Lower-Extremity Amputation

Incidence, Risk Factors, and Mortality in the Oklahoma Indian Diabetes Study

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Oklahoma Indians with NIDDM (n = 1012) underwent a baseline examination in 1972–1980. The incidence of and risk factors for first lower-extremity amputation were estimated. The mortality rates of amputees using data from 875 patients who had no previous history of amputation and who underwent follow-up examination between 1987 and 1991 are presented. The mean age of the 875 patients was 51.6 ± 10.8 yr, and the mean duration of diabetes was 6.6 ± 6.1 yr. After a mean follow-up time of 9.9 ± 4.3 yr, the incidence rate of first LEA among diabetic Oklahoma Indians was 18.0/1000 person-yr. The incidence rate was two times higher in men than in women. In both sexes, significant risk factors ($P < 0.05$) were retinopathy and duration of diabetes. Fasting plasma glucose, use of insulin, and systolic blood pressure were significant for men only. For women, plasma cholesterol and diastolic blood pressure were additional risk factors. Compared with the mortality rate of 33.5/1000 person-yr among nonamputees, the rate among amputees was 55.5/1000 person-yr. The 5-yr survival rate after first amputation was 40.4%. For the amputees, the most common causes of death were diabetes (37.3%), cardiovascular disease (29.1%), and renal disease (7.3%). The incidence and mortality rates in diabetic Oklahoma Indians were higher than those reported in Pima Indians and other diabetic populations. To lower the incidence of lower-extremity amputation in this high-risk population, preventive action through education, foot care programs, and early detection of lesions must be intensified. *Diabetes* 42:876–82, 1993

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NIDDM, non-insulin-dependent diabetes mellitus; LEA, lower-extremity amputation; BP, blood pressure; sBP, systolic blood pressure; dBP, diastolic blood pressure; FPG, fasting plasma glucose; WHO, World Health Organization; ICD-9, International Classification of Disease, ninth revision; BMI, body mass index; CI, confidence interval; IHS, Indian Health Service.

LEA is a significant and common complication of diabetes mellitus, generally arising from vascular and neuropathic complications. The 1978 age-adjusted rate of LEA has been estimated to be 59.7/1000 diabetic patients in the U.S. (1). This rate of LEA in the diabetic population is ~15 times that of the nondiabetic population (1) and poses an especially significant problem in medical care cost for the diabetic patient. With ~5.8 million people diagnosed with diabetes (1987 estimates; 2), more than 50,000 LEAs are performed on diabetic patients each year. The direct medical care (excluding rehabilitation) cost for LEAs in the diabetic population is ~$500 million dollars/yr in the U.S. (3).

In Oklahoma Indians, NIDDM is regarded as one of the most serious health problems and affects ~33% of adults >30 yr of age (4). In this study, the incidence of and risk factors for first LEA in diabetic Oklahoma Indians were determined. Mortality rates and causes of death among amputees and nonamputees also are presented. To our knowledge, no such study of the incidence of and risk factors for LEA has been conducted previously in Oklahoma Indians. These results are compared with reports from the Pima Indians of Arizona and other populations.

RESEARCH DESIGN AND METHODS

At the IHS facilities in Oklahoma, 1012 Oklahoma Indians with NIDDM were examined from 1972 to 1980. This sample, including recruitment methods and examination procedures, has been described elsewhere (5,6). Diabetes was defined as having FPG (o-toluidine method) ≥7.8 mM (140 mg/dl) or a 2-h postload plasma glucose level ≥11.1 mM (200 mg/dl). At baseline examination, the

TABLE 1
Comparison of incidence of first LEA for diabetic Oklahoma and Pima Indians by age and sex

	Male					Female					
	Oklahoma Indians			Pima	Oklahoma/ Pima Indians	Oklahoma Indians			Pima	Oklahoma/ Pima Indians	Oklahoma Male/female
Age (yr)	Person-yr at risk	Cases (*n*)	Incidence*	Indians incidence*	incidence rate ratio	Person-yr at risk	Cases (*n*)	Incidence	Indians incidence	incidence rate ratio	incidence rate ratio
<45	984.6	25	25.4	8.4	3.0	1782.6	15	8.4	2.9	2.9	3.0
45–64	1892.0	48	25.4	18.1	1.4	3265.0	52	15.9	8.4	1.9	1.6
≥65	229.8	8	34.8	28.4	1.2	522.0	8	15.3	12.4	1.2	2.3
Overall	3106.4	81	26.1	15.3	1.7	5569.6	75	13.5	7.1	1.9	1.9

*Per 1000 person-yr.

cohort had a mean duration of diabetes of 6.9 ± 6.4 yr with a mean age of 52.0 ± 11.3 yr. The baseline examination consisted of a physical examination and an interview. All of the examiners followed the protocol of the WHO Multinational Study of Vascular Disease in Diabetes (7). At baseline, amputation status was known for 1011 (379 men and 632 women) patients. Of these, 21 (2.1%) reported a history of LEA, and 990 (374 men and 616 women) reported no LEA before baseline examination. In addition to amputation status, information on dorsalis pedis pulse and ulceration of the foot was also available.

From 1987 to 1991, a follow-up study was conducted. Of the 990 patients who had no amputations at baseline, 434 (43.8%) had died, 498 (50.3%) were re-examined, and 58 (5.8%) did not participate in the follow-up. Information on amputation status was obtained in addition to foot pressure, foot pulse, and problems with numbness in the foot. Medical records of 377 patients who were not examined at follow-up, including 328 deceased, were reviewed for amputation status. Thus, of the 990 who reported no LEA at baseline, amputation status was known for 875 (88.4%) at follow-up. For these 875 (332 men and 543 women) patients, the mean follow-up time was 9.9 ± 4.3 yr. The mean age was 51.6 ± 10.8 yr with a mean duration of diabetes of 6.6 ± 6.1 yr. These 875 patients formed the cohort for this report.

Incidence rate was defined as the number of first amputations/1,000 person-yr at risk for first LEA. Each person who underwent a first amputation was counted only once in the numerator. Person-years were calculated from the baseline examination date to the date of first amputation for amputees and to the date of follow-up examination for those who were re-examined. For those who died or were lost to follow-up, person-years were computed from the baseline examination date to the date of last entry in medical charts. Cause of death among amputees and nonamputees was determined by reviewing death certificates obtained from the Oklahoma State Department of Health using ICD-9.

Many baseline variables were analyzed as possible risk factors, including therapeutic regimen (insulin, oral agent, and diet restriction), the presence of renal disease (defined by plasma creatinine >133 μM [1.5 mg/dl], or slight or heavy proteinuria by the salicylsulphonic acid test), and the presence of coronary heart disease (defined by the Rose and Blackburn questionnaire on angina [8], history of myocardial infarction, or evidence of ischemic heart disease by ECG). BMI was calculated by the ratio of weight (in kg) to height (in m^2), whereas hypertension was defined as sBP ≥160 mmHg, dBP (4th phase) ≥95 mmHg, or the use of antihypertensive medication. Patients with visual problems that could not be corrected by ordinary eyeglasses were defined as visually impaired. The diagnostic criteria for retinopathy were established previously (5). The level of amputation was also specified: toe, foot, below the knee, and above the knee were classifications for amputation levels.

Univariate analyses were performed first to identify significant predictors of LEA. CIs for rate ratios (9) were calculated, and the binomial test (9) and trend test (10) were performed. The SAS computer package (11) was used to calculate the two-tailed Student's *t* test. Bivariate analyses were performed using the Mantel-Haenszel extension test (9). The survival analysis techniques (12) and Cox proportional hazards model (13) using a stepwise procedure were performed using BMDP software (14).

RESULTS

Selected baseline characteristics of participants and nonparticipants (including those who died, had missing medical charts, or were lost to follow-up) were reviewed. Similar to previous findings (15), the nonparticipants generally did not differ significantly from the participants. However, they did have longer duration of diabetes, higher sBP, more severe proteinuria, higher prevalence of background or proliferative retinopathy, and were older.

Of the 875 patients who had no LEA at baseline, 156 (81 men and 75 women) had undergone first LEA during the follow-up period, giving a 10-yr cumulative incidence of 17.8%. The incidence rate of first LEA among these diabetic Oklahoma Indians was 18.0/1000 person-yr with 95% CI 10.6–29.8 (16). Table 1 compares the incidence in this study cohort with that in Pima Indians (17) by sex and age. The incidence in this study population was higher in every age-group and sex group, particularly in those <45 yr of age for both sexes.

Of the 156 first LEAs performed during the study period, the level of amputation was known from either

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interview or medical charts for 84 patients: 44 (52.4%) were of the toe, 5 (6.0%) were of the foot, 32 (38.1%) were below the knee, and 3 (3.6%) were above the knee. The level of amputation was not found to be directly related to age, sex, or duration of diabetes.

To determine the risk factors for first LEA, we performed univariate analyses for the following characteristics: age at baseline, sex, duration of diabetes, age at diagnosis of diabetes, FPG, plasma cholesterol, plasma triglyceride, sBP, dBP, therapeutic regimen, and BMI. We also included renal disease, education, smoking status, hypertension, retinopathy, visual impairment, dorsalis pedis pulse, foot ulceration, and coronary heart disease.

We found the sex of the subjects to be a significant risk factor ($P < 0.0001$). The incidence rate of first LEA in men was 26.1/1000 person-yr (95% CI 12.6–51.3), which was ~2 times that of women (13.5/1000 person-yr, 95% CI 6.0–28.4). The univariate analyses were consequently performed by sex (Table 2). For both men and women, the following were found to be significant risk factors ($P < 0.05$): duration of diabetes, FPG, sBP, dBP, therapeutic regimen, and presence of retinopathy. Additional significant predictors for men were younger age at diagnosis, hypertension, coronary heart disease, and renal disease; foot ulceration was also found to be a suggestively significant factor. For women, additional significant risk factors consisted of plasma cholesterol level, plasma triglyceride level, visual impairment, nonpalpable dorsalis pedis pulse, foot ulceration, and poor education. Coronary heart disease, hypertension, and younger age at diagnosis were found to be suggestively significant in women.

The Student's *t* test was performed to compare the group means of selected continuous variables at baseline for participants who did and did not undergo first LEA during the follow-up period. For both sexes, the amputees had significantly ($P < 0.05$) greater means for sBP, dBP, duration of diabetes, and FPG than the nonamputees. In women, mean plasma cholesterol and mean plasma triglyceride were also significantly higher ($P < 0.05$) in amputees than in nonamputees.

Figure 1 shows that when stratified by duration of diabetes, hypertension remained a significant predictor of LEA in men ($P < 0.03$) and a suggestive predictor in women ($P = 0.1$). Hypertensive men had a significantly higher incidence of LEA regardless of the duration of diabetes. In addition, hypertension remained highly significant when stratified by therapeutic regimen ($P < 0.02$) and FPG ($P < 0.03$) in men only. Therapeutic regimen ($P < 0.04$) and FPG ($P < 0.004$) remained significant when stratified by hypertension in both sexes (Fig. 2). Patients with coronary heart disease and elevated FPG at baseline had a very high incidence (53/1000 person-yr) of LEA in men.

To identify the most important risk factors, multivariate analyses including Cox proportional hazards regression were performed by sex. The response variable was time to amputation or to last follow-up from baseline examination. The covariates examined included baseline age, duration of diabetes, use of insulin, smoking status, retinopathy, coronary heart disease, renal disease, BMI, plasma triglyceride, plasma cholesterol, sBP, dBP, and FPG. Table 3 displays the significant variables ($P < 0.05$) for each sex in the order of entry into the regression equation.

Of patients at risk for first LEA, 347 of 875 died during the follow-up. Of the 719 (251 men and 468 women) who did not undergo a LEA, 254 (104 men and 150 women) died. Of the 156 who did, 93 (48 men and 45 women) died. The crude mortality rate for amputees was thus 59.6%, in contrast to a rate of 35.3% for nonamputees. When person-years are used, the mortality rates for the amputees and nonamputees were 55.5/1000 and 33.5/1000 person-yr, respectively. Death rates among diabetic amputees and nonamputees by age and sex are compared in Table 4. In all age and sex groups except men ≥65, amputees had higher death rates than nonamputees. The difference was particularly large in patients <45 yr of age.

A general trend was found in the mortality rates by the level of first amputation—the higher the level of amputation, the higher the mortality rate. Of the 49 known toe or foot amputees, 38.8% died; of the 32 below-the-knee amputees, 43.8% died; and of the 3 above-the-knee amputees, 66.7% died. However, the number of known above-the-knee amputees was small. The median survival times ranged from 8.1 yr for toe and foot amputees to 5.7 yr for below-the-knee amputees and 4.0 yr for above-the-knee amputees. Thus, the higher on the leg the amputation occurred, the shorter the survival time. However, this trend was not significant at 0.05 level. The 3-yr survival rate after first LEA was 59.8%, whereas 40.4% survived 5 yr after amputation.

Of the 93 amputees who died during the study period, death certificates were obtained for 91 (97.8%). The most common cause of death was diabetes (ICD-9 codes 250–251.2), which appeared on 32 (35.2%) of the death certificates of the amputees. Circulatory disease (ICD-9 codes 390–459.9) was the cause of death in 29 (31.9%) of the amputees. Seven (7.7%) of the amputees died from renal disease (ICD-9 codes 580- 589.9), and the remaining 23 (25.3%) died of other causes.

DISCUSSION

Few population-based or prospective studies that focus on the incidence of and risk factors for LEA in NIDDM patients have been conducted (1,17–19). These studies of diabetic populations have found much lower incidence rates (1,18,19). For example, Moss et al. (18) conducted a population-based 4-yr follow-up study of older-onset diabetic individuals. Moss et al. (18) reported a 4-yr incidence of 2.2%. The Pima Indian study (17) has been the only study concerning Native Americans. The incidence rate in this study of first LEA, 18.0/1000 person-yr, was higher than that reported by the study of Pima Indians (13.7/1000 person-yr). When the incidence rates of this study were compared by age and sex (Table 1), the incidence for Oklahoma Indians was higher in all groups. The incidence rate typically increased with age and duration of diabetes. Although the Pima Indian study conducted biennial examinations, no examinations were

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TABLE 2
Incidence of first LEA by baseline risk factors and sex

Risk factors	Male					Female				
	Person-yr at risk	Cases (*n*)	Incidence*	*P*	Rate ratio (95% CI)†	Person-yr at risk	Cases (*n*)	Incidence*	*P*	Rate ratio (95% CI)†
Duration of diabetes (yr)										
<4	1296.7	21	16.2		1.00	2452.8	13	5.3		1.00
4–7	1079.8	23	21.3	<0.001	1.32 (0.73–2.38)	1613.2	21	13.0	<0.001	2.46 (1.23–4.91)
≥8	481.0	13	27.0		1.67 (0.84–3.33)	859.5	17	19.8		3.73 (1.81–7.68)
Age at diagnosis (yr)										
<30	207.3	8	38.6		1.00	285.5	6	21.0		1.00
30–44	1355.4	45	33.2	0.007	0.86 (0.41–1.82)	2710.5	42	15.5	0.052	0.74 (0.31–1.73)
≥45	1543.8	28	18.1		0.47 (0.21–1.03)	2573.7	27	10.5		0.50 (0.21–1.21)
FPG (mM)										
<7.8	1103.9	13	11.8		1.00	1777.6	12	6.8		1.00
7.8–11.0	1011.4	22	21.8	<0.001	1.85 (0.93–3.67)	1416.7	23	16.2	0.006	2.40 (1.20–4.83)
≥11.1	991.2	46	46.4		3.94 (2.13–7.29)	2364.5	40	16.9		2.51 (1.31–4.78)
sBP (mmHg)										
<130	1172.4	21	17.9		1.00	2349.3	20	8.5		1.00
130–159	1579.7	43	27.2	<0.001	1.52 (0.90–2.56)	2319.9	33	14.2	<0.001	1.67 (0.96–2.91)
≥160	263.3	16	60.8		3.39 (1.77–6.50)	701.8	21	29.9		3.52 (1.91–6.48)
dBP (mmHg)										
<90	1833.5	40	21.8		1.00	3590.7	43	12.0		1.00
90–94	611.3	18	29.5	0.024	1.35 (0.77–2.35)	865.0	14	16.2	0.050	1.35 (0.74–2.47)
≥95	535.0	21	39.3		1.80 (1.06–3.05)	833.6	17	20.4		1.70 (0.97–2.99)
Hypertension status										
No	1916.2	41	21.4	0.021	1.00	3366.6	39	11.6	0.053	1.00
Yes	1063.6	38	35.7		1.67 (1.07–2.60)	1932.1	35	18.1		1.56 (0.99–2.47)
Plasma cholesterol (mM)										
<5.2	1542.4	34	22.0		1.00	2763.1	27	9.8		1.00
5.2–6.1	980.5	30	30.6	0.146	1.39 (0.85–2.27)	1701.1	26	15.3	0.001	1.56 (0.91–2.68)
≥6.2	500.6	16	32.0		1.45 (0.80–2.63)	899.9	22	24.5		2.50 (1.42–4.39)
Plasma triglyceride (mM)										
<18.1	1369.3	30	21.9		1.00	2558.0	23	9.0		1.00
18.1–25.9	539.7	16	29.7	0.177	1.35 (0.74–2.48)	1325.2	18	13.6	<0.001	1.51 (0.82–2.80)
≥26.0	1114.4	34	30.5		1.39 (0.85–2.28)	1480.8	34	23.0		2.55 (1.50–4.33)
Therapeutic regimen										
Diet alone	794.5	9	11.3		1.00	1543.2	9	5.8		1.00
Oral agents	1793.6	45	25.1	<0.001	2.21 (1.08–4.53)	3211.5	48	15.0	<0.001	2.56 (1.26–5.22)
Insulin	461.4	27	58.5		5.17 (2.43–10.98)	784.5	18	22.9		3.93 (1.77–8.76)
Coronary heart disease										
No	2231.7	49	22.0	0.010	1.00	3457.0	40	11.6	0.053	1.00
Yes	756.3	30	39.7		1.81 (1.15–2.85)	1877.2	34	18.1		1.57 (0.99–2.47)
Renal disease										
No	2149.4	46	21.4	0.009	1.00	4111.2	51	12.4	0.122	1.00
Yes	856.2	33	38.5		1.80 (1.15–2.82)	1259.7	23	18.3		1.47 (0.90–2.41)
Retinopathy										
No	2450.6	44	18.0		1.00	4268.5	39	9.1		1.00
Yes	492.6	33	67.0	<0.001	3.73 (2.77–5.03)	831.0	33	39.7	<0.001	4.35 (3.17–5.96)
Visual impairment										
No	2612.3	67	25.6		1.00	4325.5	54	12.4		1.00
Yes	345.8	11	31.8	0.507	1.24 (0.66–2.35)	897.7	20	22.3	0.023	1.80 (1.08–3.00)
Dorsalis pedis pulse										
Present	1390.0	35	25.2	0.132	1.00	2885.0	28	9.7	0.004	1.00
Absent‡	492.8	19	38.6		1.53 (0.88–2.68)	795.9	18	22.6		2.33 (1.29–4.21)
Ulceration of foot										
No	1308.2	36	27.5	0.058	1.00	2625.8	32	12.2	<0.001	1.00
Yes	36.8	3	81.5		2.96 (0.91–9.61)	46.4	4	86.2		7.08 (2.50–20.01)

*Per 1000 person-yr.
†95% CI computed using methods in Rothman (9).
‡Absent in at least one foot.

conducted during the follow-up period in this study. The biennial exams may have promoted earlier detection, prevention, and treatment in those at risk, thereby resulting in a lower incidence rate in the Pima Indian population.

Univariate and multivariate analyses results concur with the findings of the Pima Indian study (17) and other studies that indicate a significantly higher incidence of amputation in men than in women (1,18,20). Duration of diabetes, presence of retinopathy, FPG, and presence of renal disease were also found to be risk factors for amputation in the Pima Indian study. However, additional

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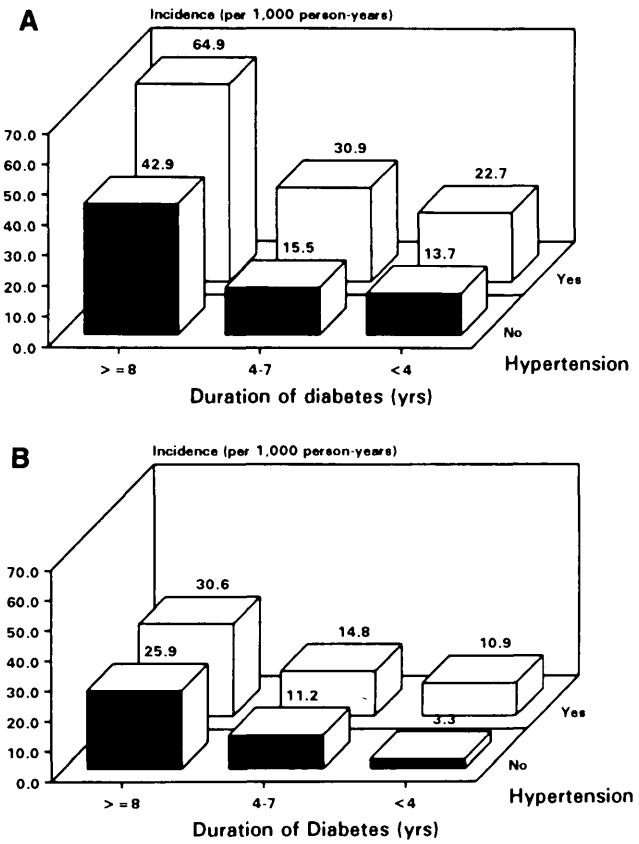

FIG. 1. Incidence of first LEA stratified by hypertension and duration of diabetes in men (*A*) and women (*B*).

risk factors were identified, including sBP and therapeutic regimen (insulin treatment being most predictive) in men and dBP and plasma cholesterol level in women, suggesting that Oklahoma and Pima Indians share many but not all risk factors for LEA. This may be the result of various environmental and genetic factors that deserve future study.

These findings that renal disease and plasma cholesterol are risk factors are consistent with evidence that they predict lower-extremity atherosclerotic occlusive disease in diabetic patients (21). Not surprisingly, both a nonpalpable dorsalis pedis pulse and foot ulceration were found to be a risk factor or a highly suggestive factor, because they also can both be manifestations of peripheral vascular disease (18,19). Finally, plasma triglyceride level and poor education were additional risk factors for women only.

The incidence of first LEA among men is two times that of women, indicating that being male was an important risk factor in this study. When comparing risk factors at baseline between men and women, men had a significantly ($P < 0.05$) higher mean dBP and plasma triglyceride and a lower mean BMI. The rate of coronary heart disease was also higher in men than in women. These facts may contribute to the difference in LEA rates between men and women. Possibly, as in atherosclerotic coronary heart disease, women may be protected from peripheral vascular disease, at least before menopause. Such hypotheses await future studies. To our knowledge, a breakdown of LEA risk factors by sex has not been done, and thus comparison of these to other findings is also for future study.

In this study, retinopathy was found to be a significant risk factor in both sexes, and visual impairment was significant only in women. Visually impaired patients may be especially susceptible to lower-extremity injuries as a result of accidental trauma. The Pima Indian study (17) also found retinopathy to be a significant risk factor, although visual impairment as a risk factor was not mentioned.

Regrettably, no data on peripheral polyneuropathy were available at baseline. At follow-up, a question on numbness in the feet was asked at the interview, and evidence of neuropathic joint disease was noted from X rays. Of the 54 amputees who were interviewed, 32 had numbness (14 for the first time before amputation, 14 after amputation, and 4 gave no dates of first occurrence). Which foot had numbness was unknown. Of the 444 nonamputees, 151 experienced numbness in the feet (133 patients for the first time during the follow-up period, 10 before baseline examination, and 8 gave no dates of first occurrence). Among the 453 patients who had readable foot X rays, 19 (4%) had evidence of neuropathic joint disease. Of these patients, 8 were toe amputees.

The death rate among diabetic Oklahoma Indian amputees was higher than among nonamputees in almost every sex and age-group. This finding that men 25–44 yr of age had the highest death rate ratio of amputees to nonamputees among men agrees with Pima Indian study findings (17). In men and women without amputation, the age-specific death rates in Oklahoma Indians were higher than in the Pima Indians. As was found in the Pima Indian study, toe amputations were the most common in this study cohort; however, only a few foot amputations were observed (6%), and nearly three times as many leg amputations occurred (41%) as in the Pima Indians. Lindegard et al. (22) found that the higher the level of amputation the shorter the survival time. This is consistent with the notion that higher amputations indicate more severe disease and also delayed and possibly even impaired recovery. This may explain the much lower 5-yr survival rate (40.4%) after first amputation in this cohort compared with that of the Pima Indians (61%).

Similar to the Pima Indian study, diabetes was found to be the most common cause of death, followed by cardiovascular disease. Other studies have also found that cardiovascular disease and renal disease are common causes of death for diabetic amputees (22,23).

The physical, psychological, and economical consequences of LEA are severe. LEA hinders mobility and independence and may limit employment opportunities and overall quality of life and predisposes to future morbidity. Diabetic populations, especially Native-American populations, must focus more attention on these problems. Financial limitations may exacerbate the problem; e.g., failure to purchase properly fitting shoes can lead to calluses and foot ulcers that can require amputation.

Debate about the most effective type of treatment and

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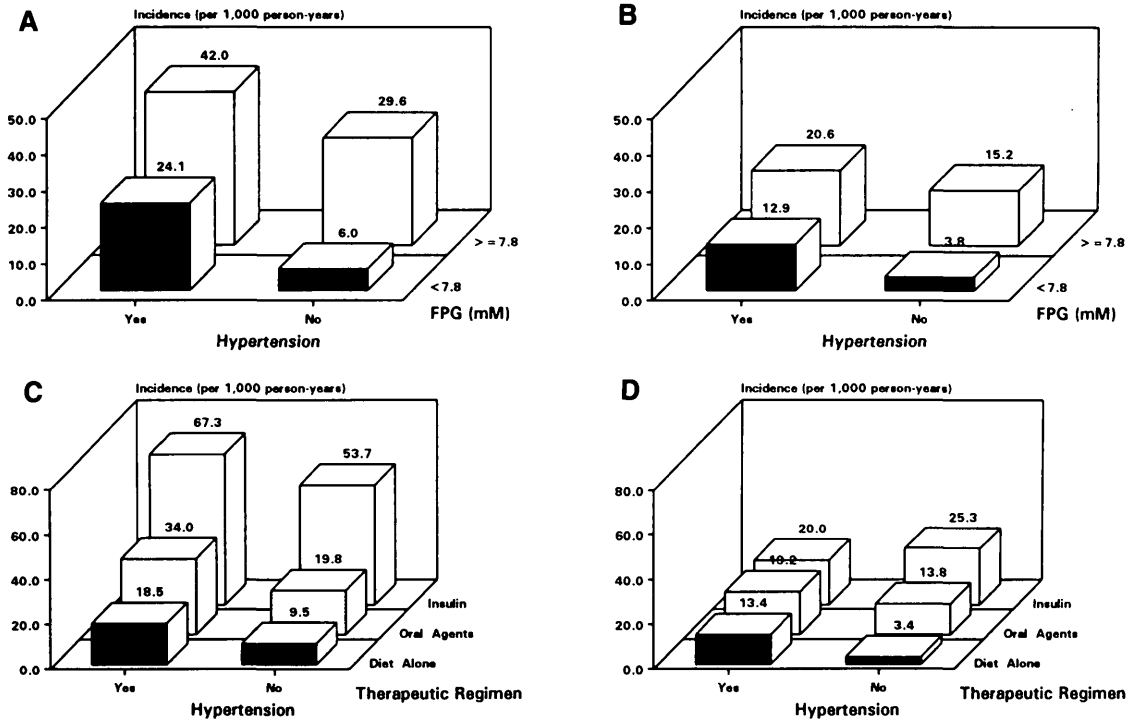

FIG. 2. Incidence of first LEA stratified by hypertension status and FPG in men (*A*) and women (*B*) and therapeutic regimen in men (*C*) and women (*D*).

therapy continues (24). Of diabetic amputees, 34% have been shown to have nonhealing amputations that require an even higher level of amputation (25,26). To preserve the amputee's way of life as much as possible, early rehabilitation with prostheses currently is encouraged. However, although below-the-knee amputations offer more promise of rehabilitation compared with above-the-knee amputations (27), the success rate of prosthetic rehabilitation for the former is only 60–66% (28,29). Limb preservation strategies such as revascularization may prove a more effective and desirable alternative if performed early and on a selective group of patients.

Although current means of therapy have improved, the cost for surgery is higher. On average for patients with primary amputations or vascular reconstruction, the cost is $40,500/patient (30). If vascular reconstruction is successful, the cost averages $28,374/patient; however, the cost of an unsuccessful reconstruction has been estimated at $56,809/patient (30). Prevention must be undertaken in high-risk populations such as the diabetic Oklahoma Indian population. A well-organized program of diabetic education and prevention has been shown to decrease the rate of amputation by >50% (31). These stratified and multivariate analysis identified several controllable risk factors, e.g., BP, plasma glucose, and plasma cholesterol. Better control of these risk factors may be beneficial in the diabetic Oklahoma Indian population. In addition, health education stressing the importance of foot care and early detection of lower-extremity lesions would likely help lower the incidence of amputation in diabetic Oklahoma Indians.

TABLE 3
Risk factors for first LEA from the Cox proportional hazards model

	Coefficient	SE	*P*	Rate ratio (95% CI)
Male				
Retinopathy	1.1613	0.2759	<0.001	3.19 (1.86–5.49)
Use of insulin	0.9392	0.2578	<0.001	2.56 (1.54–4.24)
sBP*	0.1390	0.0560	0.002	1.15 (1.03–1.28)
Duration of diabetes (yr)	0.0471	0.0197	0.005	1.05 (1.01–1.09)
FPG (mM)	0.0738	0.0234	0.011	1.08 (1.03–1.13)
Female				
Retinopathy	1.2021	0.2643	<0.001	3.33 (1.98–5.59)
Duration of diabetes (yr)	0.0806	0.0191	<0.001	1.08 (1.04–1.13)
Plasma cholesterol (mM)	0.1664	0.0464	0.012	1.18 (1.08–1.29)
dBP*	0.2450	0.1020	0.013	1.28 (1.05–1.56)

*Per 10 mmHg change.

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TABLE 4
Mortality rate (per 1000 person-yr) by sex, age, and LEA status

Baseline age (yr)	Male			Female		
	Amputation	No amputation	Rate ratio	Amputation	No amputation	Rate ratio
<45	48.7	16.7	2.9	33.1	8.6	3.8
45–64	53.5	39.9	1.3	55.6	31.2	1.8
≥65	88.6	140.1	0.6	124.4	91.7	1.4
Total	58.7	40.4	1.5	56.0	29.9	1.9

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