doi: 10.2490/prm.20240021 Progress in Rehabilitation Medicine 2024; Vol. 9, 20240021

ORIGINAL ARTICLE

# Impact of Early Rehabilitation after Endovascular Treatment for Peripheral Arterial Disease

**Yuki Kato, MD [a,b] Kenta Ushida, RPT, MMSc [a,b] Miho Shimizu, RPT, PhD [b] and Ryo Momosaki, MD, PhD, MPH [a,b]**

**Objectives:** The prevalence of peripheral arterial disease (PAD) is on the rise, with endovascular treatment being a widely accepted surgical intervention. Patients with PAD often experience reduced activities of daily living (ADL). Therefore, we conducted a retrospective cohort study to investigate the impact of early rehabilitation after endovascular treatment in patients with PAD. **Methods:** Using data from the JMDC hospital database, the study included 529 patients who were hospitalized for PAD and underwent endovascular treatment. Patients were classified into two independent variables: early rehabilitation group (rehabilitation started within 2 days postoperatively) and control group (rehabilitation started within 3–7 days postoperatively). The outcome measures were the occurrence of hospital-associated disability (HAD) and duration of hospitalization. **Results:** Unadjusted data showed that the early rehabilitation group (n=469) had fewer HAD events (8.5% vs. 23.3%, P <0.001) and a shorter mean hospitalization duration (4.4 vs. 18.9 days, P <0.001) than the control group (n=60). The difference remained significant after adjustment by propensity score analysis. **Conclusions:** In patients with PAD, early rehabilitation after endovascular treatment may be beneficial in preventing the development of HAD and reducing the duration of hospitalization.

**Key Words:** activities of daily living; arteriosclerosis obliterans; hospital-associated disability; retrospective studies

## INTRODUCTION

Peripheral arterial disease (PAD) affects more than 200 million people worldwide, primarily older adults, and its incidence is increasing.[1] PAD typically results in limb-related complications, such as intermittent claudication, lower-extremity pain at rest, and ischemic ulcers, leading to reduced physical activity and decreased activities of daily living (ADL).[2] Decreased gait ability associated with PAD also increases the number of patients needing nursing care.[3] In addition, patients with PAD suffer from systemic atherosclerosis and have a high incidence of cerebrovascular disease and myocardial infarction.[4]

The benefits of rehabilitation and exercise therapy for patients with PAD are widely known. Active gait training is always recommended from initial treatment through to after surgery and endovascular treatment.[5] Several studies have investigated the effectiveness of postoperative rehabilitation for patients with PAD, but they were conducted in the outpatient setting after hospital discharge.[6]

Approximately 30% of older adults with independent ADL on admission develop hospital-associated disability (HAD), implying a decline in ADL after admission.[7,8] Patients who develop HAD are often readmitted to the hospital after discharge and often require discharge to a long-term care facility. Therefore, HAD is strongly associated with increased medical care costs; thus, countermeasures are needed.[9,10] The activity of inpatients is often considerably reduced, and lower activity levels during hospitalization have been linked to the onset of HAD.[11] Inpatient rehabilitation has

Received: January 30, 2024, Accepted: May 28, 2024, Published online: June 8, 2024
[a] Department of Rehabilitation Medicine, Mie University Graduate School of Medicine, Tsu, Japan
[b] Department of Rehabilitation, Mie University Hospital, Tsu, Japan
Correspondence: Ryo Momosaki, MD, PhD, MPH, 2-174 Edobashi, Tsu, Mie 514-8507, Japan, E-mail: momosakiryo@gmail.com

been reported to be potentially effective in mitigating the development of HAD.[12,13] Patients with PAD also experience decreased mobility and ADL following acute treatment, and the medical costs associated with hospitalization are increasing.[14,15] In several diseases, early rehabilitation after surgery can effectively maintain physical function and ADL.[16] Although early rehabilitation after surgery for patients with PAD may also reduce HAD, its effect has not yet been investigated.

Surgical treatments for PAD include bypass surgery and endovascular treatment using catheters. These methods are equally effective, but endovascular treatment, which can be performed under local anesthesia, is less invasive than bypass surgery, which requires general anesthesia.[17] Less invasive treatment is important for older patients with PAD, and, in recent years, endovascular treatment has become the first choice of several facilities and has been performed in an increasing number of cases.[18,19]

Some reports indicate that even brief periods of hospitalization carry a risk of the onset of HAD. Patients with PAD, typically inactive before admission, are at risk of developing HAD even with less invasive endovascular treatment.[8] In this study, we utilized a large inpatient database to investigate the impact of early rehabilitation after endovascular treatment on the outcomes of patients with PAD.

## MATERIALS AND METHODS

### Data Source

This study used a hospital-based database created by JMDC (Tokyo, Japan). The JMDC database is an epidemiological database that has been accumulating medical information requests and Diagnosis Procedure Combination (DPC) survey data from contracted hospitals since 2014. As of August 2020, the JMDC database contained information from approximately 12 million patients.[20] The DPC database is based on a medical payment system that was introduced in Japan in 2003.[21] It includes data such as institutional information, patient age, sex, diagnoses based on the International Classification of Diseases Version 10 (ICD-10) codes, surgeries and procedures performed, medications, special reimbursement for specific diseases, hospitalization duration, and ADL index.[22] JMDC maintains a database of medical claims from 400 hospitals. These data can be tracked even if the patients are transferred to another hospital or if they use multiple facilities.[23]

Diagnoses were defined according to ICD-10 and the Medical Information Systems Development Center (MEDIS-DC). MEDIS-DC is a Japanese foundation that supports the introduction and updating of medical information systems, standardizes medical information, and creates and manages ICD10-compliant standard disease names corresponding to ICD-10.[24] Given that all data were anonymized, the requirements for consent and approval were waived. In addition, the Ethics Committee of our institution determined that studies using the JMDC database do not require ethical review.

### PAD

Using the JMDC survey data (April 2014 to August 2020), we collected information for patients admitted to hospital with PAD diagnoses (ICD-10 code: I702) and received endovascular treatment only. The following patients were excluded: those who did not undergo rehabilitation within 0–7 days after endovascular treatment and those for which ADL data were missing for admission or discharge. We considered that if patients who started rehabilitation much later were included, causal inference would not work well because of causal inversion. To maintain internal validity, we excluded patients whose rehabilitation commenced more than 8 days after surgery.

### Rehabilitation

All rehabilitation types and intensities were covered by physiotherapists and occupational therapists. In Japan, the rehabilitation cost is reimbursed by the national health insurance system based on the number of rehabilitation units, where 20 min of rehabilitation is equivalent to 1 unit.[25] Therefore, only data on the number of rehabilitation units and the dates performed were available in the administrative claims database. The specific indications of rehabilitation for patients with PAD were left to the discretion of the attending physician.

### Endovascular Treatment

In the Japanese reimbursement system, vasodilatation and thrombectomy of the extremities are assigned the code K616. Patients who received this treatment were included in this study. However, we excluded those who underwent other spectroscopic surgery types or who received invasive treatment for comorbidities.

### Selection of Variables

The primary independent variable was the number of days between endovascular treatment and the introduction of rehabilitation. We divided the included patients into two groups: the early rehabilitation group (rehabilitation started within 0–2 days after endovascular treatment) and the control group (rehabilitation started within 3–7 days after endovascular treatment). The study outcomes were HAD development and hospitalization duration. In this study, HAD was defined as a decrease in ADL at discharge compared with ADL at admission.[26,27]

## Covariates

Rehabilitation-related covariates were sex, age, ADL at admission (Barthel Index), number of days to surgery after admission, Body Mass Index (BMI), Charlson Comorbidity Index (CCI), place of living before admission, number of beds, and admission year. These parameters were obtained from hospitalization insurance claims. Barthel Index is a scale used to evaluate ADL, and is expressed on a scale of 0–100, with higher scores indicating more independent ADL.[28] CCI is a weighted index that combines the number and severity of complications; it is highly reliable, with higher scores indicating higher mortality.[29]

## Statistical Analysis

Baseline characteristics are expressed as mean (± standard deviation; SD) for continuous variables and as number (percentage) for categorical variables. To compare between groups, we used the *t*-test for continuous variables and the $\chi^2$ test for categorical variables. Outcomes were compared using inverse probability weighting (IPW) with propensity scores to determine the association between the outcome and the number of days the rehabilitation started after endovascular treatment. Propensity scores were estimated by logistic regression analysis, with early rehabilitation as the dependent variable and age, sex, Barthel Index at admission, number of days to surgery after admission, BMI, number of beds, place of living before admission, CCI, and admission year as baseline covariates. IPW is widely used to correct for selection bias and covariate imbalance in observational studies. It employs logistic analysis with covariates to estimate the probability of each patient being assigned to the intervention group (propensity score).[30] We calculated the C statistic from the area under the ROC curve using the propensity score and covariates to assess the adequacy of the model for propensity score analysis.[31] The inverse of the propensity score is used to weigh each individual to reduce patient background bias.[32] Statistical significance was recognized for P<0.05. All statistical data were analyzed using SPSS version 25.0 (IBM, Armonk, NY, USA).

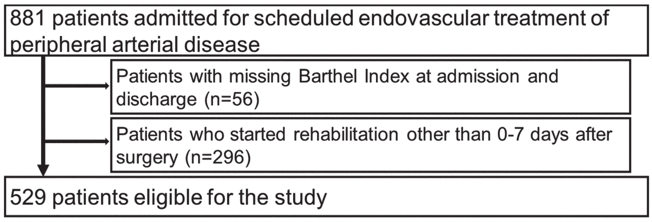


**Fig. 1.** Flowchart of patient selection process.

# RESULTS

A total of 881 patients with PAD were admitted for scheduled hospitalization, receiving endovascular treatment followed by rehabilitation within the study period. We excluded patients with a missing Barthel Index at admission or discharge (n=56) and those who underwent rehabilitation other than 0–7 days postoperatively (n=296 patients). Finally, 529 patients were included in this study (**Fig. 1**).

**Table 1** shows the patient characteristics. The mean number of days to start rehabilitation after surgery was 0.84 days in the early rehabilitation group and 4.28 days in the control group. Overall, 69.8% of the patients were men, the mean age was 74 years, the mean Barthel Index on admission was 93, most of the patients were independent in ADL, and 13.6% were underweight (BMI $\leq$18.5 kg/m$^2$). The mean number of days to endovascular treatment from admission was 1.2 days. Barthel Index at admission, number of days before operation, BMI, place of living before operation, and number of hospital beds showed significant difference between the groups. After weighting by IPW, **Table 1** demonstrates balanced background characteristics, with a C statistic of 0.783 suggesting model adequacy.[33] Standardized differences post-IPW were <0.25, which meet balancing standards.[34]

**Table 2** shows the outcomes between the two groups. The early rehabilitation group had significantly shorter hospitalization duration (4.4 vs. 18.9 days) and significantly lower incidence of HAD development (8.5% vs. 23.3%) than the control group. After the application of IPW, hospitalization duration was still significantly shorter (4.9 vs. 19.8 days) and the incidence of HAD development remained significantly lower (9.0% vs. 18.7%) in the early rehabilitation group than in the control group.

# DISCUSSION

This study used a national inpatient database to investigate the association between the time to start rehabilitation after

**Table 1.** Baseline characteristics of study participants

| Characteristic | Unadjusted | | | | Adjusted by IPW | | | |
|---|---|---|---|---|---|---|---|---|
| | Overall | Control group | Early rehabilitation group | P value | Control group | Early rehabilitation group | P value | Standardized difference |
| n | 529 | 60 | 469 | | | | | |
| Sex (male) | 369 (69.8) | 39 (65.0) | 330 (70.4) | 0.394 | 298 (62.0) | 370 (69.7) | 0.010 | 0.162 |
| Age, years | 74.0 (±8.8) | 75.5 (±8.2) | 73.8 (±8.8) | 0.176 | 74.8 (±8.3) | 74.0 (±8.8) | 0.186 | 0.093 |
| Barthel Index on admission | 93.3 (±18.5) | 85.3 (±26.6) | 94.3 (±17.0) | <0.001 | 91.7 (±18.7) | 93.0 (±19.5) | 0.319 | 0.068 |
| Days to surgery[a] | 1.2 (±1.9) | 1.8 (±1.9) | 1.1 (±1.9) | 0.009 | 1.37 (±1.5) | 1.23 (±2.1) | 0.983 | 0.077 |
| Underweight[b] | 72 (13.6) | 14 (23.3) | 58 (12.4) | 0.020 | 68 (14.1) | 70 (13.2) | 0.650 | 0.026 |
| Number of beds | | | | <0.001 | | | 0.783 | 0.031 |
| 20–99 | 1 (0.2) | 0 (0.0) | 1 (0.2) | | 0 (0.0) | 1 (0.2) | | |
| 100–199 | 36 (6.8) | 13 (21.7) | 23 (4.9) | | 37 (7.7) | 37 (7.0) | | |
| 200–299 | 188 (35.5) | 15 (25.0) | 173 (36.9) | | 159 (33.1) | 188 (35.3) | | |
| 300–499 | 286 (54.1) | 263 (56.1) | 23 (38.3) | | 264 (55.0) | 287 (53.9) | | |
| 500– | 18 (3.4) | 9 (15.0) | 9 (1.9) | | 20 (4.2) | 19 (3.6) | | |
| From home[c] | 512 (96.8) | 53 (88.3) | 459 (97.9) | <0.001 | 462 (96.3) | 514 (96.6) | 0.753 | 0.016 |
| CCI | | | | 0.212 | | | 0.067 | 0.114 |
| 0 | 0 (0.0) | 0 (0.0) | 0 (0.0) | | 0 (0.0) | 0 (0.0) | | |
| 1 | 122 (23.1) | 10 (16.7) | 112 (23.9) | | 87 (18.1) | 121 (22.7) | | |
| 2 | 407 (76.9) | 50 (83.3) | 357 (76.1) | | 394 (81.9) | 411 (77.3) | | |
| Admission year | | | | 0.572 | | | 0.175 | 0.074 |
| 2014 | 27 (5.1) | 3 (5.0) | 24 (5.1) | | 25 (5.2) | 27 (5.1) | | |
| 2015 | 40 (7.6) | 4 (6.7) | 36 (7.7) | | 36 (7.5) | 41 (7.7) | | |
| 2016 | 32 (6.0) | 6 (10.0) | 26 (5.5) | | 38 (7.9) | 32 (6.0) | | |
| 2017 | 96 (18.1) | 9 (15.0) | 87 (18.6) | | 110 (22.9) | 98 (18.4) | | |
| 2018 | 129 (24.4) | 11 (18.3) | 118 (25.2) | | 86 (17.9) | 128 (24.1) | | |
| 2019 | 144 (27.2) | 17 (28.3) | 127 (27.1) | | 136 (28.3) | 143 (26.9) | | |
| 2020 | 61 (11.5) | 10 (16.7) | 51 (10.9) | | 50 (10.4) | 63 (11.8) | | |

Data given as number (percentage) or mean (±SD).
[a] Number of days to surgery after admission; [b] BMI <18.5 $kg/m^2$; [c] Patient was at home before admission.

**Table 2.** Outcomes before and after adjustment by IPW

| Outcome | Unadjusted | | | | Adjusted by IPW | | |
|---|---|---|---|---|---|---|---|
| | Overall | Control group | Early rehabilitation group | P value | Control group | Early rehabilitation group | P value |
| Hospitalization duration, days | 6.1 (±9.9) | 18.9 (±21.7) | 4.4 (±5.2) | <0.001 | 19.8 (±27.2) | 4.9 (±6.0) | <0.001 |
| Hospital-associated disability, n (%) | 54 (10.2) | 14 (23.3) | 40 (8.5) | <0.001 | 90 (18.7) | 48 (9.0) | <0.001 |

endovascular treatment, hospitalization duration, and HAD development in patients with PAD. Results showed that the group that started rehabilitation earlier after endovascular treatment had lower incidence of HAD development and shorter hospitalization duration.

Recommended as first-line treatment in all major guidelines, exercise-based rehabilitation for PAD improves patient walking ability and the overall quality of life regardless of the presence or degree of PAD symptoms.[5] Therefore, the benefits of exercise in PAD are multifaceted. Mechanisms underlying these improvements include expanded circulatory capacity, decreased blood viscosity, enhanced mitochondrial function, recovery from metabolic muscle disease, and alleviation of endothelial inflammation. Exercise can also help to alleviate several PAD-exacerbating risk factors, such as adipose tissue mass, poor glycemic control, and hypertension.[35]

Our study is consistent with previous studies that described the feasibility of postoperative rehabilitation in patients with lower-extremity PAD without a concurrent increase in adverse events.[36] A previous study on functional prognosis after angioplasty for patients with lower-extremity PAD reported that 88% of these patients could walk before the operation, 82.7% could maintain their walking ability, and 84.5% could independently perform ADL.[37] Although strict comparisons cannot be made because of varied patient characteristics, the fact that more patients in the early rehabilitation group in our study maintained their ADL than in the previous study indicates that early rehabilitation is useful in maintaining ADL.

Despite being able to walk preoperatively, symptomatic patients with lower-extremity PAD often show decreased walking distance and activity after treatment.[38] Bed rest causes many adverse events, including muscle weakness, and early postoperative rehabilitation may lead to earlier gains in ambulation and shorter hospitalization duration by improving disuse caused by pre-morbid inactivity.[39]

On average, postoperative rehabilitation for the early rehabilitation and control groups commenced approximately 3 days after surgery. Low activity during hospitalization, even for a short period, can cause HAD.[8] Therefore, early rehabilitation may benefit ADL maintenance and contribute to shorter hospital stays by promoting increased activity levels and accelerated mobility.

Given that endovascular treatment for patients with PAD is widely considered as the first choice for surgical treatment, the implications of this finding are profound and relevant for both clinicians and policymakers. Early rehabilitation, initiated within 0–2 days after endovascular treatment, may help reduce the risk of developing HAD and shorten the duration of hospitalization, thereby preserving patients' quality of life and counteracting increasing healthcare costs.

## Limitations

This study had some limitations. First, we did not obtain information on the clinical severity of PAD, such as the Fontaine or Rutherford classification. In addition, we did not acquire measures of walking ability commonly used in clinical practice, such as the 6-min walk test, and mobility was assessed inclusively as an ADL. Therefore, we could not evaluate or provide correction for variables that might have impacted the results. Second, information on the rehabilitation treatment undertaken by the patients was limited to the number of rehabilitation units and the start date. Information on the content, intensity, and type of rehabilitation provided was unavailable. Third, decisions about whether rehabilitation was to be provided (and its timing) were made by individual clinicians according to their own judgment. Fourth, we restricted eligibility to patients initiating rehabilitation within 0–7 days after surgery to ensure internal validity, leading to the exclusion of 296 patients. Despite these measures to uphold internal validity, the exclusion of a large number of patients may have impacted the data quality.

## CONCLUSION

Early rehabilitation after endovascular treatment for PAD was associated with shorter hospitalization duration and fewer HAD events. Further research, including randomized controlled trials, is needed to confirm the effect of providing rehabilitation to patients admitted for PAD.

## ACKNOWLEDGMENTS

This investigation was supported by a Grant-in-Aid from the Japan Society for the Promotion of Science (Grant Number: 22K19669). We thank students of the Department of Rehabilitation Medicine, Mie University Graduate School of Medicine, for their participation in discussions on this study.

## CONFLICTS OF INTEREST

The authors declare no conflict of interest.

## REFERENCES

1. Fowkes FG, Rudan D, Rudan I, Aboyans V, Denenberg JO, McDermott MM, Norman PE, Sampson UK, Williams LJ, Mensah GA, Criqui MH: Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. Lancet 2013;382:1329–1340. https://doi.org/10.1016/S0140-6736(13)61249-0, PMID:23915883
2. Abu Dabrh AM, Steffen MW, Undavalli C, Asi N, Wang Z, Elamin MB, Conte MS, Murad MH: The natural history of untreated severe or critical limb ischemia. J Vasc Surg 2015;62:1642–1651. https://doi.org/10.1016/j.jvs.2015.07.065, PMID:26391460
3. Brach JS, Solomon C, Naydeck BL, Sutton-Tyrrell K, Enright PL, Jenny NS, Chaves PM, Newman AB, Cardiovascular Health Study Research Group: Incident physical disability in people with lower extremity peripheral arterial disease: the role of cardiovascular disease. J Am Geriatr Soc 2008;56:1037–1044. https://doi.org/10.1111/j.1532-5415.2008.01719.x, PMID:18384579
4. Caro J, Migliaccio-Walle K, Ishak KJ, Proskorovsky I: The morbidity and mortality following a diagnosis of peripheral arterial disease: long-term follow-up of a large database. BMC Cardiovasc Disord 2005;5:14. https://doi.org/10.1186/1471-2261-5-14, PMID:15972099
5. Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, Fleisher LA, Fowkes FG, Hamburg NM, Kinlay S, Lookstein R, Misra S, Mureebe L, Olin JW, Patel RA, Regensteiner JG, Schanzer A, Shishehbor MH, Stewart KJ, Treat-Jacobson D, Walsh ME: 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. Circulation 2017;135:e686–e725. https://doi.org/10.1161/CIR.0000000000000470, PMID:27840332
6. Kruidenier LM, Nicolaï SP, Rouwet EV, Peters RJ, Prins MH, Teijink JA: Additional supervised exercise therapy after a percutaneous vascular intervention for peripheral arterial disease: a randomized clinical trial. J Vasc Interv Radiol 2011;22:961–968. https://doi.org/10.1016/j.jvir.2011.02.017, PMID:21571547
7. Covinsky KE, Pierluissi E, Johnston CB: Hospitalization-associated disability: "She was probably able to ambulate, but I'm not sure". JAMA 2011;306:1782–1793. https://doi.org/10.1001/jama.2011.1556, PMID:22028354
8. Loyd C, Markland AD, Zhang Y, Fowler M, Harper S, Wright NC, Carter CS, Buford TW, Smith CH, Kennedy R, Brown CJ: Prevalence of hospital-associated disability in older adults: a meta-analysis. J Am Med Dir Assoc 2020;21:455–461. https://doi.org/10.1016/j.jamda.2019.09.015, PMID:31734122
9. Kortebein P, Bopp MM, Granger CV, Sullivan DH: Outcomes of inpatient rehabilitation for older adults with debility. Am J Phys Med Rehabil 2008;87:118–125. https://doi.org/10.1097/PHM.0b013e3181588429, PMID:17912135
10. Hoyer EH, Needham DM, Atanelov L, Knox B, Friedman M, Brotman DJ: Association of impaired functional status at hospital discharge and subsequent rehospitalization. J Hosp Med 2014;9:277–282. https://doi.org/10.1002/jhm.2152, PMID:24616216
11. Brown CJ, Friedkin RJ, Inouye SK: Prevalence and outcomes of low mobility in hospitalized older patients. J Am Geriatr Soc 2004;52:1263–1270. https://doi.org/10.1111/j.1532-5415.2004.52354.x, PMID:15271112
12. Smith TO, Sreekanta A, Walkeden S, Penhale B, Hanson S: Interventions for reducing hospital-associated deconditioning: a systematic review and meta-analysis. Arch Gerontol Geriatr 2020;90:104176. https://doi.org/10.1016/j.archger.2020.104176, PMID:32652367

13. Ortiz-Alonso J, Bustamante-Ara N, Valenzuela PL, Vidán-Astiz M, Rodríguez-Romo G, Mayordomo-Cava J, Javier-González M, Hidalgo-Gamarra M, Lopéz-Tatis M, Valades-Malagón MI, Santos-Lozano A, Lucia A, Serra-Rexach JA: Effect of a simple exercise program on hospitalization-associated disability in older patients: a randomized controlled trial. J Am Med Dir Assoc 2020;21:531–537. https://doi.org/10.1016/j.jamda.2019.11.027, PMID:31974063
14. Rollins KE, Coughlin PA: Functional outcomes following revascularisation for critical limb ischaemia. Eur J Vasc Endovasc Surg 2012;43:420–425. https://doi.org/10.1016/j.ejvs.2012.01.015, PMID:22305646
15. Mahoney EM, Wang K, Keo HH, Duval S, Smolderen KG, Cohen DJ, Steg G, Bhatt DL, Hirsch AT, Reduction of Atherothrombosis for Continued Health (REACH) Registry Investigators: Vascular hospitalization rates and costs in patients with peripheral artery disease in the United States. Circ Cardiovasc Qual Outcomes 2010;3:642–651. https://doi.org/10.1161/CIRCOUTCOMES.109.930735, PMID:20940249
16. Tazreean R, Nelson G, Twomey R: Early mobilization in enhanced recovery after surgery pathways: current evidence and recent advancements. J Comp Eff Res 2022;11:121–129. https://doi.org/10.2217/cer-2021-0258, PMID:35045757
17. Adam DJ, Beard JD, Cleveland T, Bell J, Bradbury AW, Forbes JF, Fowkes FG, Gillepsie I, Ruckley CV, Raab G, Storkey H, BASIL Trial Participants: Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. Lancet 2005;366:1925–1934. https://doi.org/10.1016/S0140-6736(05)67704-5, PMID:16325694
18. Faglia E, Dalla Paola L, Clerici G, Clerissi J, Graziani L, Fusaro M, Gabrielli L, Losa S, Stella A, Gargiulo M, Mantero M, Caminiti M, Ninkovic S, Curci V, Morabito A: Peripheral angioplasty as the first-choice revascularization procedure in diabetic patients with critical limb ischemia: prospective study of 993 consecutive patients hospitalized and followed between 1999 and 2003. Eur J Vasc Endovasc Surg 2005;29:620–627. https://doi.org/10.1016/j.ejvs.2005.02.035, PMID:15878541
19. Nasr MK, McCarthy RJ, Hardman J, Chalmers A, Horrocks M: The increasing role of percutaneous transluminal angioplasty in the primary management of critical limb ischaemia. Eur J Vasc Endovasc Surg 2002;23:398–403. https://doi.org/10.1053/ejvs.2002.1615, PMID:12027466
20. Nagai K, Tanaka T, Kodaira N, Kimura S, Takahashi Y, Nakayama T: Data resource profile: JMDC claims databases sourced from medical institutions. J Gen Fam Med 2020;21:211–218. https://doi.org/10.1002/jgf2.367, PMID:33304714
21. Yasunaga H, Ide H, Imamura T, Ohe K: Impact of the Japanese diagnosis procedure combination-based payment system on cardiovascular medicine-related costs. Int Heart J 2005;46:855–866. https://doi.org/10.1536/ihj.46.855, PMID:16272776
22. Yamana H, Moriwaki M, Horiguchi H, Kodan M, Fushimi K, Yasunaga H: Validity of diagnoses, procedures, and laboratory data in Japanese administrative data. J Epidemiol 2017;27:476–482. https://doi.org/10.1016/j.je.2016.09.009, PMID:28142051
23. Yasunaga H: Real world data in Japan: chapter II the diagnosis procedure combination database. Ann Clin Epidemiol 2019;1:76–79. https://doi.org/10.37737/ace.1.3_76
24. Sakamoto N: The construction of a public key infrastructure for healthcare information networks in Japan. Stud Health Technol Inform 2001;84:1276–1280. PMID:11604934
25. Uda K, Matsui H, Fushimi K, Yasunaga H: Intensive in-hospital rehabilitation after hip fracture surgery and activities of daily living in patients with dementia: retrospective analysis of a nationwide inpatient database. Arch Phys Med Rehabil 2019;100:2301–2307. https://doi.org/10.1016/j.apmr.2019.06.019, PMID:31421098
26. Palleschi L, De Alfieri W, Salani B, Fimognari FL, Marsilii A, Pierantozzi A, Di Cioccio L, Zuccaro SM: Functional recovery of elderly patients hospitalized in geriatric and general medicine units. The PROgetto DImissioni in GEriatria Study. J Am Geriatr Soc 2011;59:193–199. https://doi.org/10.1111/j.1532-5415.2010.03239.x, PMID:21288230
27. Fimognari FL, Pierantozzi A, De Alfieri W, Salani B, Zuccaro SM, Arone A, Palleschi G, Palleschi L: The severity of acute illness and functional trajectories in hospitalized older medical patients. J Gerontol A Biol Sci Med Sci 2017;72:102–108. https://doi.org/10.1093/gerona/glw096, PMID:27257216
28. Mahoney FI, Barthel DW: Functional evaluation: the Barthel index. Md State Med J 1965;14:61–65. PMID:14258950

29. Charlson ME, Pompei P, Ales KL, MacKenzie CR: A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–383. https://doi.org/10.1016/0021-9681(87)90171-8, PMID:3558716
30. McDonald RJ, McDonald JS, Kallmes DF, Carter RE: Behind the numbers: propensity score analysis—a primer for the diagnostic radiologist. Radiology 2013;269:640–645. https://doi.org/10.1148/radiol.13131465, PMID:24261493
31. Westreich D, Cole SR, Funk MJ, Brookhart MA, Stürmer T: The role of the *c*-statistic in variable selection for propensity score models. Pharmacoepidemiol Drug Saf 2011;20:317–320. https://doi.org/10.1002/pds.2074, PMID:21351315
32. Halpern EF: Behind the numbers: inverse probability weighting. Radiology 2014;271:625–628. https://doi.org/10.1148/radiol.14140035, PMID:24848956
33. Šimundić AM: Measures of diagnostic accuracy: basic definitions. EJIFCC 2009;19:203–211. PMID:27683318
34. Stuart EA: Matching methods for causal inference: a review and a look forward. Stat Sci 2010;25:1–21. https://doi.org/10.1214/09-STS313, PMID:20871802
35. Stewart KJ, Hiatt WR, Regensteiner JG, Hirsch AT: Exercise training for claudication. N Engl J Med 2002;347:1941–1951. https://doi.org/10.1056/NEJMra021135, PMID:12477945
36. Tsuchia H: Importance of vascular rehabilitation in the treatment of chronic critical limb ischemia [in Japanese]. Jpn J Vasc Surg. 2011;20:927–932.
37. Taylor SM, Kalbaugh CA, Blackhurst DW, Langan EM III, Cull DL, Snyder BA, Carsten CG III, Jackson MR, York JW, Youkey JR: Postoperative outcomes according to preoperative medical and functional status after infrainguinal revascularization for critical limb ischemia in patients 80 years and older. Am Surg 2005;71:640–646. https://doi.org/10.1177/000313480507100805, PMID:16217945
38. Gerage AM, Correia MA, Oliveira PM, Palmeira AC, Domingues WJ, Zeratti AE, Puech-Leão P, Wolosker N, Ritti-Dias RM, Cucato GG: Physical activity levels in peripheral artery disease patients. Arq Bras Cardiol 2019;113:410–416. https://doi.org/10.5935/abc.20190142, PMID:31365605
39. Greenleaf JE: Physiological responses to prolonged bed rest and fluid immersion in humans. J Appl Physiol 1984;57:619–633. https://doi.org/10.1152/jappl.1984.57.3.619, PMID:6386766