Thailand Diabetes Registry Project: Prevalence and Risk Factors Associated with Lower Extremity Amputation in Thai Diabetics

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Objective: To determine the prevalence and risk factors associated with lower extremity amputation (LEA) in Thai diabetics.

Material and Method: A cross-sectional, multicenter, hospital-based diabetes registry was carried out from April to December 2003. Baseline characteristics and risk factors were analysed from 9,419 diabetic patients. peripheral vascular disease (PVD) was defined as absent or diminished dorsalis pedis (DP) and posterior tibialis (PT) pulses to palpation in the same limb. LEA was defined as surgical removal of part of a lower extremity.

Results: The prevalence of LEA was 1.5% (142). Mean diabetes duration was 10 years (SD = 7.6). Out of 556 patients with a history of foot ulcer, 123 (22.1%) underwent amputation. PVD was present in 370 patients. Most of LEAs were toe amputations (64.1%). Multiple logistic regression analysis of risk factors (adjusted OR, [95% confidence interval], p value) revealed a high risk of LEA in patients with a history of ulcer (59.2, [32.8-106.8], $p < 0.001$), peripheral vascular disease (5.3, [3.1-9.2], $p < 0.001$), diabetic retinopathy (2.2, [1.3-3.8], $p = 0.004$), and insulin injection (1.9, [1.1-3.2], $p < 0.023$).

Conclusion: Patients at risk for LEA were those with a history of foot ulcer, absence of peripheral pulse, diabetic retinopathy and insulin injection. Preventive strategies should be considered in these groups of patients. Data should be interpreted with caution as the number of patients with amputation was few and information on neuropathy was not available.

Keywords: Lower extremity amputation, Revascularization, Semmes-Weinstein monofilament

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Lower extremity amputation (LEA) is a debilitating complication of diabetes. Patients with diabetes have a 10-15 fold increased risk for lower extremity amputation compared with nondiabetics[1]. The age-adjusted incidence rates for nontraumatic lower limb amputations in persons with diabetes ranged from 2.1/1,000 to 13.7/1,000[2]. Reasons for the wide variation in incidence rates include discipline-specific training, which may support the aggressive limb salvage strategies and preventive guideline in high-risk groups. Other factors are the experience and judgment of surgeons, patients' preferences, level of education, access to care, and socioeconomic status.

Major independent risk factors for amputation from multivariate analytic studies are long duration of diabetes, selected measurements for peripheral neuropathy (PN) and peripheral vascular disease (PVD), high level of HbA1c or fasting plasma glucose, history of foot ulcer or amputation and retinopathy[3-7,8]. Several published clinical intervention studies demonstrated that the frequency of amputation can be reduced with improved foot care program including professional education, podiatric service, and patient education[9,10]. Self-management education can lower ulceration and amputation rates especially for patients with high-risk foot conditions[5,11].

The purpose of the present study was to determine the prevalence and risk factors associated with foot amputation in Thai diabetics.

Material and Method
Study population

A cross-sectional, multicenter, hospital-based diabetes registry was carried out from April through December 2003. The participating centers were university-based and tertiary-care hospitals. Patients eligible for the present study were diabetic patients in the out patient diabetic clinic who were able to return for follow-up visits for at least one year. Data were collected from 9,419 patients who agreed to participate and gave written informed consent.

Data collection

Each participant underwent an interview, a physical examination and laboratory testing. History of foot ulcer, foot amputation, and vascular intervention were included in the interview. Assessment of palpation of posterior tibialis (PT) and dorsalis pedis (DP) pulses were included in the physical examination. PVD was defined as absent or diminished DP and PT on palpation in the same limb. LEA was defined as surgical removal of part of a lower extremity. Other definitions were described elsewhere[19].

Statistical analyses

Descriptive statistics such as frequency, percent, mean and standard deviation were used for analysis. The Student's t-test was performed to compare the means of selected continuous variables at baseline for subjects who did and did not undergo amputation. Categorical data of studied variables were compared with Chi-square test or Fisher's exact test. Univariate analysis was used to define each associated factor with amputation by calculating the odds ratio (crude OR) and 95% confidence interval of crude odds ratio. Multiple logistic regression was used to calculate odds ratios for amputation after controlling for multiple covariates simultaneously. All statistical analyses were performed with STATA 8.0. (STATA Corporation, College Station, Tx, USA)

Results

The mean age of the subjects was 59.4 years (SD = 13.5). Most participants had type 2 diabetes (94.6%). The mean duration of diabetes was 10.0 years (SD = 7.6). Of the 9,419 participants, 142 (53 men, 89 women) underwent amputation. The prevalence of amputation was similar in both sexes (1.6% in men and 1.4% in women). Of the 142 amputations, 91 (64.1%) were toe amputations, 45 (31.7%) were below-knee amputations, and 6 (4.2%) were above-knee amputations. History of ulcer was found in 556 participants, and 123 of 556 (22%) underwent amputation. PVD was detected in 370 participants.

Table 1 shows the characteristics of patients with and without amputation. Participants with amputation were older, had longer duration of diabetes, were more likely to have a history of foot ulcer, were more likely to be under insulin treatment, had higher HbA1c, had lower HDL-cholesterol and had higher systolic blood pressure when compared with participants without amputation.
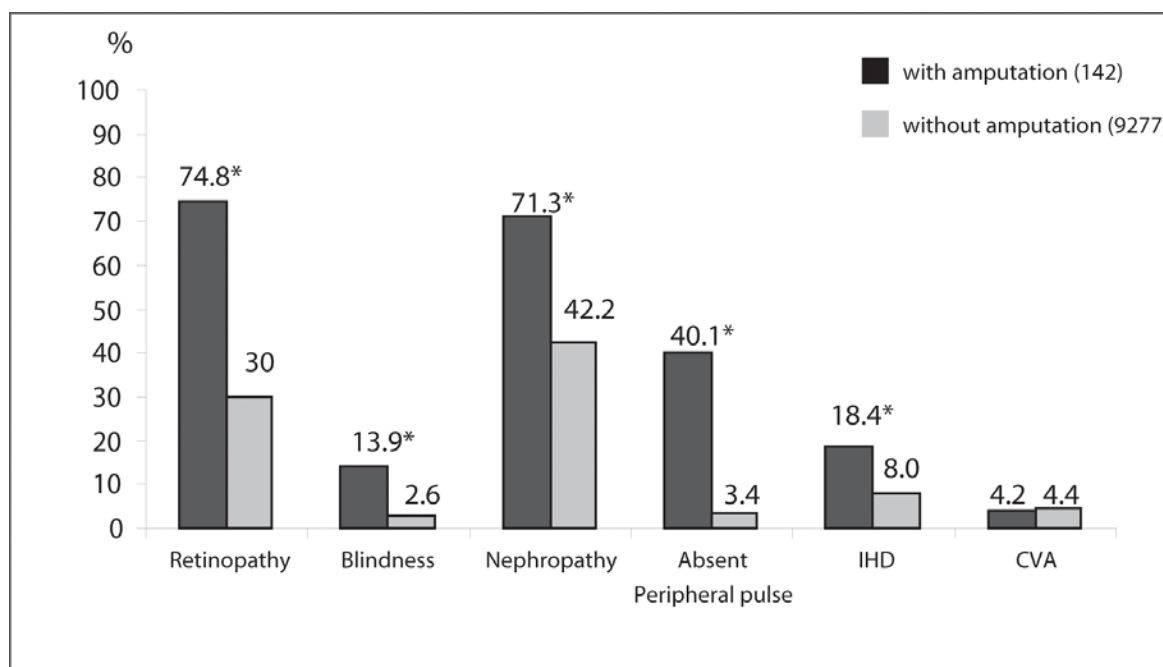
All components of microvascular and macrovascular complications except for cerebrovascular accident were more common in the group with amputation as shown in Fig. 1.

Risk factors for amputation were analyzed using multiple logistic regression models as shown in Table 2. History of foot ulcer was associated with a 59.2-fold and peripheral vascular disease with a 5.3-fold risk for amputation. Retinopathy and insulin treatment were associated with 2-fold risk for amputation.

Table 1. Baseline characteristics of patients with and without amputation (N = 9419)

Variable	Without amputation (n = 9,277)	With amputation (n = 142)	p-value
Male Gender(%)	34%	37 %	0.414
Age (yrs)*	59.3±13.5	63.4±10.5	<0.001
BMI (kg/m^2)	25.5±4.3	25.9±5.4	0.489
Duration of DM (yrs)*	10.3±7.5	15.9±8.9	<0.001
Type 2 DM (%)	95.4	95.8	0.972
History of foot ulcer (%)*	4.7	86.6	<0.001
Smoking (%)	20.0	26.1	0.076
Alcohol (%)	18.6	22.5	0.236
Insulin use (%)*	28.4	67.6	0.023
FPG (mg/dl)	153.5±56.5	156.6±71.5	0.615
HbA1c (%)*	8.2±1.9	8.7±2.1	0.002
Total Cholesterol (mg/dl)	197.1±42.4	195.2±50.1	0.652
Triglyceride (mg/dl)	150.7±105.5	156.6±100	0.518
HDL-chol (mg/dl)*	53.9±35.7	50.6±18.9	0.044
LDL-chol (mg/dl)	114.5±35.7	115.7±41.8	0.753
Systolic BP (mmHg)*	142.2±22.8	152.7±29.2	<0.001
Diastolic BP (mmHg)	78.8±11.3	77.1±12.4	0.086

* p-value < 0.05

* p < 0.001, IHD = Ischemic heart disease, CVA = Cerebrovascular accident

Fig. 1 Microvascular and macrovascular complications in patients with and without amputation (N = 9419)

Table 2. Risk factors of lower extremity amputation calculated by multiple logistic regression model (N = 142)

Factors	Adjusted OR (95%CI)	p-value
HbA1c > 7%	0.6 (0.4-1.1)	0.082
Cr > 2 mg/dl	1.9 (1.0-3.7)	0.054
Presence of retinopathy	2.2 (1.3-3.8)	0.004
Blindness	1.7 (0.8-3.6)	0.159
History of foot ulcer	59.2 (32.8-106.8)	<0.001
Absent pulse	5.3 (3.1-9.2)	<0.001
Insulin treatment	1.9 (1.1-3.2)	0.023
Smoking	1.0 (0.6-1.8)	0.935

Discussion

The 1.5% prevalence of LEA may not reflect the true prevalence of amputation in the population because most data were collected from university-based hospitals where there were more specialists and diabetes care teams than other care settings.

The risk factors for LEA identified in the present study were PVD, history of foot ulcer, diabetic retinopathy, and insulin treatment. The history of foot ulcer was a stronger risk factor when compared with previous studies that reported 2.2-2.5- fold risk for amputation[7,8]. This can be explained by different definition of history of ulcer. Both previous ulcer and ulcer at the time of amputation were included in the definition in our study. The number of ulcers at the time of amputation should have a very important effect on the calculated risk factor because most amputations were preceded by ulcers.

PVD was an important risk factor that was consistent with other studies. Whether the methods of measurement were ankle brachial index (ABI), transcutaneous oximetry (TcPO$_2$) or palpation, PVD was associated with a 3-fold increased risk for LEA[3,7,8].

The present study demonstrated that retinopathy increased the chance of LEA twofold. Most studies reported association between retinopathy and LEA even when there is no visual impairment[3,4,8,12,13]. Insulin users had a 2-fold increased risk for LEA even after adjustment for duration of diabetes. Past studies demonstrated both positive and negative results for this association[6,7,13]. Being treated with insulin may itself reflect more severe diabetes or hyperglycemia.

The combination of PN to the development of foot ulcer could not be ascertained in the present study since the data on PN were not controlled. However, the importance of PN should not be underrated. Diminished or absent peripheral sensation decreases patients' awareness of foot pressure, discomfort, and pain, and increases the risk of ulceration and amputation. Different measures of PN were identified as risk factors for amputation. Several studies reported association between impairment of sensation measured by Semmes-Weinstein monofilament examination with foot ulcer[14-16] and amputation risk[7,8]. PN measured with other means such as absent or diminished vibration sensation and absent ankle reflexes were also reported to increase the risk of amputation[3,4,8].

Poor glycemic control, measured by either HbA1c or plasma glucose, was demonstrated to be an independent predictor of amputation[3,5,6,8,13]. Hyperglycemia may contribute to PN and impairment of defense mechanisms against infection. However, hyperglycemia was not a risk factor for LEA in the present study.

Smoking has been considered a strong risk factor for PVD, but was not identified as a risk factor for LEA in many studies[5-7] except for one that did not include PVD in the analysis[17]. Former smokers may have quit smoking because of the development of macrovascular diseases, which subsequently increases the risk for amputation. Therefore, data on smoking should be interpreted with caution.

Conclusion

The present study demonstrated that PVD, history of foot ulcer, diabetic retinopathy and insulin treatment are risk factors for LEA. Other factors that should be included in the next cohort study are history of previous amputation and PN, which are important for risk analyses.

Individuals with diabetes should receive annual complete foot evaluation, including inspection and assessment of peripheral nerve status, peripheral vasculature and type of footwear in use. Foot examination should be repeated at regular intervals based on the risk status. Peripheral vasculature can be assessed

with palpation. Semmes-Weinstein monofilament examination is a reliable method to screen for PN.

Individuals with diabetes, especially those high risk, should learn the principles of self-foot examination and care. Previous studies demonstrated that self management education helped reduce amputation rate especially in high-risk groups[5,11].

Professional education strategies should be the targeted at all members of the comprehensive health care team. These strategies should stress the identification of high-risk patients, treatment methods, and when to refer the patients to a specialist, such as podiatrists, orthopedic and vascular surgeons.

Appropriate footwear plays an important role in the prevention of amputation[9,10]. Distal bypass grafting delivers excellent outcome for limb-threatening ischemia[18]. Risks of LEA can be greatly reduced with effective preventive interventions.

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ความชุกและปัจจัยเสี่ยงต่อการถูกตัดเท้าในผู้ป่วยเบาหวานไทย

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วัตถุประสงค์: เพื่อประเมินความชุกของการถูกตัดเท้าในผู้ป่วยเบาหวาน รวมทั้งหาปัจจัยทางด้านคลินิกที่มีผลต่อการถูกตัดเท้า

วัสดุและวิธีการ: ข้อมูลนี้เป็นส่วนหนึ่งของงานวิจัยโครงการลงทะเบียนผู้ป่วยเบาหวาน ซึ่งโครงการได้เริ่มเก็บข้อมูลภาคตัดขวางในช่วงระหว่างเดือนเมษายนถึงเดือนธันวาคม พ.ศ. 2546 แหล่งข้อมูลส่วนใหญ่ได้จากโรงพยาบาลศูนย์หรือคณะแพทยศาสตร์จำนวนทั้งสิ้น 11 แห่ง รวบรวมจำนวนผู้ป่วยได้ทั้งหมด 9,419 ราย คำจำกัดความของโรคหลอดเลือดส่วนปลายอุดตันหมายถึง การคลำชีพจร dorsalis pedis และ posterior tibial ของขาข้างเดียวกันไม่ได้หรือคลำได้เบาลงกว่าปกติ

ผลการศึกษา: พบความชุกของการถูกตัดเท้าร้อยละ 1.5 ผู้ป่วยส่วนใหญ่เป็นเบาหวานชนิดที่ 2 (94.6%) โดยพบว่าเป็นการตัดนิ้วเท้า 91 ราย (64.1%) ตัดใต้เข่า 45 ราย (31.7%) และตัดเหนือเข่า 6 ราย (4.2%) พบว่ามีประวัติมีแผลก่อนถูกตัดเท้าทั้งสิ้น 556 ราย และในจำนวนนี้ 123 ราย (22%) ถูกตัดเท้า ตรวจพบมีหลอดเลือดอุดตันจำนวน 370 ราย พบว่าปัจจัยเสี่ยงที่มีผลต่อการถูกตัดเท้า (adjusted OR, [95% confidence interval], p value) ได้แก่ ประวัติการมีแผลมาก่อน (59.2, [32.8-106.8], < 0.001), หลอดเลือดส่วนปลายอุดตัน (5.3, [3.1-9.2], < 0.001) ภาวะเบาหวานขึ้นจอประสาทตา (2.2, [1.3-3.8], 0.004) และการใช้ยาฉีดอินซูลิน (1.9, [1.1-3.2], 0.023)

สรุป: ปัจจัยทางคลินิกที่มีผลต่อการตัดเท้า ได้แก่ ประวัติการมีแผลมาก่อน ภาวะหลอดเลือดส่วนปลายอุดตัน ภาวะเบาหวานขึ้นจอประสาทตา และการใช้ยาฉีดอินซูลิน อย่างไรก็ตามอาจมีข้อจำกัดในการแปลผลเนื่องจากจำนวนผู้ป่วยที่ถูกตัดเท้าน้อยและยังขาดปัจจัยอื่นในการวิเคราะห์ข้อมูลได้แก่ ข้อมูลเรื่องปลายประสาทเสื่อมซึ่งเป็นปัจจัยที่สำคัญ ต่อการถูกตัดเท้า