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Nontraumatic lower extremity amputations in the Medicare end-stage renal disease population

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Background. Nontraumatic lower limb amputation is a serious complication of both diabetic neuropathy and peripheral vascular disease. Many people with end-stage renal disease (ESRD) suffer from advanced progression of these diseases. This study presents descriptive information on the rate of lower limb amputation among people with ESRD who are covered by the Medicare program.

Methods. Using hospital bill data for the years 1991 through 1994 from the Health Care Financing Administration's ESRD program management and medical information system (PMMIS), amputations were based on ICD9 coding. These hospitalizations were then linked back to the PMMIS enrollment database for calculation of rates.

Results. The rate of lower limb amputation increased during the four-year period from 4.8 per 100 person years in 1991 to 6.2 in 1994. Among persons whose renal failure was attributed to diabetic nephropathy, the rates in 1991 and 1994 were 11.8 and 13.8, respectively. The rate among diabetic persons with ESRD was 10 times as great as among the diabetic population at large. Two thirds died within two years following the first amputation.

Conclusions. The ESRD population is at an extremely high risk of lower limb amputation. Coordinated programs to screen for high-risk feet and to provide regular foot care for those at high risk combined with guidelines for treatment and referral of ulceration are needed.

Prior to the Social Security Amendments of 1972 extending Medicare coverage to persons with end-stage renal disease (ESRD), diabetes was a contraindication to treatment for persons in need of dialysis or transplant. Since that time, the number of treated incident cases of ESRD has risen dramatically. In 1994, there were 62,266 persons who began renal replacement therapy in the Medicare ESRD program. This is four times the 15,327 who began treatment in 1978. In addition, diabetes is the most common cause of renal failure, accounting for 38% of all new cases in 1994, which is up from 17% from 1978 [1]. The progression of diabetes to end-stage renal failure is associated with the progression of multiple other complications of diabetes, including neuropathy and peripheral vascular disease [2]. Not uncommonly, lower extremity amputation (LEA) results in the loss of part of the toe, foot, or leg in the persons being treated for end-stage renal failure. In addition, problems leading to amputations often recur in the ipsilateral or contralateral extremity, further impairing mobility and rehabilitation from the initial amputation.

The pathogenesis of LEA in diabetes is multifactorial. The initial lesions are often initiated by minor trauma leading to ulcerations, which progress because of the combination of ischemia and peripheral neuropathy complicated by faulty wound healing and gangrene [3–6]. Diabetic ESRD patients are at high risk for these conditions. Similar predisposing conditions (that is, peripheral neuropathy and vascular disease) exist in ESRD patients who do not have diabetes [7–9]. Many amputations in diabetic patients are initiated by a potentially preventable event such as minor trauma or ill-fitting footwear. In a series from the Veterans Administration, such events were identifiable in 86% of the diabetic persons undergoing amputation [10]. Thus, the diabetic ESRD patients and those with uremia from other causes are at high risk for potentially preventable LEAs.

The epidemiology of LEA has been described in diabetic populations using hospital discharge records [4, 11]. Age-adjusted rates of 8 out of 1000 per year were reported from the National Health Discharge Data in 1990 [12]. Most studies have shown higher rates among males than among females and significant racial and ethnic variation with African Americans and Native Americans experiencing higher rates than non-Hispanic whites [4, 12–14]. Mortality is high in follow-up, with a two-year survival rate reported at 50% from the United Kingdom [4, 15].

Key words: diabetic nephropathy, peripheral vascular disease, leg amputation, ulceration, gangrene.

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In a preliminary study, Hill et al identified a higher rate of foot problems in diabetic ESRD patients (25%) compared with 10% of diabetic patients who were not receiving renal replacement therapy [16].

Several intervention studies have been published showing reductions in amputation rates [17–20]. In general, successful programs have used a multidisciplinary approach targeting patient education and regular foot care services to diabetic individuals known to be at high risk for lower extremity problems [21–25]. In one case, a special foot clinic organized for diabetic renal transplant patients reduced gangrene and major amputations in a group of patients with both diabetes and renal disease [26]. Because of the growing recognition that the identification and intervention among high-risk persons may reduce rates of LEA, this study was undertaken to examine the rates of LEA among the Medicare ESRD population. This article describes variation among population subgroups, recent trends in amputation, and postamputation mortality.

METHODS

Data for this study were obtained from the ESRD Program Management and Medical Information System (ESRD-PMMIS) maintained by the Office of Clinical Standards and Quality at the Health Care Financing Administration (HCFA). The ESRD-PMMIS is a longitudinal file of patients with ESRD who are entitled to Medicare benefits. In addition to the basic enrollment data available for all Medicare beneficiaries such as sex, race, date of birth, date of death, and entitlement dates, the PMMIS contains information unique to ESRD beneficiaries. The medical evidence form (HCFA 2728) is used to determine date and cause of renal failure. Since July of 1994, kidney transplant data have been collected by the Organ Procurement and Transplant Network (OPTN) and are routinely forwarded to HCFA. Prior to that time, transplant data were collected through the HCFA 2745. The ESRD-PMMIS file used in this study was updated through May 1996. This update of the ESRD-PMMIS contained 706,952 people, the complete count of Medicare ESRD patients ever entitled since 1978.

In addition to entitlement records, HCFA receives bill data on all ESRD persons served by fee-for-service providers. Hospitalization data include the principal diagnosis for the inpatient stay and up to 10 additional comorbid or complicating conditions. In addition, the hospitalization data include up to six procedures. Coding for both the diagnoses and procedures are based on the International Classification of Diseases version 9, current modification (ICD9-CM). Medicare pays for ESRD beneficiaries who belong to risk-based managed care organizations on a monthly capitation basis and does not receive hospitalization data for these persons. In the 1991 to 1994 period, it is estimated that 2 to 3% of ESRD beneficiaries belonged to HMOs.

This analysis is based on hospitalizations during 1991 through 1994 during which a lower limb amputation was performed. ICD9-CM codes 84.10 through 84.19 were used to select stays in which an amputation occurred. Between 1991 and 1994, there were 24,886 Medicare ESRD beneficiaries with at least one hospitalization in which an amputation occurred. Because of multiple amputations, there were 35,898 hospitalizations during these years among ESRD beneficiaries for whom there was at least one amputation. Although there were 35,898 hospital stays in which an amputation occurred, a patient could have received more than one amputation during a single stay.

Amputation rates were calculated based on the number of ESRD persons ever enrolled during a year. A logistic regression analysis was performed to estimate the independent effects of demographic variables on the probability of amputation. The analyses were limited to persons for whom Medicare is the primary payer of services. For patients with other health insurance, Medicare is the secondary payer of medical care for the first 18 months following renal failure. HCFA does not receive hospitalization records for these patients; therefore, they were excluded from the analyses. (During 1991 through 1994, Medicare was the secondary payer for approximately 15% of all Medicare ESRD beneficiaries.) Survival was calculated using standard life table estimates with right censoring for end of observation (May 1996). To control for confounding effects of age and treatment status, a multivariate proportional hazards model was constructed.

RESULTS

Descriptive characteristics

Table 1 shows the demographic characteristics of the persons included in this study. Also shown in Table 1 are the demographic characteristics of the Medicare-prevalent ESRD population as of December 31, 1994, including both dialysis and functioning graft patients. Amputees were older and much more likely to have diabetes than the overall ESRD population (68.2 vs. 29.1%).

Table 2 shows the level of the amputation for all hospitalizations included in this study. The 24,886 patients accounted for 35,898 amputations. The two most common sites of initial amputation were other amputation below the knee (38.5%) and amputation of toe (27.4%). Table 2 also shows the level of amputation by cause of renal failure. Persons whose renal failure was attributed to diabetic nephropathy were less likely to have had an amputation above the knee (18.1%) than were people whose renal failure was attributed to other causes (25.3%). In subsequent analyses, amputations were grouped into three categories: (*a*) toe amputations (code 84.11), (*b*)

Table 1. Demographic characteristics of ESRD amputation patients and total ESRD population during 1991 to 1994

	ESRD amputation population		Total Medicare ESRD population	
	Persons	Percent	Persons	Percent
All persons	24,886	100.0%	232,193	100.0%
Age				
Under 15 years	1	0.0	1,769	0.8
15–24 years	28	0.1	6,039	2.6
25–34 years	823	3.3	19,545	8.4
35–44 years	2,343	9.4	34,208	14.7
45–54 years	4,039	16.2	40,433	17.4
55–64 years	6,369	25.6	44,767	19.3
65–74 years	7,958	32.0	53,816	23.2
75 years or over	3,325	13.4	31,616	13.6
Sex				
Male	13,343	53.6	125,983	54.3
Female	11,543	46.4	106,210	45.7
Race				
Asian	365	1.5	5,644	2.4
African American	8,289	33.3	75,574	32.5
White	15,345	61.7	143,359	61.7
Native American	553	2.2	2,841	1.2
Other/unknown	334	1.3	4,775	2.1
Primary diagnosis				
Diabetes	16,974	68.2	67,460	29.1
Glomerulonephritis	884	3.6	36,859	15.9
Hypertension	4,062	16.3	58,189	25.1
Cystic kidney disease	201	0.8	9,228	4.0
Interstitial nephritis	246	1.0	7,626	3.3
Obstructive nephropathy	171	0.7	4,890	2.1
Other	375	1.5	15,927	6.9
Unknown	715	2.9	13,097	5.6
Not reported	1,258	5.1	18,917	8.1

all other below-knee amputations (codes 84.12 through 84.15), and (*c*) all above-knee amputations (codes 84.16 through 84.19).

Table 3 shows the principal diagnosis associated with each amputation stay. Over 40% of the stays had diabetes mellitus listed as the principal diagnosis. Of these, 82% (or 33.2% of all hospital stays) had diabetes with peripheral circulatory disease as the principal diagnosis (data not shown). The second most common diagnosis was atherosclerosis (18.5%), followed by gangrene with 7.1% of cases. However, gangrene was listed as either the principal or secondary diagnosis in two thirds of all the amputations (data not shown). For persons whose renal failure was attributed to diabetic nephropathy, diabetes mellitus was the principal diagnosis in almost one half of the amputations. For persons whose renal failure was not attributed to diabetes, diabetes was still the principal diagnosis in almost one fourth of the amputations. Hypertension and atherosclerosis are often comorbid with diabetes and may explain the lack of concurrence between the cause of LEA and the cause of ESRD.

Amputation rates

Table 4 shows the amputation rates for the ESRD population in 1994 by treatment status. The overall rate of amputation was 4.3 per 100 persons. This ranged from 4.9 among persons on dialysis to 1.5 for persons receiving a transplant. Although the transplant group is younger, rates of amputation are higher for the dialysis group in every age strata except under 15 years. Subsequent tables and figures (except for the tables on mortality) show amputation rates for the dialysis population only.

Figure 1 displays time trends for annualized amputations per 100 persons on dialysis, by year for diabetic and nondiabetic ESRD separately. In 1991, the rate of amputation among diabetic patients on dialysis was 11.8 per 100. This increased each subsequent year up to 13.8 per 100 in 1994. Amputation rates for all other dialysis patients were approximately one fifth as great as for diabetic patients, but also showed an increasing rate during the period of 1991 through 1994. Increasing rates with time were seen in the majority of age, sex, and race strata (data not shown).

Figure 2 displays LEA incidence by age for diabetic and all other ESRD. Those aged 45 to 54 years had the highest rate among diabetic ESRD patients. The peak incidence was older (55 to 64 years of age) for all other ESRD.

Figure 3 displays the rates by race. The lowest rates were found for Asian beneficiaries, and the highest rates were found for Native Americans among diabetic ESRD. In contrast to the general population, Caucasians have higher LEA rates than African Americans. Among all other ESRD patients, the other/unknown race category had the highest rates of LEA, but African Americans were a close second (2.8 vs. 2.7). The lowest rates were again among Asian beneficiaries.

Because the presence of diabetes varies considerably across racial and age groups, the bivariate analyses in Table 4 and Figures 1 to 3 may not adequately show the relative rates across demographic groups. Table 5 shows a multivariate analysis of the hospitalization rate for amputation. There was a steep gradient in the probability of hospitalization with increasing age up to ages 65 to 74. Males were 23% more likely to have an amputation than were females. Compared with whites, amputation was 6% greater among blacks and 28% greater among Native Americans. Asian Americans were only 58% as likely to get an amputation as were whites. Persons whose renal failure was caused by diabetes were almost nine times as likely to get an amputation as were persons with glomerulonephritis. Rates were also higher for persons with hypertension and an unknown or not reported cause of renal failure. The higher rates for the latter two categories could be due to comorbid diabetes. Finally, persons who received a transplant and persons with a functioning graft were only 37 and 77% as likely to get an amputation as were persons on dialysis.

Table 2. Level of lower limb amputation Medicare ESRD patients during 1991 to 1994

		Cause of renal failure		
		All persons	Diabetic nephropathy	All other causes
ICD9-CM	Location	*N* (%)		
Total		35,898 (100.0)	25,037 (100.0)	10,861 (100.0)
84.10	Lower limb amputation, not otherwise specified	23 (0.1)	16 (0.1)	7 (0.1)
84.11	Amputation of toe	9,830 (27.4)	7,051 (28.2)	2,779 (25.6)
84.12	Amputation through foot	4,387 (12.2)	3,172 (12.7)	1,215 (11.2)
84.13	Disarticulation of ankle	73 (0.2)	60 (0.2)	13 (0.1)
84.14	Amputation of ankle thorugh malleoli of tibia and fibula	244 (0.7)	180 (0.7)	64 (0.6)
84.15	Other amputation below knee	13,835 (38.5)	9,885 (39.5)	3,950 (36.4)
84.16	Disarticulation of knee	163 (0.5)	110 (0.4)	53 (0.5)
84.17	Amputation above knee	7,275 (20.3)	4,523 (18.1)	2,752 (25.3)
84.18	Disarticulation of hip	66 (0.2)	38 (0.2)	28 (0.3)
84.19	Abdominopelvic amputation	2	2	0 (*)

Data are: Number of hospitalizations (percent). Diabetic patients are defined as those whose renal failure was attributed to diabetes. The other patients may have diabetes but their renal failure was not attributed to diabetes.

Table 3. Principal diagnoses for amputations in Medicare ESRD beneficiaries

		Cause of renal failure		
		All LEA persons	Diabetic nephropathy	All other
ICD9 causes	Diagnosis	*N* (%)		
	All hospitalizations	35,898 (100.0)	25,037 (100.0)	10,861 (100.0)
038	Septicemia	1,059 (3.0)	741 (3.0)	318 (2.9)
250	Diabetes mellitus	14,539 (40.5)	12,019 (48.0)	2,520 (23.2)
440	Atherosclerosis	6,650 (18.5)	3,690 (14.7)	2,960 (27.3)
443	Other peripheral vascular disease	1,276 (3.6)	644 (2.6)	632 (5.8)
444	Arterial embolism and thrombosis	1,015 (2.8)	504 (4.6)	511 (2.0)
682	Other cellulitis and abscess	445 (1.2)	329 (1.3)	116 (1.1)
707	Chronic ulcer of skin	794 (2.2)	497 (2.0)	297 (2.7)
730	Osteomyelitis, periostitis, and other infections involving bone	1,414 (3.9)	1,057 (4.2)	357 (3.3)
785	Symptoms involving cardiovascular system including gangrene	2,548 (7.1)	1,546 (6.2)	1,002 (9.2)
996	Complications peculiar to certain specified procedures including grafts	1,239 (3.5)	745 (3.0)	494 (4.5)
997	Complications affecting specified body systems (including amputation stump complication)	1,487 (4.1)	1,109 (4.4)	378 (3.5)
	All other	3,350 (9.3)	2,067 (8.3)	1,283 (11.8)

Diabetic patients are defined as those whose renal failure was attributed to diabetes. The other patients may have diabetes but their renal failure was not attributed to diabetes.

Mortality

Table 6 shows the cumulative survival following the first amputation. [Note that this is actually the first amputation following renal failure, during the 1991 through 1994 time period and after Medicare became the primary payer. Amputations that occurred (*a*) prior to 1991, (*b*) and/or prior to renal failure, (*c*) and/or during a period when Medicare was the secondary payer will have been missed. Tracking patients prior to their Medicare entitlement date is not possible in the Medicare database. Of those patients who received an amputation after renal failure, 3% had at least one amputation prior to renal failure.] The survival at 30 days postamputation was 88.9%. At one year, the survival rate was 49.3%, and at two years, it was 32.7%. In comparison, survival rates for the entire ESRD dialysis population from the date of renal failure are 78.7% at one year and 63.2% at two years (HCFA, 1997).

Age had a strong effect on postamputation survival. The two-year survival for persons under age 25 was over 60%. This declined to 15.8% among persons aged 75 and over. Males had slightly higher survival rates than did females. By racial category, two-year postamputation survival rates ranged from a low of 27.4% among Asian beneficiaries to a high of 39.1% among Native American beneficiaries.

Interestingly, persons whose renal failure was attributed to diabetes have a somewhat better survival following amputation than do other persons. At two years postamputation, there is an approximate 6 to 10% differential in

Table 4. Hospitalizations for amputation among ESRD beneficiaries by age, sex, race, and diagnosis by treatment category during 1994

	All persons (N = 239,170)	Dialysis (N = 190,147)	Transplant (N = 6,408)	Functioning graft (N = 40,702)	Graft failure (N = 1,913)
	Number of discharges per 100 persons				
All persons	4.3	4.9	1.5	2.0	3.0
Age					
Under 15 years	0.1	0.2	0.3	0.1	0.0
15–24 years	0.6	0.7	0.4	0.4	0.6
25–34 years	2.3	2.4	1.8	2.1	3.1
35–44 years	3.3	3.8	1.7	2.5	2.5
45–54 years	5.4	6.2	2.1	2.9	7.3
55–64 years	6.2	6.8	1.8	2.1	2.8
65–74 years	5.3	5.4	0.8	1.2	16.0
75 years or over	3.1	3.1	0.0	0.0	0.0
Sex					
Male	4.4	5.0	1.8	2.4	3.3
Female	4.2	4.7	1.1	1.5	2.5
Race					
Asian	3.0	3.9	1.0	0.1	0.0
African American	4.5	5.0	1.2	1.7	1.3
White	4.1	4.8	1.7	2.2	4.0
Native American	8.2	9.1	4.4	4.2	0.0
Other/unknown	3.8	4.2	1.0	0.5	10.5
Primary diagnosis					
Diabetes	10.0	10.4	3.0	7.6	12.4
Glomerulonephritis	0.9	1.2	0.3	0.3	0.0
Hypertension	2.6	2.8	0.4	0.5	1.5
Cystic kidney disease	0.7	1.0	0.0	0.4	1.3
Interstitial nephritis	1.3	1.6	0.0	0.3	0.0
Obstructive nephropathy	1.0	1.2	0.8	0.4	0.0
Other	0.9	1.1	13.9	0.3	0.0
Unknown	1.8	2.2	0.8	0.4	1.3
Not reported	3.3	3.8	0.0	1.8	2.6

Excludes Medicare secondary payer patients.

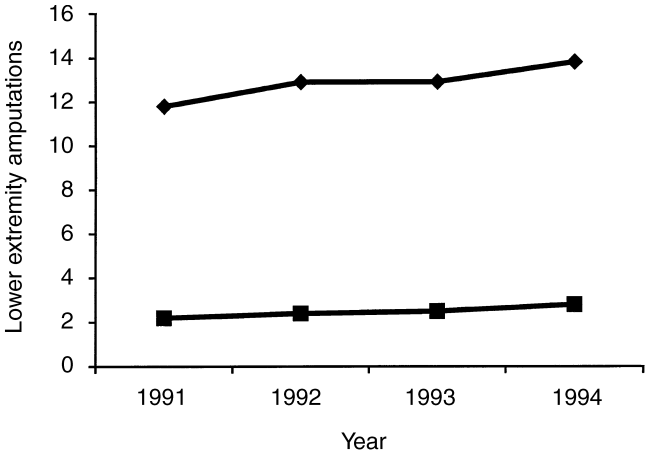

Fig. 1. Time trends in annualized lower extremity amputation (LEA) incidence by diabetes mellitus (◆) and all other causes (■).

favor of diabetic persons compared with persons whose renal failure was due to other factors.

Not surprisingly, the extent of the initial amputation was strongly associated with subsequent mortality. A two-year survival for persons whose initial amputation was the toe was 44.8%. This decreased to 31.7% for amputations below the knee and to only 15.2% for above-the-knee amputation patients. The diabetic survival advantage may be partially explained by the fact that diabetic patients on average had amputations at lower levels (Table 2).

The treatment status at the time of amputation was also associated with postamputation survival. Persons on dialysis who had never received a transplant had the worst survival rate (28.1% at two years). Persons who were on dialysis following a failed transplant did slightly better at 36.0%. Persons with a functioning transplant at the time of amputation did much better, with a two-year survival rate of 75.6%.

It is highly likely that some of these differences are due to selection effects. For example, both the functioning graft patients and the dialysis patients with a failed transplant are significantly younger than the average dialysis patient. Therefore, in order to help control for confounding effects of these variables on survival, a multivariate proportional hazards model was constructed. The results are displayed in Table 7 as relative risk ratios.

In general, the univariate results shown in Table 6 were consistent with the multivariate results in Table 7. There was a strong age effect. Persons under the age of 25 had one half (52%) of the mortality of persons aged 45 to 54, whereas the mortality rate was 81% greater for

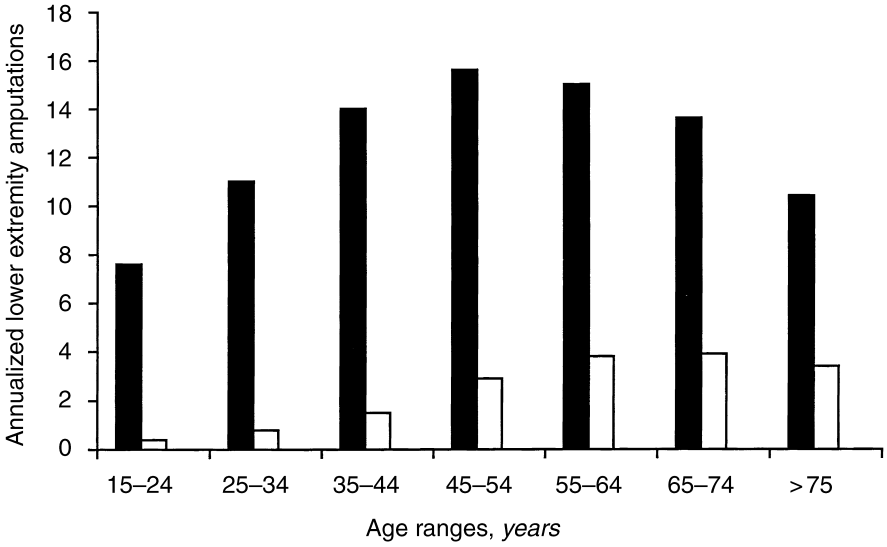

Fig. 2. Annualized LEA by age strata for diabetes mellitus (■) and all other causes (□) in 1994.

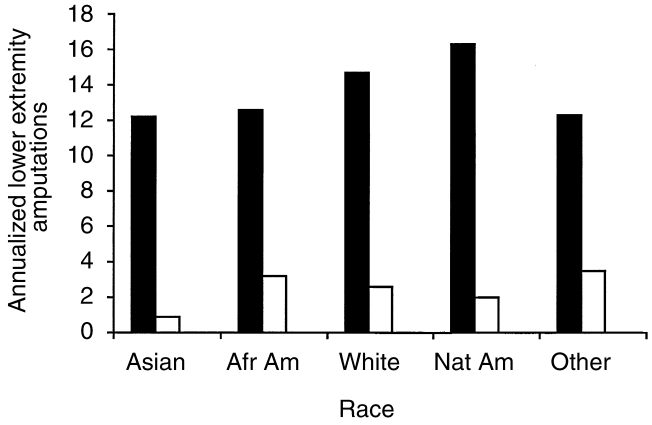

Fig. 3. Annualized incidence of LEA by race in 1994. Symbols are: (■) diabetes mellitus; (□) non-diabetes mellitus.

persons over age 75. Males had a 6% lower mortality rate than did females. Mortality was 32% lower for African Americans and 26% lower for Native Americans than for whites. Compared with persons whose renal failure was attributed to glomerulonephritis, persons with diabetes had an 11% lower mortality rate, and persons with obstructive nephropathy had a 27% lower mortality rate.

As expected, the extent of the original amputation had a significant effect on subsequent mortality. Compared with toe amputations, persons with below-the-knee amputations had a 37% greater mortality rate, whereas persons with above the knee amputations had a more than twice the mortality rate. Gangrene, either as a principal diagnosis or a secondary diagnosis, was associated with a 10% increase in postamputation mortality.

Finally, persons with a functioning kidney transplant had one third the postamputation mortality of persons on dialysis. There was no difference in mortality between persons on dialysis who had never been transplanted and those who had lost a transplanted kidney.

Table 5. Patient hospitalization for amputation: Odds ratio model

Variable	Comparison	Odds ratio	*P* value
Ages			
0 to 14	Ages 45 to 54	—	NS
15 to 24	Ages 45 to 54	0.04	<0.0001
25 to 34	Ages 45 to 54	0.52	<0.0001
35 to 44	Ages 45 to 54	0.79	<0.0001
55 to 54	Ages 45 to 54	1.07	0.0579
65 to 74	Ages 45 to 54	1.14	0.0004
75 and over	Ages 45 to 54	—	NS
Gender			
Male	Female	1.23	<0.0001
Race			
African American	White	1.06	0.0002
Native American	White	1.28	0.0022
Asian	White	0.58	0.0001
Other/unknown race	White	—	NS
Primary diagnosis			
Diabetes	Glomerulonephritis	8.93	<0.0001
Hypertension	Glomerulonephritis	2.11	<0.0001
CKD	Glomerulonephritis	—	NS
Interstitial Nephropathy	Glomerulonephritis	—	NS
Obstructive Nephropathy	Glomerulonephritis	—	NS
Other	Glomerulonephritis	—	NS
Unknown	Glomerulonephritis	1.83	<0.0001
Not reported	Glomerulonephritis	2.24	<0.0001
Kidney status			
Transplant	Dialysis (never Tx)	0.37	<0.0001
Functioning Graft	Dialysis (never Tx)	0.77	<0.0001

DISCUSSION

Treatment for ESRD identifies a group of patients at very high risk for lower extremity problems. To our

Table 6. Cumulative survival following first amputation after renal failure for Medicare ESRD patients during 1991 through 1994

		Days postamputation					
	N	30	60	90	182	365	730
All persons	24,877	88.9%	80.1%	74.2%	62.8%	49.3%	32.7%
Age							
0 to 24	29	86.2	86.2	86.2	79.3	69.0	65.0
25 to 34	419	96.4	93.2	89.7	83.0	73.8	61.3
35 to 44	2,342	95.8	91.3	88.0	78.6	67.3	53.3
45 to 54	4,038	93.8	88.0	84.0	74.1	60.7	44.0
55 to 64	6,365	90.2	82.0	76.5	65.1	51.3	33.1
65 to 74	7,956	86.0	75.7	68.7	56.5	41.7	24.5
75 and over	3,324	80.4	66.3	57.0	43.9	30.9	15.8
Gender							
Male	13,339	89.4	81.1	75.7	64.9	51.5	35.0
Femlae	11,538	88.3	78.9	72.4	60.5	46.7	29.9
Race							
Asian	363	89.0	79.9	73.6	63.4	47.1	27.4
African American	8,287	90.0	81.9	76.3	66.6	54.1	37.3
Native American	553	93.1	85.9	80.8	70.9	59.7	39.1
Other/unknown	333	91.0	82.3	77.2	68.2	49.6	35.3
White	15,341	88.1	79.9	72.7	60.4	46.4	30.0
Primary diagnosis							
Diabetes	16,970	90.5	82.4	76.7	65.7	51.7	34.8
Glomerulonephritis	892	83.7	74.3	66.8	54.6	41.3	27.8
Hypertension	4,059	84.7	73.7	66.6	55.3	42.3	26.2
Cystic kidney disease	201	79.1	69.7	62.7	50.3	41.8	26.0
Interstitial nephritis	246	82.9	74.0	69.1	53.3	39.0	23.4
Obstructive nephritis	170	88.2	77.1	71.8	61.2	48.2	32.0
Other	363	84.6	75.2	70.5	55.4	44.9	29.2
Unknown	718	85.9	75.4	68.0	55.6	42.9	25.6
Not reported	1,258	89.4	81.3	77.0	64.9	52.5	36.5
Amputation							
Toe	7,806	95.2	89.8	85.4	75.8	63.0	44.8
Below knee	12,380	89.6	81.0	75.2	63.2	49.0	31.7
Above knee	4,691	76.3	61.3	52.7	40.3	27.1	15.2
Kidney status							
Dialysis (nev tx)	21,898	87.8	78.3	71.9	59.7	45.4	28.1
Functioning graft	2,277	98.3	96.4	95.0	91.4	85.3	75.6
Dialysis (tx fail)	702	92.6	84.1	78.1	66.5	52.4	36.0

knowledge, this is the first report documenting the disproportionate burden of LEA among ESRD patients. Medicare beneficiaries 65 years of age and older experienced over 65,500 discharges from short-stay hospitals in 1994 during which LEA was performed. ESRD patients comprised only 0.3% of Medicare beneficiaries in this age group but over 6% of the hospitalizations in this age group. Two previous reports estimated the overall rates of LEA in the general population at 0.72 out of 10,000 person years in Rochester, Minnesota, and 1.6 out of 10,000 nondiabetic population in New Jersey for the three-year period of 1985 through 1987 [27, 28]. The age structure of the ESRD population, however, is very different from the general population so that direct comparisons may be misleading. The age-specific rate for the nondiabetic population in New Jersey aged 65 and over was 9.3 out of 10,000 for the three-year period, and although not strictly comparable, the annualized rate of 2.3 out of 100 hospital discharges per year found in this study for nondiabetic ESRD patients is likely much higher than LEA rates found among the oldest nondiabetic individuals who have the highest rates of LEA [28].

Among the entire population of diabetic patients, the relative risk of LEA has ranged from 15 to 24 times that of the nondiabetic patient [29–31]. Several previous reports identified the association of foot ulcers and amputation in diabetic patients with documented renal disease. Among older onset diabetic patients in Wisconsin, the relative risk of amputation in the diabetic patients with proteinuria was 2.7 (95% CI, 1.3 to 5.5) compared with diabetic patients who did not have proteinuria [32]. The relative risk (3.9) for LEA with proteinuria was even higher (95% CI, 2.2 to 7.0) for the younger onset diabetic individuals [32]. Among diabetic Pima Indians, proteinuria was associated with a similar risk ratio for LEA of 2.2 (95% CI, 1.4 to 3.6) [33]. A recent case control study among Pima Indians reported a relative risk of 5.1 (95% CI, 1.4 to 18) for LEA among diabetic persons with renal failure as defined by treatment for ESRD, transplant, or a serum creatinine of greater than 4 mg/dl [34].

The actual rates of LEA among diabetic persons receiving treatment for ESRD are not easily compared with other published rates of LEA in diabetic patients,

Table 7. ESRD patient mortality following first amputation after renal failure: Cox proportional hazards model

Variable	Comparison	Relative Risk	*P* value
Age			
0 to 24	Ages 45 to 54	0.52	<0.0196
25 to 34	Ages 45 to 54	0.68	<0.0001
35 to 44	Ages 45 to 54	0.85	<0.0001
55 to 64	Ages 45 to 54	1.17	<0.0001
65 to 74	Ages 45 to 54	1.38	<0.0001
75 and over	Ages 45 to 54	1.81	<0.0001
Gender			
Male	Female	0.94	<0.0001
Race			
Black	White	0.68	<0.0001
Native American	White	0.74	<0.0001
Asian	White	—	NS
Other/unknown	White	0.85	0.0089
Primary diagnosis			
Diabetes	Glomerulonephritis	0.89	<0.0036
Hypertension	Glomerulonephritis	—	NS
CKD	Glomerulonephritis	—	NS
Interstitial nephritis	Glomerulonephritis	—	NS
Obstructive nephropathy	Glomerulonephritis	0.73	<0.0010
Other	Glomerulonephritis	0.85	<0.0207
Unknown	Glomerulonephritis	—	NS
Not reported	Glomerulonephritis	—	NS
Amputation			
Below knee	Toe	1.37	<0.0001
Above knee	Toe	2.23	<0.0001
Complication			
Gangrene	No gangrene	1.09	<0.0001
Kidney status			
Functional graft	Dialysis (never Tx)	0.32	<0.0001
Failed graft	Dialysis (never Tx)	—	NS

because the age structure of the overall diabetic population is likely to be different from the age structure of the diabetic ESRD group. In addition, the analyses we report here are somewhat limited by Medicare payment policy. Amputations that occur during periods when Medicare is the secondary payer are missed by our study; the extent of this bias is unknown. However, the annualized rates of 13.8 per 100 hospital discharges reported in this study are higher than the highest age-specific rates published for any group of diabetic patients [4, 11, 12]. In New Jersey, the diabetic patients aged 65 and above experienced rates of amputation of 1049 per 10,000 for the period of 1985 to 1987 [28]. In the Netherlands in 1991, the rate of LEA among diabetic persons 75 years of age and older was 107.9 out of 10,000, and in California, it was slightly less than 100 per 10,000 when comparable rates of amputation were displayed for the oldest age group during the same time period [31].

Risk factors for LEA in the diabetic ESRD patients found in this study are consistent with other studies among diabetic populations that show excess rates in males compared with females and high rates among Native Americans, African Americans, and Hispanics [4, 11–14]. The distribution of amputation sites for the diabetic ESRD patients showed proportionally more below-knee amputations (39%) compared with diabetic patients in the National Hospital Discharge Survey data from 1989 to 1992 (25%) [35]. For the nondiabetic patients, the proportion of above-knee amputations (39%) was higher in the general population compared with the nondiabetic ESRD population (25%) [4].

Mortality reported in a one-year follow-up for all diabetic patients after LEA varied from 60 to 70% depending on the series [4, 15]. The lower survival of 50% among all the ESRD patients at one year after amputation is not surprising in view of the overall morbidity and mortality in ESRD patients. Similarly, perioperative mortality (death within 30 days) among diabetic patients with LEA in the United States averaged 5.8% between 1989 and 1992 compared with a 30-day cumulative mortality of 11% in the ESRD patients [36].

In addition to increasing mortality, the morbidity and costs associated with potentially preventable LEA in ESRD patients are high [4, 37, 38]. 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 [4]. Thus, every effort should be made to avoid amputation in ESRD patients.

The risk factors for LEA have been well described and include a readily identifiable loss of protective sensation, which puts patients at risk for neuropathic ulceration from repetitive stress or minor trauma [4, 6, 22, 39, 40]. Because of the loss of protective sensation, individuals ignore early lesions and inadvertently wear damaging footwear because they experience no pain from the injury [39]. Although neuropathy and peripheral vascular disease may be more severe among diabetic ESRD patients, uremia from any cause is associated with both of these major risk factors for LEA [2, 7, 8]. In addition, healing can be significantly impaired in ESRD patients [41], and surgical grafting to increase peripheral blood flow has not been uniformly successful in this population [42, 43]. Because of the nature of neuropathy, at-risk individuals will not necessarily report foot problems at an early stage and require visual inspection by others to detect early, treatable lesions. However, over a six-month period, simple foot examinations were reported to occur in only 28% of patients undergoing dialysis (abstract; Levy et al, *Diabetes* 46:184A, 1997).

Methods to decrease the incidence of ulceration and amputation and to promote healing in diabetic patients have been reported in the literature [5, 17, 19–21, 23, 26, 44]. A well-designed clinical trial showed a reduction in lower extremity clinical abnormalities among diabetic patients when interventions for patient education in foot care were combined with guidelines and instruction for their health-care providers [45]. Coordinated programs to screen for high-risk feet and to provide regular foot care for those at high risk combined with guidelines for treatment and

referral of ulceration reduced LEA rates in several American Indian and Alaska Native communities [19, 20, 46]. A special clinic organized for renal transplant patients in the United Kingdom has reported decreases in LEA and the healing of ulcers with appropriate supportive foot care [26]. In order to reduce the rates of LEA in the U.S. ESRD population, preventive foot care and patient education must become a priority for ESRD patients. These individuals are in frequent contact with the health care system to obtain renal replacement therapy. Thus, there are numerous opportunities for prevention and early detection of foot problems. Simple interventions, patient education, and routine foot care for those at highest risk can prevent the ulcer-initiating event and can detect small ulcers at a time when they can heal [23, 47]. In the past several years, efforts to improve the quality of care for patients receiving treatment for ESRD have focused on assuring the adequacy of dialysis and the treatment of anemia [1]. This study provides baseline data showing the need for ongoing monitoring of LEA rates combined with efforts to reduce these rates in all ESRD patients. In addition, diabetic patients are at risk for other end organ disabilities such as blindness for which preventive laser therapy must be given in a timely fashion. Therefore, the frequency of eye examinations and laser treatment in diabetic patients on renal replacement therapy must also be of concern. Increasing attention to the coordination of overall preventive care for patients undergoing renal replacement therapies is challenging, but the opportunity to improve all outcomes in this patient population can have a tremendous impact on morbidity, quality of life, and cost of care for individuals receiving treatment for ESRD.

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REFERENCES

1. Health Care Financing Administration Research Report: *End Stage Renal Disease, 1993–1995.* Bethesda, DHHS, HCFA, BDMS, HCFA Publication No. 03393, October, 1997
2. Fernando DJS, Hutchison A, Veves A, Gokal R, Boulton AJM: Risk factors for non-ischemic foot ulceration in diabetic nephropathy. *Diabet Med* 8:223–225, 1991
3. Pecoraro RE, Reiber GE, Burgess EM: Pathways to diabetic limb amputation: Basis for prevention. *Diabetes Care* 13:513–521, 1990
4. Reiber GE, Boyko EJ, Smith DG: Lower extremity foot ulcers and amputations in diabetes, in *Diabetes in America* (2nd ed), Bethesda, National Diabetes Data Group, U.S. Department of Health and Human Services, NIH Publication No. 95-1468, 1995, pp 409–426
5. Caputo GM, Cavanagh PR, Ulbrecht JS, Gibbons GW, Karchmer AW: Assessment and management of foot disease in patients with diabetes. *N Engl J Med* 331:854–860, 1994
6. Boulton AJM: The pathogenesis of diabetic foot problems: An overview. *Diabet Med* 13(Suppl):S12–S16, 1996
7. Asbury AK, Victor M, Adams RD: Uremic polyneuropathy. *Arch Neurol* 8:423–428, 1963
8. Nielsen VK: The peripheral nerve function in chronic renal failure. *Acta Med Scand* 194:455–462, 1973
9. Redfern AB, Zimmerman NB: Neurologic and ischemic complications of upper extremity vascular access for dialysis. *J Hand Surg* 20A:199–204, 1995
10. Reiber GE: Who is at risk of limb loss and what to do about it? *J Rehabil Res Dev* 31:357–362, 1994
11. Most RS, Sinnock P: The epidemiology of lower extremity amputations in diabetic individuals. *Diabetes Care* 6:87–91, 1983
12. Centers for Disease Control and Prevention: *Diabetes Surveillance 1993.* Atlanta, U.S. Department of Health and Human Services, 1993, p 92
13. Lavery LA, Ashry HR, van Houtum W, Pugh JA, Harkless LB, Basu S: Variation in the incidence and proportion of diabetes-related amputations in minorities. *Diabetes Care* 19:49–52, 1996
14. Valway SE, Linkins RW, Gohdes DM: Epidemiology of lower extremity amputation in the Indian Health Service, 1982–1987. *Diabetes Care* 16(Suppl 1):349–353, 1993
15. Deerochanawong C, Home PD, Alberti KGMM: A survey of lower limb amputations in diabetic patients. *Diabet Med* 9:942–946, 1992
16. Hill MN, Geldman HI, Hilton SC, Holechek MJ, Ylitalo M, Benedict GW: Risk of foot complications in long-term diabetic patients with and without ESRD: A preliminary study. *ANNA J* 23:351–356, 1996
17. Larsson J, Apelqvist J, Agardh C-D, Stenstrom A: Decreasing incidence of major amputation in diabetic patients: A consequence of multidisciplinary foot care team approach. *Diabet Med* 12:770–776, 1995
18. Malone JM, Snyder M, Anderson G, Bernhard VM, Holloway GA Jr, Bunt TJ: Prevention of amputation by diabetic education. *Am J Surg* 158:520–524, 1989
19. Gohdes D, Schraer C, Rith-Najarian S: Diabetes prevention in American Indians in Alaska Natives: Where are we in 1994? *Diabetes Res Clin Pract* 34(Suppl):S95–S100, 1996
20. Rith-Najarian S, Braunchaud C, Beaulieu O, Simonson G, Mazze R: Reducing lower extremity amputation due to diabetes: Application of the staged diabetes management approach in the primary care setting. *J Fam Pract* 47:127–132, 1998
21. Edmonds ME, Blundell MP, Morris ME, Thomas EM: Improved survival of the diabetic foot: The role of a specialized foot clinic. *Q J Med* 60:763–771, 1986
22. Rith-Najarian S, Stolusky T, Gohdes DM: Identifying diabetic patients at high risk for lower-extremity amputation in a primary care setting. *Diabetes Care* 15:1386–1389, 1992
23. Larsson J, Apelqvist J: Towards less amputations in diabetic patients: Incidence, causes, cost, treatment, and prevention: A review. *Acta Orthop Scand* 66:181–192, 1995
24. Boulton AJM: Why bother educating the multi-disciplinary team and the patient: The example of prevention of lower extremity amputation in diabetes. *Patient Educ Couns* 26:183–188, 1995
25. Pinzur MS, Stuck R, Sage R, Pocius L, Trout B, Wolf B, Vrbos L: Benchmark analysis on diabetics at high risk for lower extremity amputation. *Foot Ankle Int* 17:695–700, 1996
26. Foster AVM, Snowden S, Grenfell A, Watkins PJ, Edmonds ME: Reduction of gangrene and amputations in diabetic renal transplant patients: The role of a special foot clinic. *Diabet Med* 12:632–635, 1995
27. Humphrey LL, Palumbo PJ, Butters MA, Hallett JW, Chu CP, O'Fallon M, Ballard DJ: The contribution of non-insulin-dependent diabetes to lower-extremity amputation in the community. *Arch Intern Med* 154:885–892, 1994
28. VanBuskirk A, Barta PJ, Schlossbach NJ: Lower extremity amputations in New Jersey. *N J Med* 91:260–263, 1994
29. Bild DE, Selby JV, Sinnock P, Browner WS, Braveman P, Showstack JA: Lower-extremity amputation in people with diabetes: Epidemiology and prevention *Diabetes Care* 12:24–30, 1989
30. Van Houtum WH, Lavery LA: Regional variation in the incidence of diabetes-related amputations in the Netherlands. *Diabetes Res Clin Pract* 31:125–132, 1996
31. Van Houtum WH, Lavery LA: Outcomes associated with diabetes-related amputations in the Netherlands and in the state of California, USA. *J Intern Med* 240:227–231, 1996

32. Moss SE, Klein R, Klein BEK: Long-term incidence of lower-extremity amputations in a diabetic population. *Arch Fam Med* 5:391–398, 1996
33. Nelson RG, Gohdes DM, Everhart JE, Hartner JA, Zwemer FL, Pettitt DJ, Knowler WC: Lower-extremity amputations in NIDDM: 12-year follow-up study in Pima Indians. *Diabetes Care* 11:8–16, 1988
34. Mayfield JA, Reiber GE, Nelson RG, Greene T: A foot risk classification system to predict diabetic amputation in Pima Indians. *Diabetes Care* 19:704–709, 1996
35. *National Hospital Discharge Data.* Survey, 1989–1992
36. Reiber GE: The epidemiology of diabetic foot problems. *Diabet Med* 13(Suppl):S6–S11, 1996
37. Van Houtum WH, Lavery LA, Harkless LB: The costs of diabetes-related lower extremity amputations in the Netherlands. *Diabet Med* 12:777–781, 1995
38. Apelqvist J, Ragnarson-Tennvall G, Persson U, Larsson J: Diabetic foot ulcers in a multidisciplinary setting: An economic analysis of primary healing and healing with amputation. *J Intern Med* 235:463–471, 1994
39. Sims DS, Cavanaugh PR, Ulbrecht JS: Risk factors in the diabetic foot: Recognition and management. *J Am Phys Ther Assoc* 68:1887–1902, 1988
40. Reiber GE, Pecoraro RE, Koepsell TD: Risk factors for amputation in patients with diabetes: A case-control study. *Ann Intern Med* 117:97–105, 1992
41. Yue DK, McLennan MM, Mai YW, Spaliviero J, Delbridge L, Reeve T, Turtle JR: Effects of experimental diabetes and malnutrition on wound healing. *Diabetes* 36:295–299, 1987
42. Johnson BL, Glickman MH, Bandyk DF, Esses GE: Failure of foot salvage in patients with end-stage renal disease after surgical revascularization. *J Vasc Surg* 22:280–286, 1995
43. Simsir SA, Cabellon A, Kohlman-Trigohoff D, Smith BM: Factors influencing limb salvage and survival after amputation and revascularization in patients with end-stage renal disease. *Am J Surg* 170:113–117, 1995
44. Griffiths GD, Wieman TJ: Meticulous attention to foot care improves the prognosis in diabetic ulceration of the foot. *Surg Gynecol Obstet* 174:49–51, 1992
45. Litzelman DK, Slemenda CW, Langefeld CD, Hays LM, Welch MA, Bild DE, Ford ES, Vinicor F: Reduction of lower extremity clinical abnormalities in patients with non-insulin-dependent diabetes mellitus: A randomized, controlled trial. *Ann Intern Med* 119:36–41, 1993
46. Schraer CD, Adler AI, Mayer AM, Halderson KR, Trimble BA: Diabetes complications and mortality among Alaska Natives: Eight years of observation. *Diabetes Care* 20:314–321, 1997
47. Isakov E, Budoragin N, Shenhav S, Mendelevich I, Korzets A, Susak Z: Anatomic sites of foot lesions resulting in amputation among diabetics and non-diabetics. *Am J Phys Med Rehab* 74:130–133, 1995