The impact of chronic kidney disease on outcomes following peripheral vascular intervention

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Funding Information
Cardiovascular Systems, Inc. (CSI, St. Paul, MN)

Abstract

Background: Patients with chronic kidney disease (CKD) have worsened clinical outcomes following percutaneous coronary intervention; however, limited evidence exists in patients undergoing peripheral vascular intervention (PVI).

Purpose: We aimed to assess the effect of CKD on outcomes following PVI for symptomatic peripheral artery disease.

Methods: Using patients from the LIBERTY 360 study, we compared the rates of 30 day and 1 year major adverse vascular events (MAVE), a composite of all-cause mortality, major amputation, and target vessel/lesion revascularization, between patients with and without CKD (estimated glomerular filtration rate less than 60) following PVI. Multivariable adjustment was performed to assess for independent association between CKD and outcomes.

Results: Among 1189 patients enrolled, 378 patients (31.8%) had CKD. At 1 year, patients with CKD had higher rates of MAVE (34.6% vs 25.6%), all-cause mortality (11.9% vs 5.5%), and major amputation (5.9% vs 2.6%) when compared with patients without CKD (all \( P < .05 \)). After adjustment, patients with CKD had higher risks of 1-year MAVE (HR 1.30, 95% CI 1.04-1.64; \( P = .023 \)) and all-cause mortality (HR 1.88, 95% CI 1.22-2.91; \( P = .005 \)) when compared with patients without CKD. There was no statistically significant difference in risk of major amputations (HR 1.70, 95% CI 0.91-3.17; \( P = .094 \)).

Conclusions: Despite high procedural success and low amputation rates, patients with CKD remain at greater risk for MAVE and all-cause mortality after PVI. Further research is needed to determine treatment strategies to mitigate substantial mortality risk in this vulnerable population.

KEYWORDS
chronic kidney disease, mortality, peripheral artery disease, revascularization

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Peripheral artery disease (PAD) is a manifestation of systemic atherosclerosis leading to malperfusion of the lower extremities, which can cause debilitating symptoms and/or tissue loss. Despite an increasing prevalence, PAD remains underappreciated by both patients and clinicians as a significant risk factor for cardiovascular morbidity and mortality. Peripheral revascularization is frequently performed to improve symptoms among claudicants and reduce the risks of major lower extremity amputation among those with chronic limb-threatening ischemia. Endovascular revascularization has been utilized as the preferred strategy in most patients, yet little is known about risk factors and clinical outcomes following peripheral vascular intervention (PVI).

Chronic kidney disease (CKD) is a known risk factor for PAD, and patients with CKD often present with significant calcification, more severe disease, and longer lesions. Despite this higher burden of disease, there have been reports that patients with CKD are offered fewer overall revascularization procedures and more frequently suffer major amputations. Indeed, some studies have suggested that after PVI, CKD is independently associated with poor outcomes, including higher rates of death and amputation. There has also been a stronger association seen with more severe renal disease. However, evidence remains limited on the best approach for these complex medical patients.

The LIBERTY 360 study prospectively enrolled patients with symptomatic PAD undergoing PVI, captured discrete data elements at the time of PVI, and collected clinical outcomes. In order to add to the limited knowledge about success and outcomes of PVI in patients with CKD, we aimed to describe patient- and procedure-related characteristics of patients with and without CKD and characterize the impact of CKD on major cardiovascular events and ischemic limb outcomes following PVI.

2 | METHODS

2.1 | Study design and oversight

LIBERTY 360 is a prospective, observational, multicenter study that was performed to examine predictors of clinical outcomes in patients with distal lower extremity PAD who underwent PVI of the distal superficial femoral, popliteal, and/or tibial arteries. The study design, rationale, and data analysis for LIBERTY 360 have been previously published. Clinical follow-up was performed at 30 days, 6 months, 12 months, and 2 years; patients were followed up to 5 years. A steering committee consisting of LIBERTY 360 principal investigators, representatives from the study core laboratory, and the sponsor (Cardiovascular Systems, Inc) were responsible for development of the original study protocol, which was approved by the IRB at each study site. The study was registered on ClinicalTrials.gov (NCT01855412).

2.2 | Study population

Patients were enrolled if they were above the age of 18 years, presented with symptomatic PAD (at least Rutherford class 2), and had an indication for peripheral revascularization. Patients were included if they had revascularization of a stenosis located in the distal superficial femoral artery, popliteal artery, or tibial arteries (specifically any lesion distal to a point 10 cm above the medial epicondyle of the femur). Lesions needed to be present within a native vessel, be traversable with a guidewire, and be treated with an FDA-approved endovascular device. Exclusion criteria included: conversion from endovascular intervention to surgical revascularization, in-stent restenosis in all lesions in the target area, and an expected life span of less than 1 year. CKD was determined by the case report forms completed by investigators; estimated glomular filtration rate (eGFR) was measured separately by sites’ labs and recorded in the database. CKD staging was not recorded in the case report form. Patients were excluded if their CKD status was unable to be determined.

2.3 | End points

There were multiple prespecified outcomes in the observational LIBERTY 360 study. The primary outcome of our analysis was the rate of major adverse vascular events (MAVE), defined as a composite end-point including all-cause mortality, unplanned major amputation of the target limb, and clinically driven target vessel and/or lesion revascularization (TVR/TLR) at 30 days and 1 year. Major amputation was further defined as any unplanned major amputation of the target limb after the index procedure. TVR/TLR was defined as any revascularization, endovascular or surgical, of target vessel and/or lesion after index procedure. Reinterventions on the target limb at locations other than the index vessel or lesion were not captured. Acute limb ischemia was also not captured.

The secondary outcomes of this analysis consisted of rates of each individual MAVE component at 30 days and 1 year, in addition to procedural success after the index procedure and change in quality of life from baseline. Procedural success was defined as less than 50% residual stenosis for treated lesions without significant angiographic complications (flow-limiting dissections [type C-F], perforation, slow/no reflow, distal embolization, or abrupt closure). Adjudication of angiographic data was performed by SynvaCor/Prairie Educational and Research Cooperative (PERC; Springfield, IL). Quality of life was measured using the EQ-5D Visual Analog Score (VAS) at baseline and each follow-up visit.

2.4 | Statistical analysis

Categorical variables were compared between patients with CKD vs those without CKD using a Monte Carlo Approximation of the Fisher’s Exact Test. Continuous variables were compared with ANOVA tests.
and for discrete continuous variables, \( P \)-values were calculated from a Kruskal-Wallis test. For the primary and secondary outcomes, Kaplan-Meier time-to-event methodology was used to estimate unadjusted event rates through each time point; Greenwood's method used to obtain the 95% confidence interval for the estimate. A Cox proportional hazards model was analyzed controlling for the baseline characteristics of age, gender, race, body mass index, smoking status, comorbid conditions (coronary artery disease [CAD], hypertension, hyperlipidemia, diabetes, prior myocardial infarction [MI], prior stroke), Rutherford classification, ankle brachial index (ABI), and PAD history (prior endovascular treatment, bypass, or amputation on target limb).

**LIBERTY 360 study**
Enrollment: May 2013 to February 2016
Inclusion Criteria:
- Patients \( \geq 18 \),
- Symptomatic PAD
- Distal superficial femoral artery, popliteal artery, or tibial
- Indication for PVI
Consented for procedure
\( N = 1204 \)

Complete baseline and procedure data available for analysis
\( N = 1189 \)

Patients with CKD
\( N = 378 \)
Disease Severity
RC 2-3: \( N = 121 \)
RC 4-5: \( N = 217 \)
RC 6: \( N = 40 \)

Completed 1-year follow up:
\( N = 247 \)
Death: \( N = 46 \)
Lost to follow up: \( N = 81 \)
Lack of signatures on case report form: \( N = 4 \)

Patients without CKD
\( N = 811 \)
Disease Severity
RC 2-3: \( N = 379 \)
RC 4-5: \( N = 372 \)
RC 6: \( N = 60 \)

Completed 1-year follow up
\( N = 584 \)
Death: \( N = 179 \)
Lost to follow up: \( N = 43 \)
Lack of signatures on case report form: \( N = 5 \)

**FIGURE 1** Ascertainment of the study population. CKD, patients with chronic kidney disease; PAD, peripheral artery disease; PVI, peripheral vascular intervention; RC, Rutherford classification

An adjusted multivariable model was created based on a Cox proportional hazards model using stepwise selection with an entry criterion from the univariable model of 0.15 and a stay criterion of 0.05 (Supplemental Table 1). The hazard function was then used to estimate the survival function. Confidence intervals are based on back-transformed log-log of the survival function. \( P \)-values were calculated using Cox proportional hazards model for estimates at a specified time point. Imputation of significant angiographic complications for procedural success of core lab identified lesions were performed by using site data when the core lab was unable to perform angiographic assessment. Statistical analysis was performed by NAMSA.
From May 2013 to February 2016, 1204 patients who underwent PVI for symptomatic PAD were enrolled; 1189 had complete baseline and procedure data available for analysis. A total of 378 patients (31.8%) had CKD. The median eGFR was 38.1 mL/min/1.73 m² (IQR 21.9, 49.1) for patients with CKD and 72.9 mL/min/1.73 m² (IQR 60.9, 85.5) for those without CKD.

There were 87 (23.0%) of patients with CKD who were hemodialysis dependent. There were 15 patients excluded from the secondary analysis due to unknown CKD status. Follow-up was available in 247 patients with CKD (65.3%) and 584 patients without CKD (72.0%) at 1 year (Figure 1).

### TABLE 1 Baseline characteristics

|                      | With CKD (n = 378) | Without CKD (n = 811) | P value |
|----------------------|--------------------|-----------------------|---------|
| **Demographics**     |                    |                       |         |
| Age (years), median⁴ | 71 (63, 80)        | 70 (63, 77)           | .0988   |
| Male                 | 64.6               | 64.9                  | .9480   |
| **Race**             |                    |                       |         |
| White                | 78.3               | 83.4                  | .0436   |
| African American     | 18.3               | 13.4                  | .0360   |
| **Ethnicity**        |                    |                       |         |
| Hispanic or Latino   | 15.6               | 13.6                  | .3726   |
| **BMI (kg/m²), median (IQR)** | 28.9 (25.6, 32.9)  | 27.9 (24.4, 32.1)     | .0068   |
| **eGFR (mL/min/1.73 m²), median (IQR)** | 38.1 (21.9, 49.1)  | 72.9 (60.9, 85.5)     | <.0001  |
| Hemodialysis dependent | 23.0              | 0.0                   | .0003   |
| **Cardiovascular risk factors** |            |                       |         |
| Diabetes mellitus    | 72.0               | 56.1                  | <.0001  |
| Hypertension         | 96.3               | 92.0                  | .0056   |
| Hyperlipidemia       | 88.6               | 86.1                  | .2321   |
| Coronary artery disease | 69.0          | 57.5                  | .0001   |
| Previous history of MI | 28.8            | 21.7                  | .0086   |
| Previous history of CVA | 16.7          | 14.2                  | .2948   |
| **Tobacco use**      |                    |                       |         |
| Current smoker       | 10.1               | 23.2                  | <.0001  |
| Former smoker        | 51.9               | 47.7                  | .1912   |
| Never                | 38.1               | 29.1                  | .0021   |
| **PAD history**      |                    |                       |         |
| Prior PVI            |                    |                       |         |
| Target limb          | 32.5               | 29.2                  | .2499   |
| Contralateral limb   | 35.4               | 34.6                  | .7941   |
| Prior LE surgical bypass |                |                       |         |
| Target limb          | 2.9                | 4.4                   | .2632   |
| Contralateral limb   | 3.4                | 3.9                   | .7460   |
| **Prior amputation** |                    |                       |         |
| Target limb          | 6.9                | 4.2                   | .0634   |
| Contralateral limb   | 8.2                | 5.8                   | .1313   |
| Both limbs           | 5.8                | 1.0                   | <.0001  |
| **Highest level of amputation, target limb** | | | |
| Toe(s) only          | 93.8               | 95.2                  | 1.00    |
| Foot only            | 6.3                | 4.8                   | 1.00    |
| **Highest level of amputation, contralateral limb** | | | |
| Toe(s) only          | 69.8               | 47.3                  | .0203   |
| Foot only            | 11.3               | 7.3                   | .5230   |
| Below knee/above ankle | 22.6            | 47.3                  | .0090   |
| Above the knee       | 7.5                | 18.2                  | .1513   |
| **Rutherford classification** | | | |
| 2                    | 4.8                | 9.7                   | .0030   |
| 3                    | 27.2               | 37.0                  | .0010   |

(Continues)

### TABLE 1 (Continued)

|                      | With CKD (n = 378) | Without CKD (n = 811) | P value |
|----------------------|--------------------|-----------------------|---------|
| **ABI target limb⁴** |                    |                       |         |
| Abnormal ABI (<=0.90) | 53.7              | 62.9                  | .0041   |
| Borderline ABI (>0.90 to <1.00) | 8.9          | 9.5                   | .8225   |
| Normal ABI (>1.00 to <=1.40) | 18.7          | 19.2                  | .8682   |
| Noncompressible      | 18.7               | 8.3                   | <.001   |
| **Postprocedure medications** | | | |
| Aspirin              | 78.6               | 81.0                  | .3481   |
| Clopidogrel          | 69.0               | 77.9                  | .0012   |
| Prasugrel            | 4.8                | 2.6                   | .0555   |
| Dual antiplatelet therapy | 65.3          | 68.9                  | .2305   |
| Anticoagulants       | 13.5               | 8.8                   | .0138   |
| Lipid lowering therapy | 82.5            | 78.1                  | .0766   |

Note: Values are % unless otherwise specified. Abbreviations: ABI, ankle brachial index; BMI, body mass index; CKD, chronic kidney disease; CVA, cerebrovascular accident; eGFR, estimated glomerular filtration rate; IQR, interquartile range; LE, lower extremity; MI, myocardial infarction; PAD, peripheral artery disease; PVI, peripheral vascular intervention.

From May 2013 to February 2016, 1204 patients who underwent PVI for symptomatic PAD were enrolled; 1189 had complete baseline and procedure data available for analysis. A total of 378 patients (31.8%) had CKD. The median eGFR was 38.1 mL/min/1.73 m² (IQR 21.9, 49.1) for patients with CKD and 72.9 mL/min/1.73 m² (IQR 60.9, 85.5) for those without CKD. There were 87 (23.0%) of patients with CKD who were hemodialysis dependent. There were 15 patients excluded from the secondary analysis due to unknown CKD status. Follow-up was available in 247 patients with CKD (65.3%) and 584 patients without CKD (72.0%) at 1 year (Figure 1).
Table 2 highlights the anatomy and lesion characteristics of patients at the time of the index procedure. There were 489 lesions treated in a patient with no major significant angiographic complications.

Abbreviations: ATK, above the knee; BMS, bare metal stent; BTK, below the knee; CKD, chronic kidney disease; DCB, drug-coated balloon; DES, drug-eluting stent; POBA, plain old balloon angioplasty; PVI, peripheral vascular intervention.

Table 1 shows the baseline patient characteristics of patients with and without CKD. When compared with patients without CKD, those with CKD were more often African American (18.3% vs 13.4%; \( P = .0360 \)) and more frequently had diabetes mellitus (72.0% vs 56.1%; \( P < .0001 \)), CAD (69.0% vs 57.5%; \( P = .0086 \)), and had never smoked (38.1% vs 29.1%; \( P = .0021 \)). Patients with CKD more frequently had Rutherford 5 disease (33.9% vs 21.7%; \( P = .0021 \)), and had never smoked (38.1% vs 29.1%; \( P = .0021 \)). Patients with CKD more frequently had Rutherford 5 disease (33.9% vs 21.7%; \( P = .0021 \)), and had never smoked (38.1% vs 29.1%; \( P = .0021 \)). Patients with CKD who had undergone amputation of the contralateral limb were less likely to have had below- or above-knee amputations compared to patients without CKD (30.1% vs 65.5% of prior ipsilateral amputations, \( P = .0021 \)). However, patients with CKD who had higher rates of prior amputations on both limbs (5.8% vs 1.0%; \( P < .0001 \)). The median EQ-5D VAS at baseline was significantly lower among patients with CKD (70.0, IQR 50.0, 79.0) than among patients without CKD (70.0, IQR 50.0, 80.0; \( P < .0001 \)).

3.1 Baseline and PAD-specific characteristics

Table 2 shows the baseline patient characteristics of patients with and without CKD. When compared with patients without CKD, those with CKD were more often African American (18.3% vs 13.4%; \( P = .0360 \)) and more frequently had diabetes mellitus (72.0% vs 56.1%; \( P < .0001 \)), CAD (69.0% vs 57.5%; \( P = .0086 \)), and had never smoked (38.1% vs 29.1%; \( P = .0021 \)). Patients with CKD more frequently had Rutherford 5 disease (33.9% vs 21.7%; \( P = .0021 \)), and had never smoked (38.1% vs 29.1%; \( P = .0021 \)). Patients with CKD who had undergone amputation of the contralateral limb were less likely to have had below- or above-knee amputations compared to patients without CKD (30.1% vs 65.5% of prior ipsilateral amputations, \( P = .0021 \)). However, patients with CKD who had higher rates of prior amputations on both limbs (5.8% vs 1.0%; \( P < .0001 \)). The median EQ-5D VAS at baseline was significantly lower among patients with CKD (70.0, IQR 50.0, 79.0) than among patients without CKD (70.0, IQR 50.0, 80.0; \( P < .0001 \)).
patients with CKD (1.3 ± 0.6 per patient) and 1039 lesions in those without CKD (1.3 ± 0.6 per patient). When compared with patients without CKD, patients with CKD more frequently had isolated infranpopliteal disease (57.5% vs 48.5%; P = .0012). Patients with CKD more frequently had zero patent runoff vessels (12.7% vs 8.2%; P = .0151) and more lesions that were severely calcified when compared to those without CKD (65.3% vs 55.4%; P = .0005). There were no differences between the groups when assessing mean target lesion length, degree of stenosis, and number of chronic total occlusions. The use of balloon angioplasty and stenting were similar between the groups without, but not all-cause mortality (HR 3.17, 95% CI 0.74-13.46; P = .094).

3.3 | Event rates in patients with CKD and without CKD

Table 3 shows the event rates in patients with and without CKD. When compared with patients without CKD, patients with CKD had higher rates at 30 days of the primary composite end point MAVE (5.6% vs. 1.7%; HR 3.27, 95% CI 1.66-6.43; P = .006) and major amputation (1.9% vs 0.5%; HR 3.78, 95% CI 1.11-12.92; P = .0339, Figure 1). At 1 year, patients with CKD had higher rates of MAVE (34.6% vs 25.6%; HR 1.47, 95% CI 1.17-1.84; P = .0009), all-cause mortality (11.9% vs 5.5%; HR 2.29, 95% CI 1.49-3.52; P = .0002), and major amputation (5.9% vs 2.6%; HR 2.24, 95% CI 1.21-4.17; P = .0107) compared with patients without CKD. Figure 2 depicts the Kaplan event rate curves for MAVE and its individual components.

After adjustment for baseline variables, the presence of CKD was associated with 30-day MAVE (HR 2.52, 95% CI 1.27-4.98; P = .008), but not all-cause mortality (HR 3.17, 95% CI 0.74-13.46; P = .119) or major amputation (HR 3.41, 95% CI 0.99-11.71; P = .052) compared with patients without CKD. However, at 1 year, patients with CKD had higher adjusted risks of MAVE (HR 1.30, 95% CI 1.04-1.64; P = .023) and all-cause mortality (HR 1.88, 95% CI 1.222.91; P = .005), but not major amputation (HR 1.70, 95% CI 0.91-3.17; P = .094).

There were no differences in the median change in EQ-5D VAS from baseline between patients with CKD and without CKD at 30 days (median change 3.0 in CKD and 5.0 in non-CKD, P = .8481) or 12 months (median change 5.0 in both groups, 0.8121).

4 | DISCUSSION

In this study, we examined the association of CKD with MAVE, consisting of all-cause mortality, major amputation, and TVR/TLR, after endovascular intervention in the multicenter LIBERTY 360 study. Nearly one-third of the 1204 symptomatic patients with PAD had a history of CKD. The unadjusted rates of MAVE among patients with CKD were higher at 30 days and 1 year following the initial intervention. This was largely driven by the increased rate of all-cause mortality. After adjustment, patients with CKD still had greater risk of MAVE at both time intervals, as well as higher all-cause mortality at 1 year. While patients with CKD experienced more major amputations at 30 days and 1 year, the adjusted risk was not statistically significant compared with those without CKD. Our findings underscore the substantial residual risk patients with CKD face post-PVI despite good procedural outcomes. Indeed, these findings also highlight that more work needs to be done to improve on these outcomes.

Though the relationship between CKD and PAD is well established, our analysis contributes to the more limited data on whether PVI modifies the association between PAD, CKD, and all-cause mortality. There have been a few retrospective analyses that have suggested that patients with CKD undergoing PVI had increased risks of cardiovascular mortality and ischemic limb events. However, in our analysis, the increased rate of the MAVE was driven by elevated rate of all-cause mortality with low overall rates of major amputation. Thus, only all-cause mortality at 1 year remained

### TABLE 3 Association between CKD and cardiovascular and limb outcomes

| Event Endpoint | With CKD | Without CKD | Univariable HR (95% CI) | Univariable P Value | Multivariable HR (95% CI) | Multivariable P Value |
|----------------|----------|-------------|-------------------------|---------------------|--------------------------|-----------------------|
| 30-day MAVE    | 5.4%     | 1.7%        | 3.27 (1.66, 6.43)       | .0006               | 2.52 (1.27, 4.98)        | .008                  |
| All-cause mortality | 1.3%   | 0.4%        | 3.58 (0.86, 14.98)     | .0807               | 3.17 (0.74, 13.46)       | .119                  |
| Major amputation | 1.9%   | 0.5%        | 3.78 (1.11, 12.92)     | .0339               | 3.41 (0.99, 11.71)       | .052                  |
| TVR/TLR        | 2.7%     | 1.1%        | 2.41 (0.98, 5.92)      | .0561               | 2.01 (0.82, 4.98)        | .129                  |
| 1-year MAVE    | 34.6%    | 25.6%       | 1.47 (1.17, 1.84)      | .0009               | 1.30 (1.04, 1.64)        | .023                  |
| All-cause mortality | 11.9% | 5.5%        | 2.29 (1.49, 3.52)      | .0002               | 1.88 (1.22, 2.91)        | .005                  |
| Major amputation | 5.9%   | 2.6%        | 2.24 (1.21, 4.17)      | .0107               | 1.70 (0.91, 3.17)        | .094                  |
| TVR/TLR        | 23.5%    | 20.6%       | 1.18 (0.90, 1.56)      | .2287               | 1.09 (0.83, 1.44)        | .543                  |

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; HR, hazard ratio; MAVE, major adverse vascular events (composite endpoint of all-cause mortality, major amputation, and target vessel and/or limb revascularization [TVR/TLR]).
significant after adjustment. In other words, PVI may lower the likelihood of amputation in both groups, but patients with CKD retain a substantial residual risk of death not modified by revascularization. Prior studies have also found that CKD was a strong independent risk factor for death, with heightened risk associated with worse renal function. Similarly, in a study of veteran patients undergoing PVI, those with CKD had higher rates of mortality and more frequent progression to dialysis compared to patients without CKD undergoing PVI. While our study does suggest that the mortality risks of patients with PAD and concomitant CKD may not be mediated by PVI, the kidney-specific risks of the procedure remain unclear in LIBERTY due to the lack of renal-specific follow-up. Using outcomes across many hospitals with high procedural success in both cohorts, it is clear that CKD contributes an inherent risk of higher cardiovascular mortality as a nature of the underlying disease and is an independent predictor of death post-PVI.

Patients with CKD in our study did have higher unadjusted rates of major amputation when compared with patients without CKD and had several factors that are known to elevate the risk of major amputation after PVI. Advanced age, coexisting diabetes mellitus, advanced disease with higher Rutherford classification and fewer runoff vessels, and non-compressible ABIs were all more frequent among patients with CKD in our analysis and all have been associated with worse limb-related outcomes. Also, the patients with CKD were more likely to have lesions treated below the knee than were patients without CKD, which has previously been shown to increase the risk of limb loss. Given that many of the factors associated with higher amputation rate were included in our model, the lack of significant association between CKD and major amputation after adjustment was unexpected. However, with a low overall rate of major amputations, as evidenced by broad confidence interval estimated at 30 day (0.99-11.71) and 1 year (0.91-3.17), the lack of statistical significance may reflect a lack of

![Figure 2](image)

**Figure 2**  Kaplan–Meier curves comparing major Adverse vascular events, all-cause mortality, major amputation, and target vessel/lesion revascularization in patients with and without chronic kidney disease. Kaplan Meier curves are shown for A, MAVE; B, all-cause mortality; C, major amputation; and D, target vessel/lesion revascularization in patients with and without CKD. Event rates of each outcome for patients with CKD compared with patients without CKD at 1 year after PVI. CKD, chronic kidney disease; MAVE, major adverse vascular events; PVI, peripheral vascular intervention.
power. It is also possible that the low amputation rates among both groups reflects contemporary practice and advanced technique in PVI. Ultimately, it remains prudent to continue working toward minimizing the amputation risk faced by patients with CKD following PVI.

Given our findings of poor outcomes in patients with CKD following PVI, the critical question is how to improve outcomes in this complex population. The literature has provided few alternative management strategies for patients with symptomatic PAD and concomitant CKD. These patients may benefit more from aggressive medical management with high-intensity statins and/or PCSK9 inhibitors, more aggressive control of diabetes mellitus with GLP-1 and/or SGLT2 inhibitors, and more aggressive antiplatelet or antithrombotic medications (including rivaroxaban as demonstrated in the COMPASS trial). These therapies have proven benefit and are often underprescribed in the PAD population. Of the patients with CKD in our study, 78.6% were on aspirin, 82.5% on lipid lowering therapy, 69.0% on clopidogrel, and 65.3% on dual antiplatelet therapy post index procedure. Adherence to guideline recommended therapy should remain the major focus in the care of this patient population. Given the worse post-PVI outcomes associated with CKD, there has been a trend towards lower rates of revascularization, both surgical and endovascular, even in patients with only moderate renal insufficiency. Our findings add context to the current limited knowledge of cardiovascular and limb outcomes following PVI, and it is clear that further work is needed in the CKD population. Specifically, a deficit of evidence exists about whether intervention is beneficial in patients with CKD and how to balance the kidney-specific risks of PVI. It remains imperative to find the best approach to reduce symptom burden while minimizing the risk of mortality and limb loss in this vulnerable group.

4.1 Study limitations

Our study does have some limitations. The LIBERTY 360 study was observational in nature: the choices of PVI procedure type and devices were clinician- and site-dependent, which may contribute to the more frequent rate of atherectomy use in LIBERTY than has been reported in Medicare analyses of office-based laboratories. While this may decrease the generalizability of our findings, the frequency of atherectomy use in office-based practice is increasing rapidly. Because this is a post-hoc analysis, the original study was not powered for our analysis and did not collect all variables of relevance to studying CKD, including change in eGFR or need for dialysis over the course of follow-up. Similarly, while target lesion and vessel revascularization were available, target limb revascularization was not collected, which may have lead to undercounting reinterventions. Finally, a relatively high number of patients were lost to follow up or withdrew over 1 year.

5 CONCLUSIONS

In conclusion, our results reflect contemporary practice of patients with symptomatic PAD with good procedural outcomes. After adjustment for baseline variables, CKD was independently associated with greater risk of all-cause mortality at 1 year post-PVI. There were low overall amputation rates and no significant difference in risk of amputation between the groups at 1 year. The increased risk of mortality among CKD patients suggests that PVI is not effectively mitigating the risk of death, and aggressive medical therapies with proven mortality benefit should likely be the focus in this vulnerable population. Ultimately, there is a need for more investigation into benefit and timing of endovascular intervention in patients with any degree of CKD.

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SUPPORTING INFORMATION
Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Narcisse DI, Weissler EH, Rymer JA, et al. The impact of chronic kidney disease on outcomes following peripheral vascular intervention. Clin Cardiol. 2020;43:1308–1316. https://doi.org/10.1002/clc.23444