Reduced Incidence of Lower-Limb Amputations in the Diabetic Population of a German City, 1990-2005

Results of the Leverkusen Amputation Reduction Study (LARS)

Christoph Trautner, MD, MPH[1,2]
Burkhard Haastert, PHD[3]
Peter Mauckner, MD[4]
Lena-Maria Gätcke[1]
Guido Giani, PHD[3]

OBJECTIVE — We evaluated whether the incidence of amputations in one German city (Leverkusen, population ~160,000) had decreased between 1990 and 2005.

RESEARCH DESIGN AND METHODS — From all three hospitals in the city, we obtained complete lists of nontraumatic lower-limb amputations in 1990–1991 and 1994–2005. Only the first observed amputation in residents of Leverkusen was counted. A total of 692 patients met the inclusion criteria. Data about the population stucture, separately for each year of the observation period, were received from the city administration and the Federal Office of Statistics. To test for time trend, we fitted Poisson regression models.

RESULTS — Of all subjects, 72% had known diabetes and 58% were male. Mean age was 71.7 years. Incidence rates in the diabetic population (standardized to the estimated German diabetic population per 100,000 person-years) varied considerably between years (maximum 549 in 1990, minimum 281 in 2004). In the diabetic population, the estimated relative risk (RR) per year was 0.976 (95% CI 0.958–0.996, $P = 0.0164$). The same trend was observed when only amputations above the ankle ($n = 352$) (RR 0.970 [95% CI 0.943–0.997], $P = 0.0318$) were considered. Over 15 years, an estimated reduction of amputations above the toe level by 37.1% (95% CI 12.3–54.8) results. There was no significant change of incident amputations in the nondiabetic population (RR 1.022 [0.989–1.056], $P = 0.1981$).

CONCLUSIONS — This finding is likely to be due to improved management of the diabetic foot syndrome after a network of specialized physicians and defined clinical pathways for wound treatment and metabolic control were introduced.

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In 1989, a reduction of the number of amputations in the diabetic population by at least one-half within 5 years was declared a primary objective for Europe (St. Vincent Declaration) (1). We published baseline data about the incidence rates of amputations in the city of Leverkusen, Germany, in 1990 and 1991, as well as follow-up data through 1998 (2,3). We found that the risk of having an amputation was 26-fold (95% CI 17–39) in the diabetic population compared with that in the nondiabetic population. Moreover, 96% (94–97) of the amputation risk in diabetic individuals and 70% (61–77) of the amputation risk in the entire population were due to diabetes (2,3). We estimated that ~31,000 patients in Germany underwent first amputations per year, that 23,000 of these patients had diabetes, and that 21,000 had their amputations due to their diabetes (4). No change in incidence rates over time could be detected between 1990 and 1998 (3). In the present study, we continued the collection of these data from 1999 through 2005 and combined them with the existing dataset to ascertain a potential change in incidence rates.

The incidence of amputations in diabetic individuals dropped significantly in several areas in various countries and populations, such as Alaska Natives, American Indians, Denmark, and Sweden, after various specific programs for foot care and prevention were introduced. In recent years, decreasing incidence rates of amputations were reported from several areas in the U.S., Finland, the Netherlands, and Italy (3,5–10). By contrast, no data showing a reduction of amputations since 1989 in any part of Germany have been published to date (3,11,12).

Following our publication, a group of physicians in Leverkusen analyzed why various activities had failed to reduce amputation rates. Profound changes in the structure of care for patients with diabetes followed. The Leverkusen Diabetes Wound Network was founded in 2000. Participants were the office-based physicians who specialized in diabetes, office-based surgeons, the department of vascular surgery, and the diabetologists from Remigius Hospital. Defined clinical pathways for patients with diabetes were introduced (13).

Care for patients with diabetes at Remigius Hospital changed fundamentally. Until 1999, mainly patient education on an inpatient basis, even for relatively healthy patients without serious complications or comorbidity, was carried out in the department of internal medicine. In the case of foot problems, patients were transferred to the surgical departments. Internists were only consulted—if at all—with respect to metabolic control. After three specialized physicians had opened their offices and

From [1]Medicine, Science, Consulting, Berlin, Germany; the [2]Department of Public Health, University of Applied Sciences, Wolfsburg, Germany; the [3]German Diabetes Center, Institute of Biometrics and Epidemiology, Düsseldorf, Germany; and [4]Department of Internal Medicine, Remigius Hospital, Leverkusen, Germany.

Address correspondence and reprint requests to Dr. Christoph Trautner, Stephanstr. 67, 10559 Berlin, Germany. E-mail: ct@christoph-trautner.net.

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offered patient education on an outpatient basis, treatment of complications like the diabetic foot became the new focus at the hospital. An interdisciplinary ward for inpatient treatment, including preoperative and postoperative care, was opened in 2001. This ward now serves as a central unit. After surgery was performed on infected wounds and after vascular surgery, patients return for further integrated treatment of wounds, infection, and metabolic problems. As a rule, surgery is only performed after common indication rounds with diabetologists and surgeons. After surgery, so-called problem rounds regularly follow. Standardized, phase-adapted wound care after thorough, rigorous debridement and, if possible, revascularization is an integral part of treatment. Antiseptics, antibiotics, moist semi-occlusive dressings, maggots, and vacuum-assisted closure therapy are parts of this treatment scheme (13).

When patients are discharged, they continue to be treated by the now-established outpatient network. Of 93 general practitioners' offices in the city, 63 offices with 80 physicians received specific training for diabetes treatment. This training program, followed by quality circles, could considerably reduce the problem of delayed diagnosis and referral of patients with diabetic foot problems. In recent years, nearly all diabetic patients with the temporary need for specialist care (e.g., at diagnosis or in the case of complications) are seen by a diabetologist and return to their general practitioners afterward. In addition, a seminar on up-to-date wound care was held in the years 2003 and 2004 for paramedic staff. Over 60 nurses from the hospital and retirement homes and from teams working in home care were trained. In 2001, a contract between one of the major sickness funds and shoemakers was signed so that shoes could be fitted more quickly and better adapted to the individual patient's needs.

RESEARCH DESIGN AND METHODS

Population and methods have been described in detail in previous publications (2,3). Briefly, from all three hospitals in Leverkusen, we obtained complete lists of lower-limb amputations performed in 1990–1991 and 1994–2005. We abstracted the relevant information from their hospital files. Diabetes status of the patients was defined as being diagnosed with diabetes by the hospital physicians. Patients who were not city residents or who had previous amputations were excluded. Only the first observed amputation in a patient within the observation period was counted. (Analogously, in secondary analyses considering major amputations, the first observed amputation of the level under consideration was counted.) Population data were obtained from the city administration and the Federal Office of Statistics. The total population of the city as of 31 December 1989 (used for 1990) and 31 December 2004 (used for 2005) was 159,646 and 161,543, respectively.

Statistical analysis

The population with diabetes in each stratum (defined by year, age, and sex) was estimated by multiplying the population of the study area by the age- and sex-specific prevalence of diabetes obtained from the former East German diabetes registry (2,3). Even to date, these are the only reliable age-specific prevalence data available for the German population. Both stratum-specific and directly standardized incidence rates (standard: West German population of 1991) were estimated for each calendar year for the total, the estimated nondiabetic, and the estimated diabetic populations, respectively. To assure comparability, the same standard population was used in all analyses and published papers.

To test for time trend, we fitted separate Poisson regression models for diabetic and nondiabetic patients, using year of registration (difference from the first year as an ordinal variable), age (categorized into four classes), and sex as independent variables (14). In addition, we fitted a similar common Poisson regression model to all patients and the entire population. In this model, a variable was included for diabetes, as well as an interaction term for diabetes and years since 1990. The statistical analysis using Poisson models was repeated including only amputations above the toe level and above the ankle, respectively. Calculations were carried out with the SAS statistical package (version 9.1, TS1M3).

RESULTS

We identified 728 patients who were residents of Leverkusen and had nontraumatic lower-limb amputations in the three local hospitals during the defined period. Because of previous amputations, 36 were excluded (3). Tables 1 and 2 show the distribution of the remaining 692 patients with respect to age, sex, diabetic status, and calendar year. Of all patients, 72% were known to have diabetes and 58% were male. The mean ± SD age was 71.7 ± 11.0 years (range 33–98). The mean age of women was 75.4 ± 10.7 years and of men 69.0 ± 10.4 years. Of the 501 diabetic patients, 411 were classified as having type 2 diabetes and only 3 as having type 1 diabetes. (In 87 cases, there was not sufficient information.) There were 277 patients (40% of all subjects and 55% of all diabetic patients) who were known to take insulin. We obtained known diabetes duration for 320 subjects (15.1 ± 10.7 years, median 14 [range 0–61]). (Reviewing the earlier data, we calculated diabetes duration in 131 patients from the

Table 1—*Number of patients with amputations in Leverkusen (1990–1991, 1994–2005, and all years combined)*

	Patients		
Age (years)	Total	Diabetic	Non-diabetic
Men			
0–39	3	1	2
40–59	71	50	21
60–79	262	184	78
≥80	66	40	26
Women			
0–39	2	0	2
40–59	21	17	4
60–79	156	127	29
≥80	111	82	29

Data are *n*.

Table 2—*Patients with amputations in Leverkusen per year, 1990–2005*

Year	Total	With diabetes	Without diabetes
1990	51	42	9
1991	40	27	13
1994	61	44	17
1995	47	32	15
1996	39	36	3
1997	50	36	14
1998	51	39	12
1999	55	43	12
2000	51	39	12
2001	40	27	13
2002	41	33	8
2003	54	34	20
2004	47	27	20
2005	65	42	23
All years combined	692	501	191

Data are *n*.

Table 3—*Standardized incidence rates of amputations in Leverkusen 1990–1998 according to calendar years*

Year	Incidence rate (95% CI) in total population (standard: total population)*	Incidence rate (95% CI) in diabetic population*† Standard: total population	Incidence rate (95% CI) in diabetic population*† Standard: diabetic population	Incidence rate (95% CI) in nondiabetic population (standard: total population)*
1990	33 (24–42)	224 (136–311)	549 (382–715)	7 (2–12)
1991	26 (18–34)	143 (75–210)	356 (221–491)	10 (5–16)
1994	37 (27–46)	226 (141–312)	544 (383–705)	12 (6–18)
1995	28 (20–36)	175 (96–255)	386 (252–521)	11 (5–16)
1996	22 (15–30)	180 (101–259)	426 (286–566)	2 (0–5)
1997	29 (21–37)	455 (0–989)	433 (290–576)	10 (5–15)
1998	30 (21–38)	195 (113–278)	463 (316–611)	8 (4–13)
1999	29 (21–36)	191 (113–269)	474 (330–618)	7 (3–10)
2000	27 (19–35)	165 (93–237)	415 (282–549)	8 (3–13)
2001	22 (15–28)	78 (48–107)	304 (187–421)	8 (4–13)
2002	20 (14–26)	131 (67–195)	335 (218–451)	4 (1–7)
2003	28 (21–36)	119 (67–171)	360 (237–482)	13 (7–18)
2004	24 (17–31)	113 (52–174)	281 (173–389)	12 (7–17)
2005	31 (23–38)	235 (136–335)	428 (295–560)	12 (7–17)

*Per 100,000 person-years. †Diabetic rates standardized to the diabetic population are higher because higher weights are assigned to the older age-groups.

period 1994–1998 whose values were not included in our last publication.) We found the following amputation levels (highest level in the case of more than one amputation): toe, 187; forefoot, 164; lower leg, 94; knee, 5; thigh, 236; and hip, 1. (In five patients, the amputation level was missing.)

Epidemiological measures

Table 3 shows standardized incidence rates for each year. They varied considerably between years. Table 4 shows the results of the Poisson model for the diabetic population. This model showed an estimated relative risk (RR) per year of 0.976 (95% CI 0.958–0.996, P = 0.0164) in the diabetic population. The same trend was observed when all first amputations above the toe level were considered, excluding toe amputations (n = 527) (RR 0.970 [95% CI: 0.948–0.991], P = 0.006), and when all first amputations above the ankle (n = 352) (0.970 [0.943–0.997], P = 0.0318) were considered, excluding amputations below the lower-leg level. These results are equivalent to a reduction by 3% per year. Thus, over 15 years, an estimated reduction of amputations above the toe level by 37.1% (95% CI 12.3–54.8) results.

The Poisson models showed no statistically significant change of incident amputations over time in the nondiabetic population (RR 1.022 [95% CI 0.989–1.056], P = 0.1981). The same was true when all first amputations in the nondiabetic population above the toe level (1.028 [0.990–1.068], P = 0.1578) and above the ankle (1.029 [0.987–1.074], P = 0.1864) were considered. The common model for both the diabetic and the nondiabetic populations showed no statistically significant change of incident amputations over time in the entire population (1.026 [0.994–1.061], P = 0.1200). However, both diabetes (25.685 [17.731–37.787], P < 0.01) and the interaction term for diabetes and years since 1990 (0.950 [0.914–0.986], P = 0.0078) were statistically significant predictors of amputations. The results were very similar when toe amputations were excluded and when only amputations above the ankle were considered.

Relative amputation risks of individuals with diabetes compared with nondiabetic individuals were estimated on the basis of incidence rates standardized to the general population and varied greatly between years because the random variability of both the diabetic and the nondiabetic rates contribute to RR. The maximum RR was 80 in 1996, and the minimum was 9 in 2003 and 2004. The attributable risk among the exposed (i.e., the diabetic population) varied between 99% in 1996 and 89% in 2003 and 2004. The population-attributable risk varied between 90% in 1996 and 49% in 2004.

Table 4—*Result of Poisson model (diabetic subjects): RR of amputation, depending on calendar year, age, and sex*

	RR (95% CI)	P
Calendar year*	0.976 (0.958–0.996)	0.0164
Age (years)†		
≥80	21.328 (4.769–375.415)	<0.01
60–79	11.055 (2.496–194.066)	0.0164
40–59	7.298 (1.616–128.800)	0.0458
Male	1.990 (1.662–2.386)	<0.01

*RR per 1 calendar year, baseline 1990. †Baseline 0–39 years.

CONCLUSIONS— The observations indicate a measurable reduction in the incidence of amputations in the diabetic population between 1990 and 2005, although the decrease was less pronounced than the goal set in 1989 and took considerably more time than anticipated. Whereas incidence rates in the nondiabetic population remained nearly constant, there was a statistically significant decrease in the diabetic population. This result was the same whether all amputations, only amputations above the toe level, or only amputations above the ankle were included. We conclude that a similar reduction of both major and minor amputations has taken place—not a shift from one level to the other. (There is no statistically significant decrease in the rates of amputations in the entire population because the effect in the diabetic population is diluted by the lack of a reduction in the nondiabetic population.) This consistent difference between the diabetic and the nondiabetic populations makes it very likely that this finding is due to specific improvements in the treatment of diabetic patients. Improvements taking effect in the mid-1990s or later are probably the cause, given that no reduction in the incidence of amputations could be demonstrated from 1990 through 1998.

Possible sources of error must be considered. One might imagine that a greater fraction of people with amputations had surgery performed outside the local hospitals in recent years than in the past; however, there is no empirical basis for such speculations. On the contrary, the implementation of a network of specialized physicians in the city makes it more likely that fewer patients sought specialized care and had amputations outside the city in recent years. The aging of the population might have led to increasing absolute numbers of people with diabetes or absolute numbers of amputations. However, the incidence rates are age adjusted, and Poisson models account for changes in the age structure.

Due to the lack of reliable, comparable, and regularly updated data on the age- and sex-specific prevalence of diabetes, we had to assume that the stratum-specific prevalence of diabetes remained constant between 1988 and 2005. If the stratum-specific prevalence of diabetes increased over this period of time, the actual reduction of the incidence of amputations in the diabetic population would be underestimated. However, although an increase in the prevalence of diabetes is often claimed, there are no hard data supporting such a claim. In a population-based study in Southern Germany, no change in diabetes prevalence could be detected between 1984 and 2001 (15). Even if it is likely that the true prevalence of diabetes is underestimated, this is not relevant for the analysis of a time trend as long as the underestimation remains similar over time (16).

Theoretically, increasing misclassification of diabetic patients as nondiabetic could explain our results. However, this is extremely unlikely. Lower thresholds of blood glucose for the diagnosis of diabetes and, in particular, growing financial incentives for physicians and hospitals to diagnose and document diabetes in recent years allow the expectation that fewer diabetic patients were misclassified as nondiabetic than in earlier years. If this is the case, the true reduction would be underestimated in our analysis. Other limitations have been discussed in detail in our previous articles (2,3,4).

According to the literature, a comprehensive approach is necessary to reduce amputations. Substantial success has been reported from areas with specific intervention programs for the diabetic foot with a multidisciplinary team running a hospital-based diabetic foot care clinic and close collaboration of diabetologists, surgeons, podiatrists, and other professionals as the core. Appropriate interventions like revascularization of the ischemic foot and thorough debridement of the infected foot, together with state-of-the-art wound care, were essential elements. Substantial reductions of major amputations followed the establishment of such programs (3,5–10).

As stated above, since the late 1990s core elements of successful care for patients with the diabetic foot syndrome, a specialized ward in particular, were initiated in Leverkusen and could take effect after 1998 when our last data collection had been completed. Even if everyday practice may not always perfectly meet the high-quality standards described above, these changes explain our findings of a declining incidence of amputations and are consistent with reports about successful interventions in other countries. Because of the complex nature of these interventions, it is not possible to calculate the contribution of each single measure to the overall result. Changing smoking habits, tighter blood pressure control, and the use of statins might also have had some effect. However, these factors should also be present in the nondiabetic population. In randomized controlled trials, tight blood pressure control did not significantly reduce amputations in diabetic patients (17).

Costs of diabetes in Germany have been estimated to lie between €5 and 16 billion per year. Between 1994 and 2002, costs of diabetes care increased by 64%, whereas the average costs of all diagnoses increased by 27% (12). Despite this enormous financial burden, even costly disease management programs for patients with diabetes have not been evaluated with respect to patient-oriented outcomes. Activities aiming at the reduction of amputations in other parts of Germany have not been systematically evaluated. We do not know whether any improvements have been achieved in other geographical areas. It is time now to evaluate on a larger scale which activities improve patients' outcomes in the setting of routine care. Programs with proven effectiveness urgently need to be comprehensively implemented to avoid preventable amputations everywhere.

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