Five-Year Mortality for Patients With End-Stage Renal Disease Who Undergo Upper Extremity Amputation

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Purpose To compare the 5-year survival rate of patients on dialysis requiring an upper extremity amputation with those who did not require such surgery and to analyze whether such an amputation was prognostic for mortality.

Methods The medical records of 20 consecutive patients with end-stage renal disease who received upper extremity amputations were reviewed. Control patients (n = 40) were matched based on age, sex, and duration of dialysis treatment. A Kaplan-Meier survival analysis was performed.

Results The mean survival time after the index surgery for the surgical group was 4.95 years ± 0.90 years, and the mean survival for the control group was 8.40 years ± 0.61 years. The probability of death (the event) was statistically greater in the surgical group. The overall 5-year survival rates for the surgical and the nonsurgical groups were 35% (7 of 20) and 70% (28 of 40), respectively. Patients with diabetes in the surgical group had a significantly lower 5-year survival rate, a greater number of amputations, and a greater number of wound-healing failures.

Conclusions The 5-year survival rate from the index surgery of the surgical group was half that of the nonsurgical group. Increased mortality may be partially attributed to the poor vascular health of the patient. This analysis may help the hand surgeon to more effectively counsel patients with end-stage renal disease about the prognosis associated with an upper extremity amputation and, more importantly, supports the goal of timely intervention by the multidisciplinary team to optimize care planning and to improve surgical outcomes and quality of life. *(J Hand Surg Am. 2015;40(4):666–672. Copyright © 2015 by the American Society for Surgery of the Hand. All rights reserved.)*

Type of study/level of evidence Prognostic III.

Key words Amputation, diabetes, dialysis, survival, upper extremity.

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Severe ischemia of the upper extremity necessitating amputation occurs less frequently than in the lower extremity. Approximately 5% of patients with limb ischemia have symptomatic involvement of their upper extremity.[1] Hemodialysis and/or peritoneal dialysis and vasospastic or connective tissue disorders and atherosclerotic disease are common associations of upper extremity ischemia. Indications for amputation include wet or dry gangrene and nonhealing ischemic ulcers. Some dialysates that contain calcium may exacerbate preexisting arterial disease and calcific arteritis.

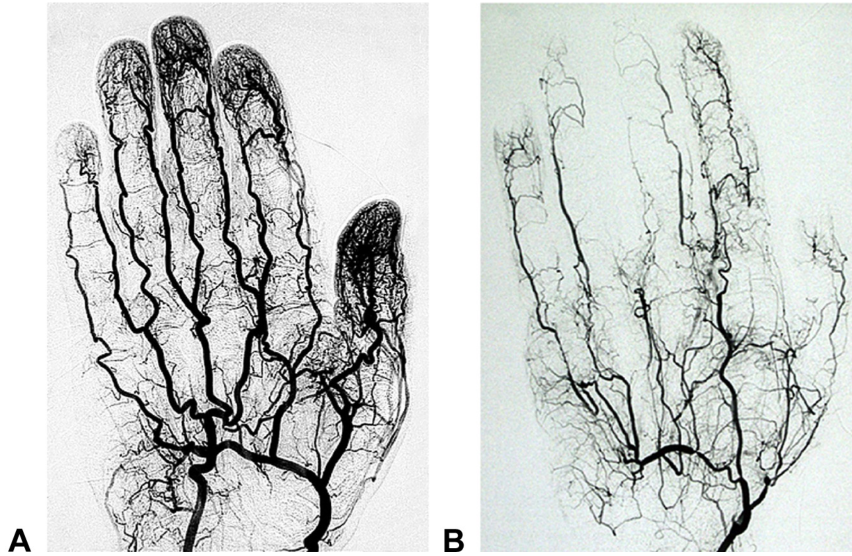

FIGURE 1: Hand arteriogram in a surgical and a nonsurgical patient. **A** The arteriogram indicates good distal filling and patent digital vessels. **B** In the surgical patient, flow is severely compromised in the distal digits, digital arteries, and ulnar artery. Irreversible poor blood flow compromises healing potential and may necessitate amputation.

In our experience, an upper extremity amputation for a patient on dialysis portends a poor prognosis for survival; however, this observation is not well documented in the literature. We hypothesized that upper extremity amputations in patients on dialysis is a prognostic indicator for increased mortality compared with patients on dialysis not requiring upper extremity amputations. We additionally hypothesized that the 5-year survival rate of patients with end-stage renal disease (ESRD) who required an upper extremity amputation was less than the survival of patients who do not require an upper extremity amputation.

MATERIALS AND METHODS

This study was approved by our institutional review board. From 2000 to 2008, 20 consecutive subjects with ESRD underwent upper extremity amputations by 3 fellowship-trained surgeons. The patients' age, age at initiation of dialysis, age at the index surgery, sex, duration of dialysis, level of amputation, number of amputations, complications, any concurrent lower extremity amputations, comorbidities, and tobacco use were included in the statistical analyses. All patients were evaluated for the possibility of revascularization; however, an amputation was performed if the finger was already necrotic, the remaining digits and hand were not compromised, and the hand had adequate radial and ulnar pulses with good capillary refill and skin turgor. Arteriography was performed if there was a possibility for revascularization (Fig. 1). Candidates who underwent revascularization were excluded. Plain radiographs were evaluated for evidence of bony erosion, osteomyelitis, and calcific arteritis. Two control patients were identified for each surgical patient and were matched for age at initiation of dialysis (± 2 y), sex, and number of years on dialysis. Two control patients per surgical patient were used to reduce the risk of statistical confounders. Because the control group did not undergo an upper extremity operation and the duration of time spent on dialysis was matched between groups, the matched patient's age at index surgery was used to compare survival after surgery between the groups. The age-adjusted Charlson Comorbidity Index (CCI) was calculated for all patients using comorbidities identified during the chart review from the notes and electronic medical

TABLE 1. Patient Group Demographics*

	Surgical (n = 20)	Control (n = 40)	*P*
Male	12 (60%)	24 (60%)	
Age at start of dialysis (y)	52 ± 12	50 ± 12	.57
Age at index surgery (y)	56 ± 10	NA	.48
Smoker	10 (50%)	22 (55%)	
Diabetes mellitus	13 (65%)	30 (75%)	
Number of medical comorbidities	4.85 ± 1.9	4.92 ± 1.9	.89
Age-adjusted CCI	7.1 ± 2.5	6.8 ± 2.2	.38

*All means reported ± SD. No statistically significant differences existed between groups.

TABLE 2. Patient Characteristics in the Surgical Treatment Group

Sex	Level and Progression of Amputation	Total Upper Extremity Amputations	Smoker	Diabetes	Lower Extremity Amputation	Vascular Calcifications	Complications	Cause of Death
M	L index PIP; R index P2; R long MCP	3	No	Yes	L BKA; R partial foot amputation	No	None	Cardiovascular
F	L middle PIP; L index PIP; L thumb IP; L little DIP	6	Yes	Yes	L second toe	No	L long MCP; L wrist disarticulation	Cardiovascular
F	L ring PIP	1	No	Yes	B Syme amputation revised to B BKA	Yes	None	Sepsis
M	R middle PIP	1	Yes	Yes	None	Yes	Revision	
M	R middle MCP, L middle P1, R ring MCP, R index MCP, R little PIP	5	No	Yes	L AKA	Yes	None	Cardiovascular
M	L middle PIP, L index DIP, R middle DIP, R ring PIP, R index MCP, R middle MCP, R ring MCP, R transmetacarpal, L ring MCP, R little PIP, L index ray resection, L middle ray resection, L wrist disarticulation	13	Yes	Yes	L BKA, R great toe amputation	Yes	Infection, and revision L ring MCP	Cardiovascular
M	R little PIP fusion, R little MCP	1	Yes	Yes	None	Yes	Infection	Cardiovascular
F	R thumb P1	1	No	No	R fourth toe amputation	Yes	None	
M	L forearm amputation	1	No	No	None	No	None	
M	L little P2, L little MCP	2	No	Yes	Fifth toe amputation		Infection, L little MCP	Cardiovascular
F	L index DIP, L index MCP, L middle DIP	3	No	Yes	None	Yes	None	Cardiovascular
F	R index MCP	1	No	No	Fourth, fifth ray amputation, B BKA	No	None	
F	R little DIP, R little MCP, R ring MCP	3	No	Yes	B BKA	Yes	Infection	Cardiovascular
M	L ring MCP	1	Yes	No	B BKA	Yes	None	
M	R wrist disarticulation, L ring P1, L ring MCP, L middle PIP, L index MCP, L little MCP	6	Yes	No	B AKA	Yes	Infection	Cardiovascular
F	L middle P2, L little ray, L middle transmetacarpal, L middle ray, L ring ray	6	No	Yes	R BKA	No	Infection	Cardiovascular

(Continued)

TABLE 2. Patient Characteristics in the Surgical Treatment Group (Continued)

Sex	Level and Progression of Amputation	Total Upper Extremity Amputations	Smoker	Diabetes	Lower Extremity Amputation	Vascular Calcifications	Complications	Cause of Death
M	R ring P2, R ring MCP, R index MCP, R little MCP, L middle DIP, L little PIP	6	Yes	Yes	L BKA	No	Infection	Cardiovascular
M	L index P3	1	Yes	No	None	No	None	
M	L middle MCP, L below elbow amputation	2	Yes	Yes	None	No	Infection	Cardiovascular
F	L index MCP, L middle MCP	2	Yes	Yes	B transmetatarsal amputation	Yes	Infection	

AKA, above-knee amputation; B, bilateral; BKA, below-knee amputation; DIP, distal interphalangeal; IP, interphalangeal; MCP, metacarpophalangeal; P1, proximal phalanx; P2, middle phalanx; PIP, proximal interphalangeal.

record problem list.[2,3] As the CCI increases (0 is lowest risk; > 5 is high risk), the patient's risk of mortality from comorbid conditions increases. The risk of the treatment could then be weighed against the patient's comorbidity.

Patient ages, age at index surgeries, and time on dialysis were all compared using Student *t* test. A chi-square analysis was performed on patient risk factors between the surgical and the control groups. Survival was calculated using Kaplan-Meyer survival curves with log-rank (Mantel-Cox) analysis. Spearman rank correlations were used for additional data analysis. Statistical significance was set at *P* of .05 or less.

RESULTS

The upper extremity amputation group consisted of 20 patients and the control group included 40 patients (Table 1). Demographic data of the surgical and the nonsurgical groups are contained in Table 1 and the differences were not statistically significant. The average time the surgical patient underwent dialysis before the index surgery was 4.5 years (range, 0.5−24 y) and the control patients underwent dialysis for an average of 4.6 years (range, 0.5−24 y). The surgical group had similar CCIs and number of comorbidities (Table 1). The 2 most common comorbidities were diabetes in 13 of 20 (65%) surgical patients and 30 of 40 (75%) control patients and hypertension in 14 of 20 (70%) surgical patients and 30 of 40 (75%) control patients. The other common comorbidities included coronary artery disease with or without coronary artery bypass grafting, congestive heart failure, previous myocardial infarction, peptic ulcer disease, peripheral vascular disease, and hepatitis C. Five (25%) of the surgical patients had bilateral upper extremity disease. Fifteen (75%) surgical patients and 32 (80%) control patients also had some type of lower extremity amputation. In addition, peripheral vascular disease in the upper extremity was common. As shown in Table 2, vascular calcifications were radiographically apparent in 55% of the surgical patients. Radiographs were not routinely obtained on nonsurgical patients. These calcifications were identified on radiographs and arteriograms. An example of the difference in flow is demonstrated in Figure 1, which compares arteriography between a surgical and a nonsurgical patient.

The mean survival time after the index surgery for the surgical group was 4.95 ± 0.90 years (95% confidence interval, 3.17−6.72 y) and the mean survival for the control group was 8.40 ± 0.61 years (95% confidence interval, 7.21−9.59 y; Fig. 2). The probability of death (the event) was statistically

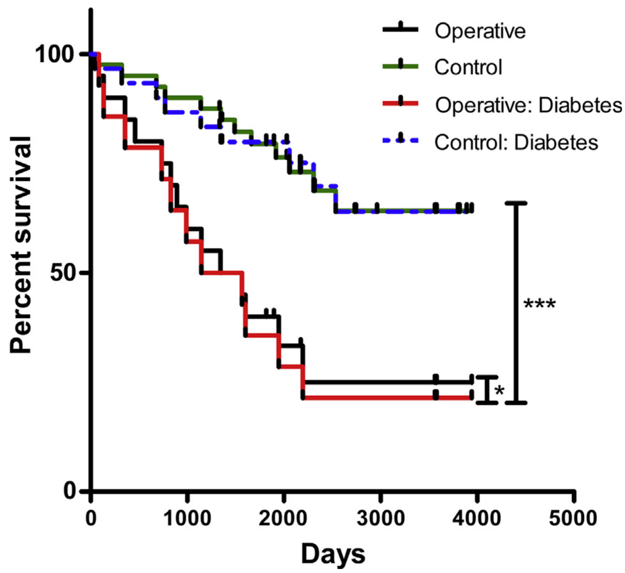

FIGURE 2: Kaplan-Meyer survival curve for surgical versus control groups. The surgical group had a significantly lower 5-year survivorship than matched controls (***$P < .001$). Patients with diabetes in the surgical group had a significantly decreased 5-year survival (*$P = .03$). Those with diabetes in the control group had a 5-year survival that was lower than patients without diabetes but the difference was not significant ($P = .42$).

greater in the surgical group ($P < .001$). The overall 5-year survival rates for the surgical and the nonsurgical groups were 35% (7 of 20) and 70% (28 of 40), respectively. The male 5-year survival rates in the surgical and the nonsurgical groups were 41.6% (5/12) and 70% (17/24), respectively. The female 5-year survival rates in the surgical and the nonsurgical groups were 25% (2 of 8) and 63% (10 of 16), respectively. The mean age-adjusted CCI did not differ significantly between the control and the surgical patients regardless of survivorship (Table 3).

Patients with diabetes had lower 5-year survival rates in both groups. Patients with diabetes in the surgical group had a 15% (2 of 13) survival compared with 71% (5 of 7) of nondiabetic patients, which was significantly different ($P = .025$). Patients with diabetes in the control group had a 5-year survival of 67% (20 of 30) compared with 80% (8 of 10) survival of nondiabetic patients, which was not significantly different ($P = .42$). The diagnosis of diabetes moderately and positively correlated with the number of amputations ($R = 0.453$, $P = .04$) and the likelihood of postoperative infections and complications ($R = .504$, $P = .02$). Postsurgical infection was reported in 11 (55%) surgical patients (Table 2). Infection was also positively correlated with the number of amputations performed ($R = 0.481$, $P = .03$) and negatively correlated with survival ($R = -0.504$, $P = .02$).

TABLE 3. Age-Adjusted CCI in Both Groups*

	Surgical	Control
Mean CCI	7.1 (5.9−8.3)	6.8 (6.1−7.5)
Mean deceased CCI	7.6 (6.7−9.1)	7.6 (6.6−8.9)
Mean alive CCI	6.0 (3.7−8.3)	6.4 (5.5−7.3)

*All means reported with 95% confidence interval. No statistically significant differences existed between groups.

In the surgical group, patients averaged 3 (range, 1−13) upper extremity amputations (including the initial amputation) with up to 11 visits to the surgical suite. The number of upper extremity operations was not independently significantly correlated with an increased mortality ($R = 0.123$, $P = .58$).

DISCUSSION

An estimated 368,544 patients with ESRD receive dialysis treatments in the United States.[4] Roughly 5% of those patients experience symptomatic ischemia of the upper extremity.[5] The development of upper extremity gangrene or nonhealing ulcers, or both, is likely multifactorial. Common associations include peripheral vascular disease, tobacco use, atherosclerotic disease, steal syndrome, and ESRD requiring dialysis. Stenosis or obstruction of large arteries proximal to the wrist was the reported cause of upper extremity ischemia in approximately 67% of the patients in 1 series.[6] In contrast, another series identified small artery spastic or occlusive disease limited to the hands and fingers as the cause of ischemia in more than 95% of patients.[7]

Our study revealed that the 5-year survival rate from the index surgery of the surgical group was half that of the nonsurgical group (35% vs 70%), thus supporting our hypothesis. Koch et al[8] concluded that the prevention of limb ischemia (and coronary artery disease) in ESRD patients on dialysis was of utmost importance to improve survival. The poor prognosis indicated by an upper extremity amputation may be attributed to associated cardiovascular disease and diabetes complications. Both groups have high CCIs, which is representative of a significant disease burden with high mortality. The need for surgical intervention is not independently captured in the CCI, but upper extremity infections and ulcerations can be manifestations of diabetes and cardiovascular disease, which is captured in the CCI. The lower survival rate in women is unclear, and the sample size precludes statistical analysis of the subset, but 75% of the women in the surgical group were diabetics versus

66% of men. Diabetes was an independent prognostic factor for increased mortality. Patients in chronic renal failure who also have skin lesions, such as ulcerations and gangrene, have widespread arterial calcification; the poor blood flow is suggestive of extensive and accelerated atherosclerosis.[7,9–11] Yeager et al[12] found clinical evidence of increased total body atherosclerosis in patients with finger gangrene compared with patients on chronic dialysis in whom gangrene did not develop. Their study reported similar survival rates in patients on chronic dialysis with upper extremity gangrene. Ischemic ulcers and gangrene are a manifestation of poor vascular flow. Poor vascular flow is likely a manifestation of cardiovascular disease, which resulted in 12 of 13 deaths (93%) in the surgical group but only 8 of 12 deaths (75%) in the control group. Both the high postoperative infection rate and the common need for multiple procedures are consistent with impaired blood flow and healing. Patients with a combination of diabetes, ESRD, and digit necrosis ultimately have a poor survival rate.[2,3,13] In our experience, calcific arteritis is a major comorbidity and the vasospastic component contributing to ischemia is small, which negates salvage with chemical or surgical sympathectomy.[14]

The diagnoses of diabetes carried a significantly worse prognosis in the surgical group. Diabetic patients underwent more amputations and experienced more postoperative complications. Although the number of postoperative complications was related in part to the number of operations, it independently correlated with the presence of diabetes. Furthermore, patients with diabetes had a significantly lower 5-year survival rate in the surgical group. A lower rate of survival in diabetic patients was not surprising because it affects all organ systems, especially the cardiovascular system. Diabetes affects terminal vessels and results in decreased perfusion and difficulty in healing, especially in the distal extremities.[13] Previous attempts at diabetic foot salvage procedures demonstrated that, with later referrals for gangrene infection, revascularization attempts failed secondary to wound healing problems and not owing to a loss of graft patency.[15] Patients with ESRD with lower extremity amputation also had higher mortality rates,[15] which is congruent with our findings that upper extremity amputation also had a poor prognosis. These findings support early referral to a microvascular surgeon before the development of extensive tissue ischemia and infection to potentially yield improved outcomes.

The retrospective nature of this study limited the amount of information that can be obtained from the medical records; however, the data were complete for all analyzed variables. The quality of the comparison was enhanced by matching each surgical patient to 2 controls based on age, sex, and number of years on dialysis. The precise day of dialysis initiation could not always be matched, so the control start of dialysis was matched within months of the surgical group's initiation of dialysis. The initial reason for dialysis was not always documented, but documented reasons for dialysis included diabetes, chronic hypertension, renal artery stenosis, failed kidney transplants, and immunoglobulin A nephropathy. The small number of proximal amputations in our study may be related to few patients surviving multiple distal amputations to require a proximal amputation. The number of patients was not sufficient to elucidate the reason for this finding.

The goal of this study was to identify whether or not upper extremity amputation was a prognostic indicator for hemodialysis patients. This study did not seek to determine causality of the amputation, but acknowledges that the index upper extremity procedure carries significant morbidity and portends a high mortality rate. Another goal of this study was to provide additional prognostic information to help the surgical and medical team counsel the patient with ESRD who requires an upper extremity amputation. It is important for the hand surgeon to be equipped with this prognostic information. Patients with ESRD who require an upper extremity amputation should receive multidisciplinary treatment aimed at aggressive restoration of adequate blood flow in an effort to improve their outcome and quality of life. Recommendations for a multidisciplinary approach to caring for a patient with ESRD include evaluation for possible revascularization and eliminating any potentially vasospastic dialysate, such as a high calcium dialysate. This approach may include referrals to a microvascular surgeon, endocrine management, and close nephrology follow-up to optimize the patient's health for wound healing and tissue preservation. Our current analysis supports the goal of timely intervention for patients with ESRD by the multidisciplinary team to optimize care planning and improve surgical outcomes and quality of life.

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