EPH36

Risk Factors for Amputation in Japanese Patients with Critical Limb Ischemia Based on a Claims Database Analysis

Kenta Takashima[1], Tomomi Takeshima[2], Midori Tateyama[2], Kosuke Iwasaki[2]
[1]Boston Scientific Japan K.K., Tokyo, Japan, [2]Milliman Inc., Tokyo, Japan

Background

- Critical limb ischemia (CLI) is the most severe clinical manifestation of peripheral artery disease (PAD) that can increase the risk of amputation.
- This study aimed to investigate the incidence of amputation and its risk factors in patients with CLI.

Methods

Study design

- Claims based study
- In patients with CLI, the time to amputation was examined by Kaplan-Meier analysis, and the risk factors were estimated by a proportional hazard analysis

Data source

- Japanese claims database provided by Medical Data Vision Co., Ltd. (Tokyo, Japan)
  - ✓ Consists of data from acute hospitals that apply the Japanese Diagnosis and Procedure Combination/Per-Diem Payment System (called DPC hospitals)
  - ✓ Data period: April 2008−September 2020
- The dataset for this study included 818,486 patients with any diagnosis associated with PAD.
- Observation period for each patient is the period between the earliest and latest dates of any medical practice recorded in the database.

Patients

- Target patients were identified from the dataset as following (Figure 1).
  1. Having diagnosis of embolism and thrombosis of arteries of lower extremities (defined as I74.3 by ICD-10) at least once
  2. Having diagnosis of CLI (defined by disease name) at least once
  3. Having first CLI diagnosis during the observation period
  4. Having a 3-month observation period after the first CLI diagnosis
     - Index date: the date 3 months after the first CLI diagnosis
     - Baseline period: from the first CLI diagnosis to the index date
  5. Not having amputation (defined by claim code) before the index date
  6. Having neither vasodilation or thrombus ablation in the limbs, nor vascular or bypass grafting in lower leg, foot aorta, or popliteal artery (defined by claim code) during the baseline period

Analysis

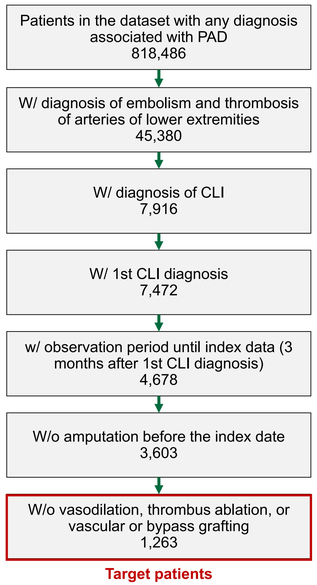
- Attributes of the target patients at the index date, including age, percentage of women, and prevalence of comorbidities were tabulated.
- A Kaplan-Meier curve for the incidence of amputation was computed.
- Hazard ratio for amputation was estimated by a proportional hazard analysis with a stepwise method.
  - ✓ Explanatory variables: age at index, sex, presence of dialysis, diabetes, chronic obstructive pulmonary disease, dementia, hypertension, dyslipidemia, cardiovascular disease, and chronic kidney disease (CKD) during baseline period
- SAS version 9.4 (SAS Institute, Cary, NC) was used for the analyses.

Results

Patients

- The dataset included 7,916 patients diagnosed as CLI, and 1,263 patients were identified for the analysis (Fig. 1).
- Average (standard deviation) of age was 75.6 (12.1) years (Table 1).
- Most common disease were hypertension (60%) followed by diabetes mellitus (53%) and dyslipidemia (40%) (Table 1).

Figure 1. Flow diagram for patients identification



CLI, critical limb ischemia; w/, with; w/o, without.

Table 1. Patient characteristics at the index

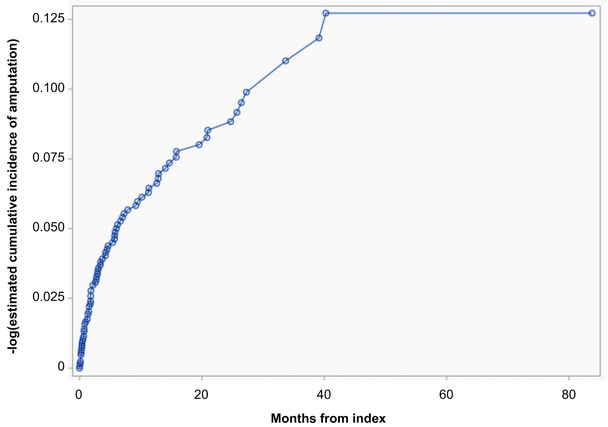
Number of patients		1,263
Age (average)		75.6
Age (SD)		12.1
Percentage of patients	**Women**	38%
	Dialysis	18%
	DM	53%
	COPD	5%
	Dementia	10%
	Hypertension	60%
	Dyslipidemia	40%
	CVD	24%
	CKD	35%

CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; DM, diabetes mellitus; SD, standard deviation.

Incidence of amputation

- 80 amputations were reported during the entire observation period.
- The cumulative incidence of amputation after 3 years from index was approximately 12% (Fig 2).

Figure 2. Kaplan-Meier curve showing estimated cumulative incidence of amputation



Risk factors for amputation

- Among the 10 explanatory variables, dialysis, diabetes, hypertension, and CKD were selected by the stepwise method.
- Dialysis showed the highest hazard ratio (HR) followed by CKD, and diabetes (Table 2).
- The HR of hypertension was lower than 1 (Table 2).

Table 2. Selected variables and their hazard ratio by the proportional hazard analysis with the stepwise method

Variables	HR	P-value
Dialysis	2.69	< 0.01
DM	1.82	0.02
Hypertension	0.47	< 0.01
CKD	1.97	0.04

CKD, chronic kidney disease; DM, diabetes mellitus; HR, hazard ratio.

Discussions

- HR was higher than 1 for CKD, dialysis, and diabetes. These characteristics may be associated with amputation risk in patients with CLI.
- HR for hypertension was lower than 1. While percentage of patients with hypertension was 60%, that with dialysis was 18%. Therefore, hypertensive patients were majority of non-dialysis patients, which may be associated with the lower amputation risk for hypertension observed in this analysis.

Limitations

- Accuracy of the claims data used in the study affects the results.
- We included patients with first CLI diagnosis during the observation period and with a 3-month period without amputation or some types of surgeries associated with CLI to exclude patients who may have been diagnosed as CLI in another institute and referred to the DPC hospital to undergo amputation. Nevertheless, not all these patients could be excluded.
- As we used the database from DPC hospitals, the patients may have more severe symptoms and/or have more complications than other Japanese patients with CLI.

Conclusions

- More than 10% of patients experienced amputation within 3 years from first CLI diagnosis.
- CKD, dialysis, and diabetes were suggested as risk factors for amputation in patients with CLI.
- Less than 1 HR was suggested for hypertension. It could be explained by the fact that hypertensive patients were majority of non-dialysis CLI patients.
- The findings may provide useful information to prevent amputation by early interventions in patients with CLI.

Boston Scientific
Advancing science for life™

Milliman