rehabilitation process. In-hospital rehabilitation after amputation may help patients achieve better functioning and longer survival.

Correspondence
Dr. A. Tsur
Dept. of Rehabilitation, Galilee Medical Center, Nahariya 22100, Israel
Phone: (972-77) 451-1012, **Fax:** (972-77) 451-1012
email: atzi_t@netvision.net.il

References

1. Collins AJ, Foley RN, Chavers B, et al. United States Renal Data System 2011 Annual Data Report: Atlas of chronic kidney disease and end-stage renal disease in the United States. *Am J Kidney Dis* 2012; 59 (1 Suppl 1): A7, e1-e420.
2. Chae JW, Song CS, Kim H, et al. Prediction of mortality in patients undergoing maintenance hemodialysis by Charlson Comorbidity Index using ICD-10 database. *Nephron Clin Pract* 2011; 117: 379-84.
3. O'Hare AM, Bertenthal D, Shlipak MG, et al. Impact of renal insufficiency on mortality in advanced lower extremity peripheral arterial disease. *J Am Soc Nephrol* 2005; 16: 514-19.
4. O'Hare AM, Glidden DV, Fox CS, et al. High prevalence of peripheral arterial disease in persons with renal insufficiency: results from the National Health and Nutrition Examination Survey 1999-2000. *Circulation* 2004; 109: 320-3.
5. O'Hare AM, Sidawy AN, Feinglass J, et al. Influence of renal insufficiency on limb loss and mortality after initial lower extremity surgical revascularization. *J Vasc Surg* 2004; 39: 709-16.
6. McGrath NM, Curran BA. Recent commencement of dialysis is a risk factor for lower-extremity amputation in a high-risk diabetic population. *Diabetes Care* 2000; 23: 432-3.
7. Margolis DJ, Hofstad O, Feldman HI. Association between renal failure and foot ulcer of lower-extremity amputation in patients with diabetes. *Diabetes Care* 2008; 31: 1331-6.
8. Reiber GE, Pecoraro RE, Koepsell TD. Risk factors for amputation in patients with diabetes: a case control study. *Ann Intern Med* 1992; 117:97-105.
9. Johnson BL, Glickman MC, Bandyk DF, et al. Failure of foot salvage in patients with end-stage renal disease after surgical revascularization. *J Vasc Surg* 1997; 174: 149-51.
10. Simsir SA, Cabellon A, Kohlman-Trigoboff D, et al. Factors influencing limb salvage and survival after amputation and revascularization in patients with end-stage renal disease. *Am J Surg* 1995; 170: 113-7.
11. Jaar BG, Astor BC, Berns JS, et al. Predictors of amputation and survival following lower extremity revascularization in hemodialysis patients. *Kidney Int* 2004; 65: 613-20.
12. Orimoto Y, Ohta T, Ishibashi H, et al. The prognosis of patients on hemodialysis with foot lesions. *J Vasc Surg* 2013; 58: 1291-9.
13. O'Hare A, Johansen K. Lower-extremity peripheral arterial disease among patients with end-stage renal disease. *J Am Soc Nephrol* 2001; 12: 2838-47.
14. Combe C, Albert GM, Bragg-Gresham MS, et al. The burden of amputation among hemodialysis patients in the dialysis outcomes and practice patterns study (DOPPS). *Am J Kidney Dis* 2009; 54: 680-92.
15. Eggers PW, Gohdes D, Pugh J. Nontraumatic lower extremity amputations in the Medicare end-stage renal disease population. *Kidney Int* 1999; 56: 1524-33.
16. Korzets A, Ori Y, Rathaus M, et al. Lower extremity amputations in chronically dialysed patients: a 10 year study. *IMAJ* 2003; 5: 501-5.
17. Dillingham TR, Pezzin L. Rehabilitation setting and associated mortality and medical stability among persons with amputations. *Arch Phys Med Rehabil* 2008; 89: 1038-45.
18. Venkataraman K, Fong NP, Chan NP, et al. Rehabilitation outcome after inpatient rehabilitation for lower extremity amputations in patients with diabetes. *Arch Phys Med Rehabil* 2016; 97: 1473-80.
19. Czerniecki JM, Turner AR, Williams RM, et al. The effect of rehabilitation in a comprehensive inpatient rehabilitation unit on mobility outcome after dysvascular lower extremity amputation. *Arch Phys Med Rehabil* 2012; 93: 1384-91.
20. Schoppen T, Boonstra A, Groothoff JW, et al. Physical, mental, and social predictors of functional outcome in unilateral lower-limb amputees. *Arch Phys Med Rehabil* 2003; 84: 803-11.
21. Reiber GE. The epidemiology of diabetic foot problems. *Diabet Med* 1996; 13(suppl): 6-11.
22. Lavery LA, Hunt NA, Ndip A, et al. Impact of chronic kidney disease on survival after amputation in individuals with diabetes. *Diabetes care* 2010; 332365-9 :.
23. Dossa CD, Shepard AD, Amos AM, et al. Results of lower extremity amputations in patients with end-stage renal disease. *J Vasc Surg* 1994; 20: 14-9.
24. Ham R, Roberts VC, Cotton LT. Post-operative management of the amputee. *Br J Surg* 1986; 73: 508-9.
25. Singh RK, Prasad G. Long-term mortality after lower-limb amputation. *Prosthet Orthot Int* 2016; 40: 545-51.