ORIGINAL ARTICLE

Outcomes of Multidisciplinary and Evidence-Based Management of Chronic Limb Threatening Ischemia Patients: The Impacts of Protocol-Based Care Processes

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Background: Chronic limb-threatening ischemia (CLTI) represents the late stage of atherosclerotic peripheral arterial disease (PAD). Similar to atherosclerosis in other vascular beds, it is preceded by a long-standing early disease and pre-disposing conditions. Thus, the care of this patient population is theoretically best delivered by a multidisciplinary team. The authors studied the outcomes of a multidisciplinary, well-structured, and evidence-based protocol that might influence better outcomes for CLTI patients.

Materials and Methods: The present study was a retrospective study done in a single center. Between January 2018 and December 2020, data were reviewed from CLTI patients that received the multidisciplinary, well-structured, and evidence-base protocol for the treatment of CLTI. The primary outcome was the perioperative clinical outcome of the patients. The secondary outcomes were the 1-year clinical outcome and the admission cost for vascular operation.

Results: Two hundred thirty CLTI cases between January 2018 and December 2020 were retrospectively reviewed. Of the 230 cases, 87.9% were elderly (older than 60-years-old) with significant comorbidities including diabetes (74.3%) and hypertension (74.8%). The protocol implementation resulted in clinical outcomes in terms of both major adverse cardiac event (MACE) and major adverse limb event (MALE) at 1.3% and 6.52%, respectively. The survival rates at 1-and 2-years post-revascularization were 84.3% and 74.1%, and the 1-year follow-up MACE and MALE were 6.08% and 12.2%, respectively. Moreover, the protocol statistically improved the quality of life as measured by EuroQoL group-5 Dimensions-5 Levels (EQ-5D-5L) utility score. The median 1-year mean EQ-5D-5Q score increased from 0.332 to 0.863. The cost of the treatments was significantly higher with the increasing severities of CLTI.

Conclusion: A multidisciplinary, well-structured, and evidence-based protocol may potentially be effective in improving the quality of care among CLTI patients, both in terms of clinical outcomes and overall health status.

Keywords: Peripheral arterial disease (PAD); Chronic limb-threatening ischemia (CLTI); Multidisciplinary and evidence-based protocol

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Chronic limb-threatening ischemia (CLTI) represents the advanced stage of peripheral arterial disease (PAD), which has an incidence of 1% to 3% of PAD. The most common cause of CLTI and PAD is atherosclerosis[1]. Similar to other vascular beds, it has been preceded by a long-standing early disease progression and shares common pre-disposing conditions, such as diabetes mellitus, arterial hypertension, dyslipidemia, and smoking. The care of this patient population is theoretically best delivered by a multidisciplinary team. In Thailand, CLTI, presenting as tissue loss, is encountered more frequently than the earlier stages of PAD[2]. This is caused by many factors, including the lack of awareness of PAD in the high-risk population and the capacity of the health care system. Failure to access high-quality care in the early stage of the disease leads to unfavorable outcomes for the patients. To deliver the holistic care of these patients, Siriraj Hospital has established CLTI multidisciplinary care teams, incorporating a vascular surgeon, plastic and reconstruction surgeon, orthopedic surgeon, podiatrist and rehabilitation physician, anesthesiologist, radiologist, cardiologist, and vascular nurses since

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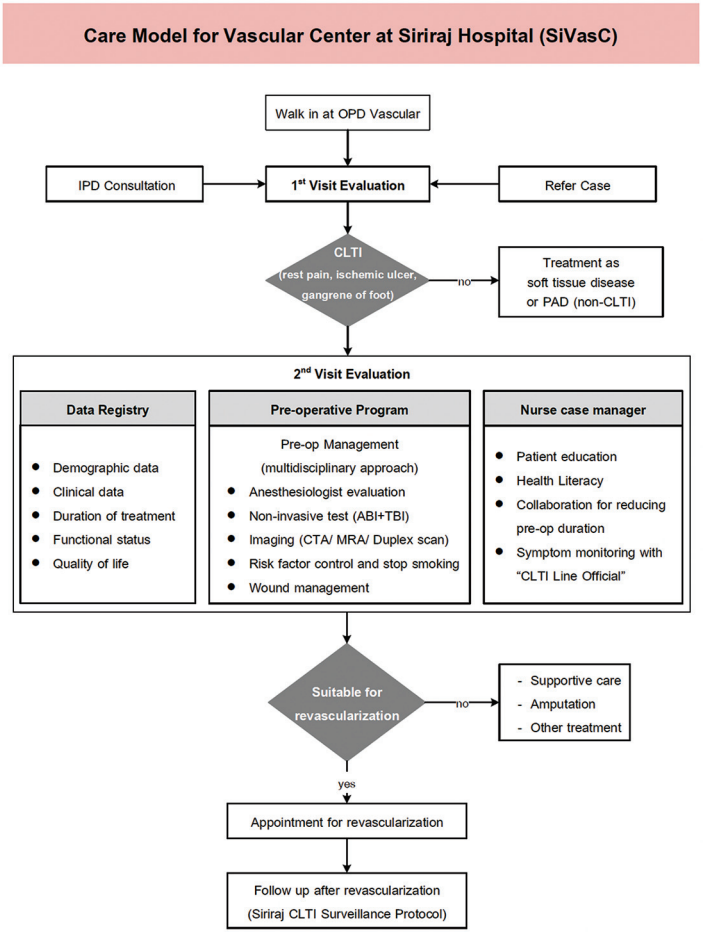


Figure 1. Algorithm of chronic limb-threatening ischemia patient management.

SiVasC=Siriaj Vascular center; OPD=outpatient department; ABI=ankle brachial index; TBI=toe brachial index; CTA=computed tomography angiogram; MRA=magnetic resonance angiography

2017. The purpose of the present study was to determine the clinical outcomes and cost of treatment of CLTI patients after the establishment of this multidisciplinary team.

Materials and Methods

Patients underwent interventions for CLTI between January 2018 and December 2020 were retrospectively reviewed. Patients were excluded if the complete follow-up medical records were not available. All the patients' demographic data, clinical data, and costs of treatments were collected. Postoperative surveillance data included both the clinical follow-up and vascular laboratory data. The research study was approved by the Siriraj Institutional Review Board, 370/2563 (EC3).

All the CLTI patients were registered with the CLTI clinic and scheduled for non-invasive vascular laboratory tests. Vascular imaging studies and pre-anesthesia evaluation for revascularization were performed during the first visit. At the second visit to the CLTI clinic, the individualized revascularization method was considered by the primary attending vascular surgeon and the vascular surgeon committee after gathering all the relevant data, based on the current guideline for revascularization[3-6] method of CLTI and the result of discussions with the patients and their families. In the case that tissue coverage was needed for a large tissue-loss area at the foot, the plastic surgeon was primarily involved.

The post-procedural surveillance protocol included interval clinical history evaluation focused on limb status and cardiovascular events, detailed physical examination of the feet and foot ulcer, physiologic tests with the ankle-brachial index and toe pressure, and blood chemistries to follow any

atherosclerosis risk modifications if applicable. The summarized algorithm of the steps in the CLTI patient management is shown in Figure 1.

The clinical outcomes of the present study were 30-day major adverse limb event (30-day MALE), 30-day major adverse cardiac event (30-day MACE), 1-year major adverse limb event (1-year MALE), 1-year major adverse cardiac event (1-year MACE), the survival rate, and the quality of life (QoL) at 1-year post-revascularization. The definitions of these parameters were listed as follows[7];

- 30-Day MALE was defined as any reintervention or amputation of the index limb within 30 days after index operation.
- 30-Day MACE included non-fatal stroke, non-fatal myocardial infraction, and any cardiovascular death within 30 days after index operation.
- 1-Year MALE was defined as any reintervention or amputation of the index limb within 1 year after index operation.
- 1-Year MACE included non-fatal stroke, non-fatal myocardial infraction, and any cardiovascular death within 1 year after index operation.

The QoL was estimated by the EuroQoL group-5 Dimensions-5 Levels EQ-5D test (EQ-5D-5L)[8] and was reported by the EQ-5D-5L utility index.

All the statistical analyses were performed using PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA). Normally distributed continuous data were expressed as the mean with standard deviation. The non-normally distributed data were reported as median with interquartile range (IQR). The Kaplan-Meier method was used to estimate the cumulative survival rate. The EQ-5D-5L utility index between preoperative and postoperative was analyzed by Wilcoxon signed-rank test. The cost of in-patient chronic limb-threatening ischemia treatment was analyzed by Independent-Sample Median test. The statistical significance alpha equal 0.05 is the cut-off point used to decide whether a hypothesis is statistically significant.

Results

During the study period, 230 patients were included with a mean age of 71±10.5 years (range 31 to 91), and 87.8% of the patients were older than 60 years. Approximately half of the patients (117, 50.9%) were male. The number of included patients in 2018, 2019, and 2020 were 80, 97, and 53 patients, respectively. The patients' demographic data are shown in Table 1. The most common presentation was minor tissue loss (Rutherford classification category 5) in 64.8%, and the remaining were major tissue loss (Rutherford classification category 6) and rest pain (Rutherford classification category 4) in 19.6% and 15.6% of the patients, respectively. The common atherosclerotic risk factors were hypertension (74.8%), diabetic mellitus (74.3%), and dyslipidemia (53.9%). The most common comorbidity was chronic renal failure, found in 40.9% of the patients in this population.

Table 1. Demographic data of the chronic limb-threatening ischemia patients

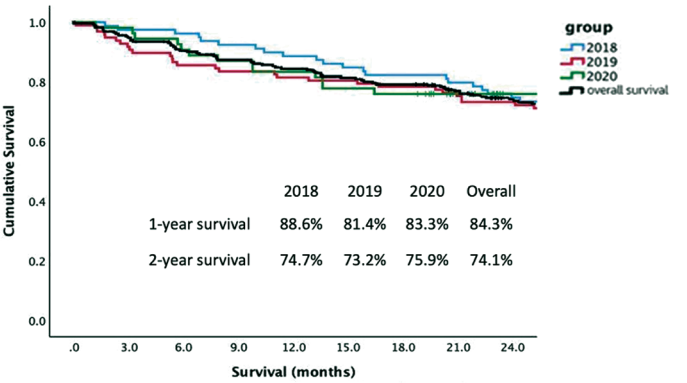
Patient characteristic	Overall (n=230)	2018 (n=80)	2019 (n=97)	2020 (n=53)
Rutherford classification				
Category 4	15.6%	19%	12%	9%
Category 5	64.8%	61%	69%	70%
Category 6	19.6%	20%	19%	21%
Risk factors and comorbidity				
Diabetic mellitus	74.3%	71.3%	76.3%	75.5%
Hypertension	74.8%	91.3%	51.5%	92.5%
Dyslipidemia	53.9%	46.3%	42.3%	69.8%
Smoking[1]	9.6%	10.0%	10.3%	7.5%
Ex-smoker[2]	25.7%	26.3%	34.0%	9.4%
Coronary artery disease	26.5%	35.0%	24.7%	35.8%
Cerebrovascular disease	11.7%	10.0%	7.2%	22.6%
Chronic renal disease	40.9%	36.3%	37.1%	54.7%

[1] Smoking defined as the practice of burning and inhaling tobacco, and cigarette smoking is the most common form of tobacco smoking.
[2] Ex-smoker defined as an individual who has given up cigarette and/or tobacco smoking[9].

The 30-day MALE rate was 6.52% with more reinterventions than perioperative amputations. The 30-day MACE rate was 1.3%. The common causes of 30-day MACE were dead from severe sepsis in two patients while one patient had perioperative stroke.

The 1-year MALE rate was 12.2% and the majority were reintervention (9.13%). The 1-year amputation rate was 3.07%. The 1-year MACE was 6.08%. Eight patients died from non-cardiac causes, five patients died from cardiac causes, and one patient suffered from non-fatal myocardial infarction. The 1-year and 2-year survival rates of the CLTI patients in the present study were 84.3% and 74.1%, respectively (Figure 2).

The median overall preoperative EQ-5D-5L utility index was 0.332. At 1-year follow-up, the overall median EQ-5D-5L utility index increased to 0.8627. The EQ-5D-5L utility index classified by severity of ischemia using the Rutherford classification category is demonstrated in Table 2. There was statistically significant improvement



Month	0	3	6	9	12	15	18	21	24
Patient at risk (2018)	80	77	76	73	70	67	65	63	59
Std Error		0.018	0.022	0.030	0.036	0.040	0.043	0.045	0.05
Patient at risk (2019)	97	89	83	81	79	78	76	73	71
Std Error		0.028	0.036	0.038	0.039	0.040	0.042	0.044	0.045
Patient at risk (2020)	53	53	49	47	45	42	41	32	21
Std Error		0.018	0.039	0.046	0.051	0.057	0.058	0.058	0.058
Patient at risk (Overall)	230	219	208	201	194	187	182	168	151
Std Error		0.014	0.019	0.022	0.024	0.026	0.027	0.028	0.029

Figure 2. Kaplan-Meier graph demonstrate the overall survival rate of chronic limb-threatening ischemia patients after revascularization.

Table 2. Comparison between the preoperative and the 1-year postoperative follow-up EQ-5D-5L utility index

Severity of CLTI	Preoperative EQ-5D-5L utility index		1-year postoperative follow-up EQ-5D-5L utility index		p-value
	Median	IQR	Median	IQR	
Rutherford 4	0.4488	0.2853	0.9710	0.2878	<0.001*
Rutherford 5	0.2954	0.3398	0.8756	0.2970	<0.001*
Rutherford 6	0.3320	0.3719	0.7611	0.2768	<0.001*
Overall	0.3320	0.3443	0.8627	0.2970	<0.001*

IQR=interquartile range; CLTI=chronic limb-threatening ischemia; EQ-5D-5L=EuroQoL group-5 Dimensions-5 Levels

* Statistic significant

Table 3. Summary of the cost of in-patient chronic limb-threatening ischemia treatment

Year	Rutherford classification category 4		Rutherford classification category 5		Rutherford classification category 6		Overall	
	Median (Baht)	Min-max	Median (Baht)	Min-max	Median (Baht)	Min-max	Median (Baht)	Min-max
2018	201,395.38	100,654.00 to 272,714.50	281,309.75	189,215.25 to 409,978.00	262,203.00	94,098.50 to 608,825.50	269,799.50	94,098.50 to 608,825.50
2019	194,309.75	71,040.50 to 552,754.50	236,402.00	176,498.19 to 310,651.75	335,914.25	70,931.00 to 1,010,721.75	240,374.88	70,931.00 to 1,010,721.75
2020	127,168.25	102,521.75 to 499,290.50	279,243.25	183,053.75 to 823,353.50	236,996.00	94,310.00 to 1,325,351.00	242,254.00	94,310.00 to 1,325,351.00
Total	194,742.75*	71,040.50 to 552,754.50	254,360.25*	176,498.19 to 823,353.50	282,026.37*	70,931.00 to 1,325,351.00	247,332.50	70,931.00 to 1,325,351.00

* Statistically significant

of EQ-5D-5L utility index between preoperative and 1-year postoperative follow-up of overall and Rutherford classification categories 4, 5, and 6. The median overall admission cost for vascular operation of CLTI patients was THB 247,332.50 (IQR 70,931, 1,325,351). There was statistically significant differences in the cost of perioperative treatment among the Rutherford classification categories, as shown in Table 3.

Discussion

This cohort of CLTI patients shared the common atherosclerosis risk factors that have been well established, except that the majority of the present study population were male. Most patients came at a very late stage, as shown by 84.4% of the

patients having tissue loss requiring aggressive revascularization. This represented a scenario that the CLTI patient care system in Thailand rarely reaches the patients at the early stages of atherosclerotic diseases. At the late stage of diseases, the treatment requires a multidisciplinary team for comprehensive care of this fragile population. The presence of complications of atherosclerotic diseases in many vascular beds sometimes precludes proper tissue loss reconstruction, rehabilitation, and overall recovery. Using the Lean management system, as seen in the present study, could deliver a patient-centered multidisciplinary care team that could shorten the previous redundant steps across the teams involved in the CLTI patient care. Satisfactory perioperative outcomes in terms of MALE and MACE could be achieved and were comparable with the objective performance goal addressed by the Society for Vascular Surgery[10] (6.2% MALE and 4.2% MACE) and the National Surgical Quality Improvement Program[11] (4.2% MALE and 9.0% MACE). The promising perioperative MALE and MACE might represent the benefits and safety of the multidisciplinary team approach and Lean management system in the care process of CLTI patients.

A low 1-year amputation rate of 3.07% stresses the sustained benefits of revascularization regardless of the patency. The 1-year follow-up MACE was 6.08% with the majority of dead patients caused by non-cardiac causes. Moreover, the CLTI patients had a stable declining survival rate, compared with Simon et al.[12] who reported a 2-year survival of 81%, and Hata et al.[13] who demonstrated a 2-year mortality rate of 32.3% in a Japanese population.

The improvement in QoL represented by the statistically increased EQ-5D-5L utility index emphasized the importance of revascularization procedures and the holistic care for the CLTI patients, given their beneficial effects beyond the hospital treatment periods. The subgroup analysis showed the best postoperative EQ-5D-5L utility index in Rutherford classification category 4, which represents an early phase of CLTI presenting without tissue loss.

One of the common concerns regarding revascularization is the cost of treatment. This was also presented in the authors' data, where the overall cost of perioperative treatment in CLTI patients was high. This could be explained by the usually encountered advanced stage of diseases in the present study center that needed more complex procedures and prolonged hospitalization for tissue loss management and tissue coverage. The high cost was confirmed by differential cost increments toward the increasing disease severity, as shown in Table 3. This may suggest the importance of access to high-quality care at the early stage of the disease to prevent limb and systemic complications of advanced atherosclerosis.

Conclusion

The timely multidisciplinary team approach for CLTI patients was potentially effective in improving the quality of care among these patients both in terms of clinical outcomes and overall QoL. Early case detection and proper health-care resource distribution in the different levels of the health care system should be implemented to establish a high-quality and cost-effective health care system, striving for a better quality of care and QoL for CLTI patients.

What is already known on this topic?

In Thailand, most of PAD patients that presented with CLTI stage had multiple underlying diseases and were a fragile population.

What this study adds?

The findings support the use of Multidisciplinary and Evidence-based Protocol in CLTI care process to improve the quality of CLTI treatment.

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Conflicts of interest

The authors declare no conflict of interest.

References

1. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG. Inter-society consensus for the management of peripheral arterial disease (TASC II). J Vasc Surg 2007;45 Suppl S:S5-67.
2. Mutirangura P, Ruangsetakit C, Wongwanit C, Sermsathanasawadi N, Chinsakchai K. Atherosclerosis obliterans of the lower extremities in Thai patients. J Med Assoc Thai 2006;89:1612-20.
3. Conte MS. Critical appraisal of surgical revascularization for critical limb ischemia. J Vasc Surg 2013;57(2 Suppl):8S-13S.
4. Aiello A, Anichini R, Brocco E, Caravaggi C, Chiavetta A, Cioni R, et al. Treatment of peripheral arterial disease in diabetes: a consensus of the Italian Societies of Diabetes (SID, AMD), Radiology (SIRM)

and Vascular Endovascular Surgery (SICVE). Nutr Metab Cardiovasc Dis 2014;24:355-69.
5. Aboyans V, Ricco JB, Bartelink MEL, Björck M, Brodmann M, Cohnert T, et al. 2017 ESC guidelines on the diagnosis and treatment of peripheral arterial diseases, in collaboration with the European Society for Vascular Surgery (ESVS): Document covering atherosclerotic disease of extracranial carotid and vertebral, mesenteric, renal, upper and lower extremity arteriesEndorsed by: the European Stroke Organization (ESO) The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). Eur Heart J 2018;39:763-816.
6. Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, et al. 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2017;69:e71-126.
7. Conte MS, Geraghty PJ, Bradbury AW, Hevelone ND, Lipsitz SR, Moneta GL, et al. Suggested objective performance goals and clinical trial design for evaluating catheter-based treatment of critical limb ischemia. J Vasc Surg 2009;50:1462-73.e1-3.
8. Kangwanrattanakul K, Parmontree P. Psychometric properties comparison between EQ-5D-5L and EQ-5D-3L in the general Thai population. Qual Life Res 2020;29:3407-17.
9. McNutt MD, Hooper MW. Ex-smokers. In: Gellman MD, Turner JR, editors. Encyclopedia of behavioral medicine [Internet]. New York, NY: Springer; 2013 [cited 2022 Aug 24]. p. 741-2. Available from: https://doi.org/10.1007/978-1-4419-1005-9_313.
10. Saraidaridis JT, Patel VI, Lancaster RT, Cambria RP, Conrad MF. Applicability of the society for vascular surgery's objective performance goals for critical limb ischemia to current practice of lower-extremity bypass. Ann Vasc Surg 2016;30:59-65.
11. Robinson WP, Mehaffey JH, Hawkins RB, Tracci MC, Cherry KJ, Eslami M, et al. Lower extremity bypass and endovascular intervention for critical limb ischemia fail to meet Society for Vascular Surgery's objective performance goals for limb-related outcomes in a contemporary national cohort. J Vasc Surg 2018;68:1438-45.
12. Simons JP, Schanzer A, Flahive JM, Osborne NH, Mills JL Sr, Bradbury AW, et al. Survival prediction in patients with chronic limb-threatening ischemia who undergo infrainguinal revascularization. Eur J Vasc Endovasc Surg 2019;58(1 Suppl):S120-34.e3.
13. Hata Y, Iida O, Asai M, Masuda M, Okamoto S, Ishihara T, et al. Risk stratification for 2-year mortality in patients with chronic limb-threatening ischemia undergoing endovascular therapy. J Atheroscler Thromb 2021;28:477-82.