Incidence of Lower-Limb Amputation in the Diabetic and Nondiabetic General Population

A 10-year population-based cohort study of initial unilateral and contralateral amputations and reamputations

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OBJECTIVE — The purpose of this study was to compare the incidence of vascular lower-limb amputation (LLA) in the diabetic and nondiabetic general population.

RESEARCH DESIGN AND METHODS — A population-based cohort study was conducted in a representative Swedish region. All vascular LLAs (at or proximal to the transmetatarsal level) performed from 1997 through 2006 were consecutively registered and classified into initial unilateral amputation, contralateral amputation, or reamputation. The incidence rates were estimated in the diabetic and nondiabetic general population aged ≥45 years.

RESULTS — During the 10-year period, LLA was performed on 62 women and 71 men with diabetes and on 79 women and 78 men without diabetes. The incidence of initial unilateral amputation per 100,000 person-years was 192 (95% CI 145–241) for diabetic women, 197 (152–244) for diabetic men, 22 (17–26) for nondiabetic women, and 24 (19–29) for nondiabetic men. The incidence increased from the age of 75 years. Of all amputations, 74% were transtibial. The incidences of contralateral amputation and of reamputation per 100 amputee-years in diabetic women amputees were 15 (7–27) and 16 (8–28), respectively; in diabetic men amputees 18 (10–29) and 21 (12–32); in nondiabetic women amputees 14 (7–24) and 18 (10–28); and in nondiabetic men amputees 13 (6–22) and 24 (15–35).

CONCLUSIONS — In the general population aged ≥45 years, the incidence of vascular LLA at or proximal to the transmetatarsal level is eight times higher in diabetic than in nondiabetic individuals. One in four amputees may require contralateral amputation and/or reamputation.

Diabetes Care 32:275–280, 2009

Severe peripheral arterial disease indicating critical ischemia has been found in 1.2% of a general population aged ≥60 years (1) and in almost 5% of primary care patients aged ≥65 years (2). It has been reported that one in four diabetic individuals develops peripheral vascular disease that, when severe, may require amputation (3). Estimating the incidence of vascular lower-limb amputation (LLA) in diabetic and nondiabetic individuals can provide important information regarding changes in the incidence over time. This can assist in the planning of preventative care and rehabilitation and facilitate assessment of the effects of interventions, such as arterial reconstruction and amputation at specific levels, and the success of prosthetic rehabilitation (4,5).

The reported annual incidence of LLA related to peripheral vascular disease has ranged from approximately 20 to 35 per 100,000 inhabitants (5,6). These incidence rates were usually based on the total population rather than on age-groups of the diabetic or the nondiabetic general population in which severe peripheral vascular disease usually occurs (7). Furthermore, different definitions and incidence estimation methods have been used, and problems of incorrectly registered diagnoses and missing data have been described (3,8). Individuals with diabetes have accounted for less than half of all patients with LLA in studies from Finland and Sweden (5,9) but for as much as two-thirds of patients with LLA in a German general population study (6).

Compared with amputations in nondiabetic individuals, amputations due to diabetes have more often involved younger individuals and lower amputation levels (10). Because vascular LLA in diabetic and nondiabetic individuals may differ with regard to patient characteristics, initial amputation level, clinical management, and prognosis (including mortality rates), it is important to study the epidemiology of LLA related to peripheral vascular disease with and without diabetes independently (10). Few population-based studies have estimated the incidence of LLA in the diabetic general population based on validated data concerning the age- and sex-specific prevalence of diabetes at the time of study. Despite the availability of data on amputations (11), the utility of these data to accurately determine the incidence of LLA in the general population may be limited because the data are usually based on hospital discharges, which do not accurately detail procedures performed and concurrent diagnosis of diabetes. Moreover, accurate incidence rates cannot be derived unless the data are related to validated estimates of the sex- and age-

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Received 5 September 2008 and accepted 30 October 2008.
Published ahead of print at http://care.diabetesjournals.org on 10 November 2008. DOI: 10.2337/dc08-1639.

specific prevalence of diabetes in the general population.

The aim of this population-based cohort study was to estimate the incidence of LLA (at or proximal to the transmetatarsal level) performed for peripheral vascular disease among the diabetic and the nondiabetic general population over a 10-year period, with particular consideration of the rate of reamputation and contralateral amputation.

RESEARCH DESIGN AND METHODS

— The study was conducted on a representative population in Northeastern Scania, a health care district in the southern part of Sweden with a total population of ~170,000. All LLAs in this region are performed at one orthopedic department by orthopedic surgeons, and patients considered for amputation related to vascular disease are assessed in agreement with vascular surgeons.

The inclusion criteria for this study were amputation performed because of peripheral vascular disease with or without diabetes at or proximal to the transmetatarsal level during the period from 1 January 1997 through 31 December 2006. Patients with infection as the primary diagnosis and peripheral vascular disease as the secondary diagnosis were also included. The exclusion criteria were residence outside the study region at the time of amputation (according to the national population register), toe or ray amputations, and amputation performed for other reasons such as trauma or tumor.

The number of diabetic individuals in the general population was estimated on the basis of the age- and sex-specific prevalence of diabetes in the region of Östergötland in the southeast area of Sweden. In that population, the prevalence of diabetes was determined using a case-finding algorithm that retrospectively searched for the diagnosis of diabetes during a 5-year period (1999–2003) in the region's administrative database (12). The two regions have similar population characteristics (13).

Data collection

All patients undergoing LLA in the operating room were recorded consecutively. The surgical procedure was recorded according to the Nordic Classification of Surgical Procedures (codes NEQ 19–NHQ 14) and included amputation level, side, and diagnosis. The amputations were classified according to the following definitions: an initial unilateral amputation is an individual's first LLA at or proximal to the transmetatarsal level (including secondary closure or two-stage amputation); a contralateral limb amputation is an amputation at or proximal to the transmetatarsal level on the opposite lower limb in an individual who had undergone an initial unilateral amputation; and a reamputation is a new amputation at a more proximal level (including procedures in which bone length was shortened within the same level) in a individual who had undergone an initial unilateral or a contralateral limb amputation.

Patients were considered to be diabetic if they had a diagnosis of diabetes treated with oral hypoglycemic agents or insulin at the time of amputation. Information from all medical records was first documented by one investigator (A.J.) and then verified by a second investigator (G.-U.L.). All postoperative care and new surgical procedures were performed at the study region's hospital. No patients included in the study moved from the region during the study period. The regional ethical committee at Lund University approved the study.

Statistical analysis

The overall sex- and age-specific incidence rates for the initial unilateral amputation were calculated for diabetic and nondiabetic individuals. Because only one diabetic individual aged ≤45 years (aged 44 years and 9 months at amputation) and no nondiabetic individuals underwent amputation at or proximal to the transmetatarsal level during the study period, the incidence rates were calculated for the diabetic and nondiabetic populations aged ≥45 years. All patients were residing in the region during the study period. The mean 10-year diabetic and nondiabetic populations were calculated as the mean value for the population for each year of the study period (obtained from the national population statistical database), adjusted for the prevalence of diabetes. The overall incidence per 100,000 person-years was calculated as the number of diabetic and nondiabetic individuals aged ≥45 years who had undergone initial unilateral amputation divided by the corresponding total population. The number of amputations over a 10-year period was assumed to have a Poisson distribution and the number of individuals with diabetes to have a binomial distribution (these were assumed to be independent). Parametric bootstrap analysis with 10,000 replications and the percentile method were used to estimate 95% CIs for incidence rate. Incidence rates for contralateral amputation and reamputation among individuals who had undergone an initial unilateral amputation were calculated per 100 amputee-years. In calculating the incidence rates (initial unilateral, contralateral, and reamputation), each patient accounted for no more than one amputation for each incidence rate. The 1-year mortality rates among diabetic and nondiabetic patients were compared using Cox regression analysis with adjustment for age and sex. For patients included during the final year of the study, mortality was recorded during 1 year after amputation. A Kaplan-Meier analysis was used to calculate median time from initial amputation to death. $P < 0.05$ was considered to indicate statistical significance. The analyses were performed with SPSS 14.0 (SPSS, Chicago, IL) and STATA 10.0 (StataCorp, College Station, TX).

RESULTS

— During the 10-year study period, 133 diabetic patients (53% men) and 157 nondiabetic patients (50% men) underwent initial unilateral amputations at or proximal to the transmetatarsal level because of peripheral vascular disease (Table 1). Among these patients, a contralateral limb amputation was performed on 22 (17%) of the diabetic patients and on 21 (13%) of the nondiabetic patients. A reamputation was performed after the initial unilateral amputation in 20 diabetic patients (15%) and after the contralateral amputation in 5 patients (3.8%); the corresponding numbers among the nondiabetic patients were 27 (17%) and 6 (3.8%). Patients >75 years of age comprised 62% of the diabetic and 81% of the nondiabetic group. The amputation was performed at the transtibial level or more distally in 120 (90%) of the diabetic patients and in 116 (74%) of the nondiabetic patients.

Incidence

During the 10-year study period the mean midyear population of individuals aged ≥45 years in the study region was 76,322, and the prevalence of diabetes was 9% (total diabetic population aged ≥45 years 6,841 and nondiabetic population 69,480). The overall incidence of initial unilateral amputation in the diabetic population was 195 (95% CI 163–231) per 100,000 person-years and in the nondiabetic population was 23 (19–26) per 100,000 person-years (Table 2). Among diabetic individuals of both sexes,

Table 1—*Characteristics of the study population stratified into diabetic and nondiabetic patients according to initial unilateral amputation, contralateral amputation, and reamputation*

	Diabetic			Nondiabetic		
	Initial unilateral amputation	Contralateral amputation	Reamputation*	Initial unilateral amputation	Contralateral amputation	Reamputation*
n	133	22	25	157	21	33
Women	62 (47)	9 (41)	10 (40)	79 (50)	11 (52)	14 (42)
Age (years)	77 ± 9			83 ± 8‡		
Men	71 (53)	13 (59)	15 (60)	78 (50)	10 (48)	19 (58)
Age (years)	76 ± 11			79 ± 8†		
Level						
Transfemoral	7 (5)	1 (5)	11 (44)	25 (16)	5 (24)	26 (79)
Knee disarticulation	6 (5)	2 (9)		16 (10)	1 (5)	3 (9)
Transtibial	108 (81)§	17 (77)	13 (52)	109 (69)§	15 (71)§	4 (12)
Midfoot (including tarsometatarsal joints)	5 (4)	1 (5)	1 (4)	2 (1)		
Transmetatarsal	7 (5)	1 (5)		5 (3)		

Data are means ± SD or *n* (%). *Reamputation (including bone revision). †$P < 0.001$ compared with diabetic patients. ‡$P = 0.007$ compared with diabetic patients. §Including one ankle disarticulation.

the incidence increased gradually with age, with similar incidence rates between 45 and 85 years, after which the incidence in men was threefold that in women. In the ≥85 years age-group the incidence in men was five times as high and in women twice as high as the incidence rate in the general population of all ages. Among nondiabetic individuals, the incidence was low up to age 75 years but increased sharply thereafter and in the ≥85 years age-group the incidence in men was 15 times and in women 12 times as high as the incidence in the total population of all ages.

Contralateral limb amputation

The incidence of contralateral amputation among diabetic amputees was 17 (95% CI 10–25) per 100 amputee-years and among nondiabetic amputees was 13 (8–20) per 100 amputee-years (Table 3). The most frequent contralateral amputation level among diabetic and nondiabetic patients was transtibial. Thirteen diabetic patients (10%) and 10 nondiabetic patients (6%) became bilateral transtibial amputees.

Reamputation

The incidence of reamputation among diabetic amputees was 19 (95% CI 12–28) per 100 amputee-years and among nondiabetic amputees was 14 (9–22) per amputee-years (Table 3). The most frequent reamputation level among diabetic patients was transtibial and among nondiabetic patients was transfemoral. Among initial transtibial amputees, reamputation

Table 2—*Incidence (per 100,000 person-years) of initial unilateral amputation at or proximal to the transmetatarsal level in the diabetic and nondiabetic general population*

		Diabetic			Nondiabetic		
Age-group	Prevalence of diabetes	No. of persons	Population	Incidence (95% CI)	No. of persons	Population	Incidence (95% CI)
Women							
45–64 years	4.3	7	9,277	75 (22–138)	0	—	—
65–74 (55–74) years	11.3 (8.0†)	11	9,179	120 (55–197)	11†	172,465	7† (3–10†)
75–84 years	14.7	30	10,100	297 (194–408)	34	58,769	58 (39–78)
≥85 years	13.4	14	4,256	329 (167–518)	34	27,548	123 (83–167)
Population ≥45 years‡	8.1	62	32,307‡	192 (145–241)	79	367,337‡	22 (17–26)
Total population	4.1	62	35,260	176 (134–221)	79	822,365	10 (8–12)
Men							
45–64 years	6.8	11	15,133	73 (33–117)	0	—	—
65–74 (55–74) years	14.6 (11.4†)	21	10,813	194 (118–282)	19†	161,088†	12† (7–17)†
75–84 years	16.7	19	8,551	222 (129–328)	39	42,767	91 (63–121)
≥85 years	14.3	20	2,153	929 (545–1,369)	20	12,945	154 (92–225)
Population ≥45 years‡	9.9	71	36,105‡	197 (152–244	78	327,467‡	24 (19–29)
Total population	4.6	71	38,860	183 (142–226	78	800,303	10 (8–12)

*Per 100,000 person-years. †The values are for the age-group 55–74 years because no lower limb amputation was performed on nondiabetic persons aged <55 years (CIs could only be calculated for the wider age interval because of small numbers). ‡All person-years generated by persons at risk do not sum to equal because this would imply that prevalence would be constant over age-groups.

Table 3—*Contralateral amputation and reamputation at or proximal to the transmetatarsal level in diabetic and nondiabetic amputees*

	Diabetic			Nondiabetic		
	n	Incidence*	Time from initial amputation (days)	*n*	Incidence*	Time from initial amputation (days)
Contralateral amputation						
Women	9	15 (7.0–26)	614 (224–1,223)	11	14 (7.2–24)	260 (140–399)
Men	13	18 (10–29)	273 (60–466)	10	13 (6.3–22)	49 (1–290)
Reamputation						
Women	10	16 (8.0–28)	30 (10–82)	14	18 (10–28)	30 (14–65)
Men	15	21 (12–32)	27 (18–49)	19	24 (15–35)	23 (12–36)

Data are incidence (95% CI) or median (interquartile range). *Incidence per 100 amputee-years, based on at-risk population of patients with prior initial amputation at or proximal to the transmetatarsal level performed during the study period (see Table 2).

was performed on 7 (6%) of the diabetic patients and 16 (15%) of the nondiabetic patients.

The time from initial amputation to reamputation showed no statistically significant differences between sexes in both groups, whereas the time to contralateral amputation was shorter in nondiabetic patients and tended to be shorter for men in both groups (Table 3).

Mortality

After an initial amputation, the median survival time for diabetic patients was 440 (95% CI 303–577) days and for nondiabetic patients was 563 (95% CI 368–758) days. During the first year after the initial amputation, 60 diabetic patients (45%) and 78 nondiabetic patients (50%) died. The 1-year mortality did not differ significantly between the two groups, with an age- and sex adjusted odds ratio of 1.03 (95% CI 0.73–1.46, $P = 0.87$).

CONCLUSIONS— This study showed that the incidence rate of initial unilateral LLA at or proximal to the transmetatarsal level in the general population aged ≥45 years was more than eight times higher among diabetic individuals than among nondiabetic individuals. When the incidence rate is calculated on the basis of the general population of all ages, the incidence of initial amputation due to diabetes would be 179 per 100,000 person-years and that due to peripheral arterial disease in nondiabetic individuals would be 10 per 100,000 person-years.

The incidence rate in the nondiabetic population is similar to that reported in previous studies. A rate of 9 per 100,000 person-years was reported in a German city population with a mean age 10 years lower than that for our study population (6), and a rate of 12 per 100,000 person-years was reported in a Dutch population (14). However, a Finnish study has reported a higher incidence of 23 per 100,000 person-years (15).

For the diabetic population, more disparity is observed when our incidence rate is compared with that reported in previous studies. This is probably due to differences in methodology (14) and/or in accuracy of the diabetes prevalence data used (6) and whether the data had been validated (12). In the German population study, relatively old data concerning the prevalence of diabetes were used, and the incidence rate (230 per 100,000 person-years) was higher than that estimated in our study. However, an incidence of 247 per 100,000 person-years was reported in a population of a Scottish city with a mean age similar to that of the German population and with diabetes prevalence data that had been validated (16). Approximately one-third of all amputations in both studies were toe amputations, which were not included in our study. A study that compared continuous registration of all amputations with the official patient register reported that only 36% of the diabetes-related amputations were noted in the official register and that the finding was in agreement with that in several other studies (8). Missing data are more likely to involve toe or ray-level amputations, as they are often performed in an emergency room or outpatient clinic and therefore are not registered in the surgical databases. The potentially high number of missing amputations can substantially influence the comparability of incidence rates in studies that do not exclude toe and ray amputation. Another aspect that needs to be considered is whether the incidence rate of diabetes-related LLA was based on the initial (first) amputation or the highest level of amputation performed on patients who had undergone more than one amputation (6). In some cases, the initial amputation is performed on a nondiabetic individual, but the last amputation is performed after a diagnosis of diabetes has been established.

The incidence of vascular LLA may be dependent on the age characteristics of the study population (7). The incidence of amputation among individuals aged ≥80 years has been reported to be almost threefold that among individuals aged 60–80 years (6). However, in our study, differences of such magnitude were found only among nondiabetic men aged ≥85 years compared with younger age-groups. The incidence of amputation in both the diabetic and the nondiabetic general population would be much lower if the rate were based on the total population of all ages rather than on the age-groups in which amputations were performed. Because amputation at the transmetatarsal level or higher, related to diabetes and/or peripheral arterial disease, is extremely uncommon in individuals aged <45 years, the incidence rate based on the population aged ≥45 years is probably more clinically important.

It has been suggested that the incidence of diabetes among adults in Sweden has not increased, although the prevalence has increased mainly because of a higher median age of diabetic individuals in the general population (17). The incidence of amputation in this Swedish population increased with age in both men and women, but the mean age at initial amputation was lower for men than for women—a finding also shown in other studies (18). Our study showed a significantly higher risk for amputation in diabetic men aged ≥85 years. A Finnish population study showed that men have a significantly higher risk of vascular amputation than women (15).

In our study, the incidence rate based

on all amputations would be 23 per 100,000 person-years, which is 35% higher than the incidence rate of initial amputation (17 per 100,000 person-years). A literature review showed that in many previous studies the reported incidence rates were based on number of all "amputations" (7), which would imply that individuals were allowed to count more than once and continue to accrue person-time after the initial amputation. Without distinguishing the initial amputation from a reamputation and contralateral amputation, the incidence rates reported in such studies are likely to reflect multiple procedures performed on the same patient, which is more common at the foot level in diabetic patients (8). According to a study involving 10 centers in six countries, the disparity in incidence rates based on initial or on all amputations ranged from 20 to 40% but was sometimes much higher (19).

The incidence rates of reamputation or contralateral amputation over the 10-year study period were similar among the diabetic and nondiabetic men and women amputees, ranging from 13 to 24 per 100 amputee-years. Few longitudinal studies have presented sex-specific incidence rates of reamputation after amputations proximal to the toe or ray level. After the initial unilateral amputation, 19% of the diabetic patients and 21% of the nondiabetic patients underwent a reamputation after a median period of 1 month, with approximately 90% occurring within 2 months. The results support the fact that once the amputated limb has healed, the risk of reamputation is small (9). Also, 17% of the diabetic initial unilateral amputees became bilateral amputees after a median time of <1 year in men and 2 years in women compared with 13% of the nondiabetic amputees after a median time of <2 months in men and 9 months in women. The rate of contralateral amputation is lower than reported previously; Andersson (20) reported that 31% (119 of 385) of vascular amputees (mean age 63 years) underwent contralateral amputation within 2 years, whereas Greant and Van den Brande (21) reported that one-third of 58 patients (mean age 72 years) required a contralateral amputation after a mean time of 8 months.

The most common level for initial amputation in our study was the transtibial level; the ratio of transtibial to higher-level amputation in diabetic patients was 8.2:1 and in nondiabetic patients was 2.6:1, which is better than the ratio of 2.5:1 usually considered as the "gold standard" (22). This conservative surgical approach in diabetic patients did not seem to increase the reamputation rate.

The high 1-year mortality in our study is related to the high mean age of the study population and is consistent with previous reports from Sweden (9). In a study from the U.S., the 1-year mortality was 30% with a mean age of the patients of 67 years (23).

The strengths of the present study are that it was performed on a well-defined general population over a 10-year period, with all amputations performed at the same department and data verified for accuracy, and that validated diabetes prevalence estimates from a representative population were used. One limitation was that residents from the study region may have had an amputation performed at hospitals outside the region and were not included. This would probably involve very few patients because, according to the health care system, such patients would usually be seen for follow-up and rehabilitation at the regional hospital unless they died or did not come for follow-up. Although all of the vascular amputations were performed by orthopedic surgeons, a different practice from that in other countries, the indication for amputation was considered in agreement with vascular surgeons. Consequently, the specialty of the surgeon (vascular or orthopedic) who performs the amputation procedure itself is not likely to influence the incidence rates.

The use of 45 years as the lower age limit for estimating the incidence rate in the general population may limit comparability with other studies. However, only one patient had an amputation before this age, and this age has also been shown to be the starting point of LLA in patients with type 1 diabetes (24). Another limitation may be the exclusion of toe and ray amputations, which may make some comparisons with studies that classified amputations on the basis of other criteria more difficult. However, the definitions of "major" and "minor" amputation used in various studies have been inconsistent, making comparisons difficult. For example, a major amputation has been defined in various studies as one extending from the tarsometatarsal joint (19), the "midfoot" (18), or the ankle (Symes) (8) and even beginning from the transtibial level (9). Furthermore, incidence rates based on amputations from the transmetatarsal level that exclude the most distal amputations are probably more accurate and have greater clinical significance with regard to the effects on functional mobility of the patients and the total cost of hospitalization (25).

Acknowledgments— No potential conflicts of interest relevant to this article were reported.

We thank Ulf Strömberg, Professor of Epidemiologic Methods, Lund University, Lund, Sweden, for his advice and Philippe Wagner, MSc, at the Swedish National Competence Centre for Musculoskeletal Disorders, Lund University, Sweden, for statistical assistance.

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