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ORIGINAL RESEARCH

Survival and Causes of Death Among Veterans With Lower Extremity Revascularization With Paclitaxel-Coated Devices: Insights From the Veterans Health Administration

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BACKGROUND: The long-term safety of paclitaxel-coated devices (PCDs; drug-coated balloon or drug-eluting stent) for peripheral endovascular intervention is uncertain. We used data from the Veterans Health Administration to evaluate the association between PCDs, long-term mortality, and cause of death.

METHODS AND RESULTS: Using the Veterans Administration Corporate Data Warehouse in conjunction with *International Classification of Diseases, Tenth Revision* (*ICD-10*) Procedure Coding System, Current Procedural Terminology, and Healthcare Common Procedure Coding System codes, we identified patients with peripheral artery disease treated within the Veterans Administration for femoropopliteal artery revascularization between October 1, 2015, and June 30, 2019. An adjusted Cox regression, using stabilized inverse probability–weighted estimates, was used to evaluate the association between PCDs and long-term survival. Cause of death data were obtained using the National Death Index. In total, 10 505 patients underwent femoropopliteal peripheral endovascular intervention; 2265 (21.6%) with a PCD and 8240 (78.4%) with a non-PCD (percutaneous angioplasty balloon and/or bare metal stent). Survival rates at 2 years (77.4% versus 79.7%) and 3 years (70.7% versus 71.8%) were similar between PCD and non-PCD groups, respectively. The adjusted hazard for all-cause mortality for patients treated with a PCD versus non-PCD was 1.06 (95% CI, 0.95–1.18, P=0.3013). Among patients who died between October 1, 2015, and December 31, 2017, the cause of death according to treatment group, PCD versus non-PCD, was similar.

CONCLUSIONS: Among patients undergoing femoropopliteal peripheral endovascular intervention within the Veterans Administration Health Administration, there was no increased risk of long-term, all-cause mortality associated with PCD use. Cause-specific mortality rates were similar between treatment groups.

Key Words: paclitaxel ■ peripheral artery disease ■ peripheral endovascular intervention

See Editorial by Drachman and Garasic

The safety of paclitaxel-coated devices (PCDs; such as drug-coated balloon [DCB] or drug-eluting stent [DES]) for peripheral endovascular intervention (PVI) among patients with lower extremity peripheral artery disease is unclear. A meta-analysis and systematic review found the use of PCDs

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CLINICAL PERSPECTIVE

What Is New?

- This work uses patient-level data from the Veterans Administration Health Administration to evaluate the association between paclitaxel-coated devices, long-term mortality, and cause of death.
- Among patients undergoing femoropopliteal peripheral endovascular intervention, there was no increased risk of long-term, all-cause mortality associated with paclitaxel-coated device use.
- Furthermore, cause-specific mortality rates were similar between treatment groups.

What Are the Clinical Implications?

- This postmarket surveillance study demonstrates that within the Veterans Health Administration, peripheral endovascular intervention with paclitaxel-coated devices are not associated with an increased risk of long-term, all-cause mortality.

Nonstandard Abbreviations and Acronyms

CDW	corporate data warehouse
CLI	critical limb ischemia
DCB	drug-coated balloon
DES	drug-eluting stent
NDI	National Death Index
PCD	paclitaxel-coated device
PVI	peripheral endovascular intervention
VA	Veterans Administration
VHA	Veterans Health Administration

to be associated with increased mortality at 2 years and 4 to 5 years post-PVI when compared with non-PCDs (percutaneous angioplasty balloon and/or bare metal stent).[1] Contrary to these findings, subsequent large analyses of Centers for Medicare and Medicaid Services data did not observe an increased mortality signal among patients treated with PCDs compared with those treated with non-PCDs.[2,3] In addition, no direct association between PCDs and causes of death have been established.[2]

To address this controversy, we used data from the largest integrated health network in the United States, the Veterans Administration (VA) Health System, to evaluate the association between the use of PCDs and long-term mortality in a contemporary cohort of patients treated in clinical practice. We also specifically assessed the cause of death in this cohort.

METHODS

This study was approved by the Research and Development Committee at the Durham VA Medical Center in Durham, NC. As a retrospective cohort study design with no subject contact and minimal privacy risk, informed consent was waived. The data used in the present research belong to the Veterans Health Administration (VHA) and are not publicly available for reproduction of the study findings. The methodology, however, is characterized in sufficient detail to permit reproduction of the results by VA researchers with access to the VA Corporate Data Warehouse (CDW) and the National Death Index (NDI).

Data Source

The present study uses data from the VA CDW, which is the national data repository for VHA administrative and clinical systems. These data are obtained via the Computerized Patient Record System interface to capture medical information across 144 VA medical centers and 1221 outpatient clinics. The Computerized Patient Record System is the documentation tool for all VA clinical activities, including diagnoses, procedures, laboratory results, medications, and imaging.[4] Cause of death was obtained through a second data source, the NDI, which is a subset of the VA Suicide Repository.[5] The NDI was established in 1981 by the National Center for Health Statistics and is a centralized database that houses dates and cause of death for every death record filed in the United States as of 1979.[6] Data for any given year are uploaded to the NDI annually, approximately 1 year after the conclusion of the respective year. As such, there is a lag time of 1 to 2 years between events and availability of cause of death in the NDI. At the time of the present analysis, data through 2017 were available.

Study Population

Using the VA CDW in conjunction with diagnosis and procedure codes, we identified all patients with a diagnosis of peripheral artery disease treated within the VHA, in either inpatient or outpatient settings, for femoropopliteal artery revascularization between October 1, 2015, through June 30, 2019. Table S1 lists all diagnosis and procedural codes. PVI (consisting of any permutation of DES, DCB, bare metal stent, or percutaneous angioplasty balloon) was identified using *International Classification of Diseases, Tenth Revision* (*ICD-10*) Procedure Coding System, Current Procedural Terminology, or Healthcare Common Procedure Coding System codes. In the occurrence where a patient had multiple procedures during the study period, patients were included in the non-PCD cohort only if they never received treatment with a PCD (DES or DCB). Within the PCD cohort, the index procedure was defined as the first use of a PCD.

Study Variables and Outcomes

Baseline variables such as age, sex, race, comorbidities, and the presence of claudication and critical limb ischemia (CLI) were obtained from the VA CDW using *ICD-10–Clinical Modification* diagnosis codes present on problem lists and/or visits prior through the date of the index PVI (Table S2). The primary outcome of interest was mortality and was identified using date of death in the CDW. Social security number, date of birth, and sex were used to cross-reference the NDI to obtain cause of death, categorized as *ICD-10* codes (Table S3), and was available for 98% of patients suffering a mortality event between 2015 and 2017.

Statistical Analysis

Baseline statistics are displayed as counts and percentages for categorical variables, and means with standard deviation for continuous variables. Differences between groups were tested using χ^2 tests for categorical variables and *t* tests for continuous variables. The overall survival was defined as the time from date of procedure to the date of death from any cause. Patients alive at last contact date or the end of the study period were censored. Survival was estimated for PCD versus non-PCD and further stratified for presentation (claudication and CLI) using Kaplan–Meier estimates, and differences between groups were evaluated using the log-rank test. A Cox regression model was used to evaluate the association between PCDs and long-term survival. Both unadjusted and adjusted associations between PCDs and long-term survival were examined. To estimate adjusted associations, differences in outcomes were assessed using stabilized inverse probability–weighted estimates based on the probability of a patient undergoing treatment with a PCD (DES or DCB) determined by observed covariates.[7] Logistic regression modeling with treatment with a PCD (yes/no) as the outcome was used to determine the relationship between covariates, including presentation (claudication or CLI) and atherectomy use and treatment with a PCD to calculate weights. The adjusted association between treatment with a PCD and long-term survival was then estimated by applying these weights to the Cox model. Concordance statistics for long-term survival were performed and described (Table S4 and Figures S1–S4). Additional sensitivity analyses were performed to explore findings from the primary model. To account for potential differences in treatment time periods and subjects with varying follow-up, cohorts with specific amounts of observed follow-up time (only 2-year and 3-year follow-ups) were separately described (Tables S5 and S6) and analyzed with and without inverse probability–weighted estimates (Tables S7 and S8). A *P* value <0.05 was considered significant. All analyses were performed using SAS 9.4 for Windows.

RESULTS

Patient and Procedure Characteristics

During the study period, 10 505 patients underwent femoropopliteal PVI: 2265 (21.6%) with a PCD and 8240 (78.4%) with a non-PCD (Table 1). Among patients assigned to the PCD cohort, 803 (35.5%) underwent prior PVI with a non-PCD device. In patients treated with a PCD, 897 (39.6%) were treated with DCB alone, 1201 (53.0%) were treated with with DES alone, and 167 (7.4%) were treated with DCB+DES. Overall, adjuvant atherectomy was used in 2291 (21.8%) of cases; 606 (26.8%) among patients treated with a PCD and 1685 (20.4%) treated with a non-PCD. The mean±SD age of the overall study population was 68.9±8.2 years, of which 10 303 (98.1%) were male and 7725 (73.5%) were White. In total, 4983 (47.4%) patients had current or prior tobacco use, 6124 (58.3%) had diabetes mellitus, and 3656 (34.8%) had CLI at the time of procedure. Patients treated with a PCD were more likely to have prior or current tobacco use, valvular heart disease, and CLI at presentation compared with those treated with non-PCD.

Survival

Following femoropopliteal PVI, the median follow-up for the remaining living patients (n=8503) was 20.3 months (interquartile range, 10.0–31.8 months). Figure 1 depicts the long-term survival following PVI among patients treated with and without PCDs in the overall study population. Survival rates at 2 years (77.4% versus 79.7%) and 3 years (70.7% versus 71.8%) were similar between the PCD and non-PCD groups, respectively. Patients presenting with CLI had lower survival rates at any given time point compared with patients presenting for claudication. Within these stratified subgroups, the survival rates between patients undergoing PVI with a PCD versus non-PCD were similar (Figure 2). The hazard ratio (HR) for all-cause mortality for patients treated with a PCD versus a non-PCD was 1.05 (95% CI, 0.94–1.16; *P*=0.4045). After adjustment with inverse probability–weighted estimates, the hazard for all-cause mortality remained similar (HR, 1.06; 95% CI, 0.95–1.18; *P*=0.3013; Table 2). Concordance statistics indicated that the multivariate Cox regression model had higher prediction accuracy compared with a univariate Cox regression model without covariate adjustment.

Table 1. Baseline Characteristics

	Nonpaclitaxel, n=8240	Paclitaxel, n=2265	Total, N=10 505	*P* Value
Baseline				
Age, y				0.0214*
Mean±SD	68.8±8.2	69.2±8.2	68.9±8.2	
Sex				0.4424†
Male	8086 (98.1)	2217 (97.9)	10 303 (98.1)	
Race				0.0695†
White	6045 (73.4)	1680 (74.2)	7725 (73.5)	
Black	1750 (21.2)	442 (19.5)	2192 (20.9)	
Other	445 (5.4)	143 (6.3)	588 (5.6)	
Alcohol abuse	1121 (13.6)	288 (12.7)	1409 (13.4)	0.2715†
Anemia	990 (12.0)	300 (13.2)	1290 (12.3)	0.1141†
Arrhythmia	2558 (31.0)	685 (30.2)	3243 (30.9)	0.4649†
Coagulopathy	307 (3.7)	89 (3.9)	396 (3.8)	0.6522†
Chronic kidney disease	2120 (25.7)	585 (25.8)	2705 (25.7)	0.9235†
Chronic obstructive pulmonary disease	2606 (31.6)	748 (33.0)	3354 (31.9)	0.2062†
Collagen vascular disease	191 (2.3)	57 (2.5)	248 (2.4)	0.5814†
Congestive heart failure	2158 (26.2)	608 (26.8)	2766 (26.3)	0.5314†
Current or prior tobacco use	3867 (46.9)	1116 (49.3)	4983 (47.4)	0.0481†
Dementia	405 (4.9)	113 (5.0)	518 (4.9)	0.8856†
Depression	2056 (25.0)	582 (25.7)	2638 (25.1)	0.4696†
Diabetes mellitus	4773 (57.9)	1351 (59.6)	6124 (58.3)	0.1410†
Fluid electrolyte disorder	1305 (15.8)	362 (16.0)	1667 (15.9)	0.8672†
Hemiplegia or paraplegia	2194 (26.6)	617 (27.2)	2811 (26.8)	0.5586†
Hypertension	6802 (82.5)	1875 (82.8)	8677 (82.6)	0.7957†
Hypothyroid	643 (7.8)	143 (6.3)	786 (7.5)	0.0170†
Liver disease	836 (10.1)	234 (10.3)	1070 (10.2)	0.7960†
Malignancy	1215 (14.7)	354 (15.6)	1569 (14.9)	0.2959†
Myocardial infarction	469 (5.7)	141 (6.2)	610 (5.8)	0.3364†
Neurologic disorder	727 (8.8)	214 (9.4)	941 (9.0)	0.3560†
Obesity	1309 (15.9)	367 (16.2)	1676 (16.0)	0.7150†
Psychiatric	153 (1.9)	46 (2.0)	199 (1.9)	0.5904†
Substance abuse	610 (7.4)	182 (8.0)	792 (7.5)	0.3127†
Valvular heart disease	673 (8.2)	229 (10.1)	902 (8.6)	0.0035†
Weight loss	582 (7.1)	174 (7.7)	756 (7.2)	0.3127†
Procedural				
Adjuvant atherectomy	1685 (20.4)	606 (26.8)	2291 (21.8)	<0.0001†
Claudication	2012 (24.4)	731 (32.3)	2743 (26.1)	<0.0001†
Critical limb ischemia	2698 (32.7)	958 (42.3)	3656 (34.8)	<0.0001†

Data are provided as mean±SD or number (percentage).
*Two-sample *t* test.
†Chi-square test.

Sensitivity Analyses

Cohorts with only 2-year and 3-year follow-ups had similar distributions of baseline clinical and procedural characteristics (Tables S5 and S7). After inverse probability–weighted adjustment for these individual cohorts, there remained no significant difference in all-cause mortality (HR, 0.98; 95% CI, 0.86–1.12; *P*=0.7672 for 2-year follow-up; HR, 1.11; 95% CI, 0.91–1.35; *P*=0.3212 for 3-year follow-up; Tables S6 and S8).

Cause of Death

Cause of death was available for the 771 patients who died between October 1, 2015, and December 31, 2017. There were 169 deaths (n=1328; 12.7%) in

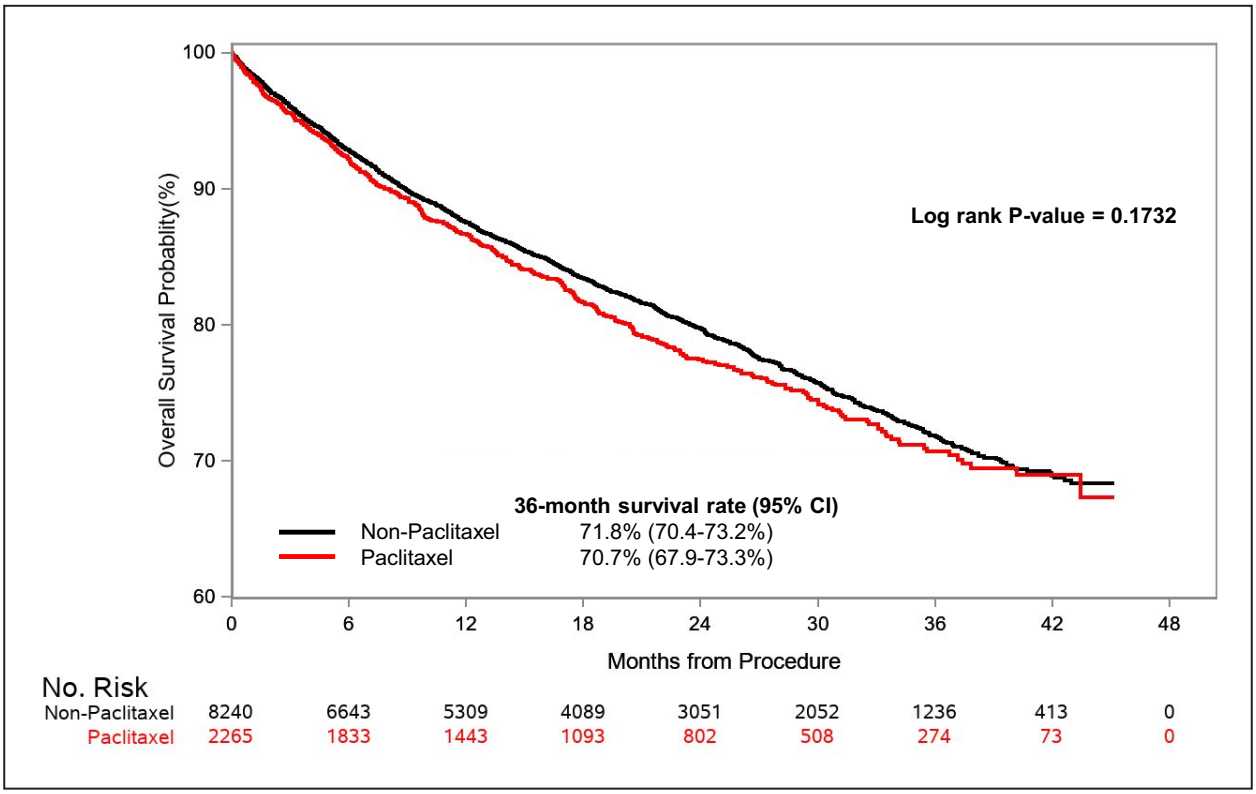

Figure 1. **Kaplan–Meier curve for overall survival: drug coated vs. non–drug coated.**

the PCD group and 602 deaths (n=4893; 12.3%) in the non-PCD group. Of these, the most common causes of death were cardiovascular (n=298, 38.7%), complications of diabetes mellitus (n=103, 13.4%), malignancy (n=86, 11.2%), and infection (n=67, 8.7%). Causes of death according to treatment group, PCD versus non-PCD, were similar: cardiovascular (34.9% versus 39.7%; *P*=0.2838), diabetes mellitus–related complication (13.0% versus 13.5%; *P*>0.999), malignancy (11.8% versus 11.0%; *P*=0.7822), and infection (9.5% versus 8.5%; *P*=0.6462; Figure 3).

DISCUSSION

This is the first study examining the impact of PCD use on mortality within the VHA and shows several important findings. First, in >10 000 veterans with peripheral arterial disease undergoing femoropopliteal PVI, the rates of 2-year and 3-year all-cause mortality were similar among patients undergoing revascularization with PCD (DCB and/or DES) and non-PCD (percutaneous angioplasty balloon and/or bare metal stent) devices. Second, all-cause mortality risk related to exposure to PCD was no different when stratified according to claudication or CLI presentations. Lastly, after adjustment for treatment assignment, no statistically significant risk in all-cause mortality was observed between the use of PCD and non-PCD devices.

Before the reporting of a late mortality signal in a 2018 meta-analysis by Katsanos et al., PCDs were frequently used in femoropopliteal endovascular procedures as they improved short-term and intermediate-term primary patency rates.[1,8–11] The late mortality signal was confirmed by the US Food and Drug Administration's analysis of long-term follow-up data from pivotal premarket randomized trials for PCD and most recently by an individual patient data meta-analysis of US commercially available PCDs.[12,13] However, limitations with these early studies have been recognized, including small sample sizes, substantial amounts of missing data, and poor patient follow-up. Nevertheless, PCDs now carry revised package labeling with information detailing the potential for late mortality. Globally, international clinical trials were initially halted (SWEDEPAD [Swedish Drug-Elution Trial in Peripheral Arterial Disease] and BASIL-3 [Bypass Versus Angioplasty in Severe Ischaemia of the Leg]), and the UK Medical and Healthcare Products Regulatory Agency has advised against PCD use in intermittent claudication.[14] The endovascular community is now left with difficult decisions regarding when to use PCDs in clinical practice, leading to wide variability in practice patterns. The

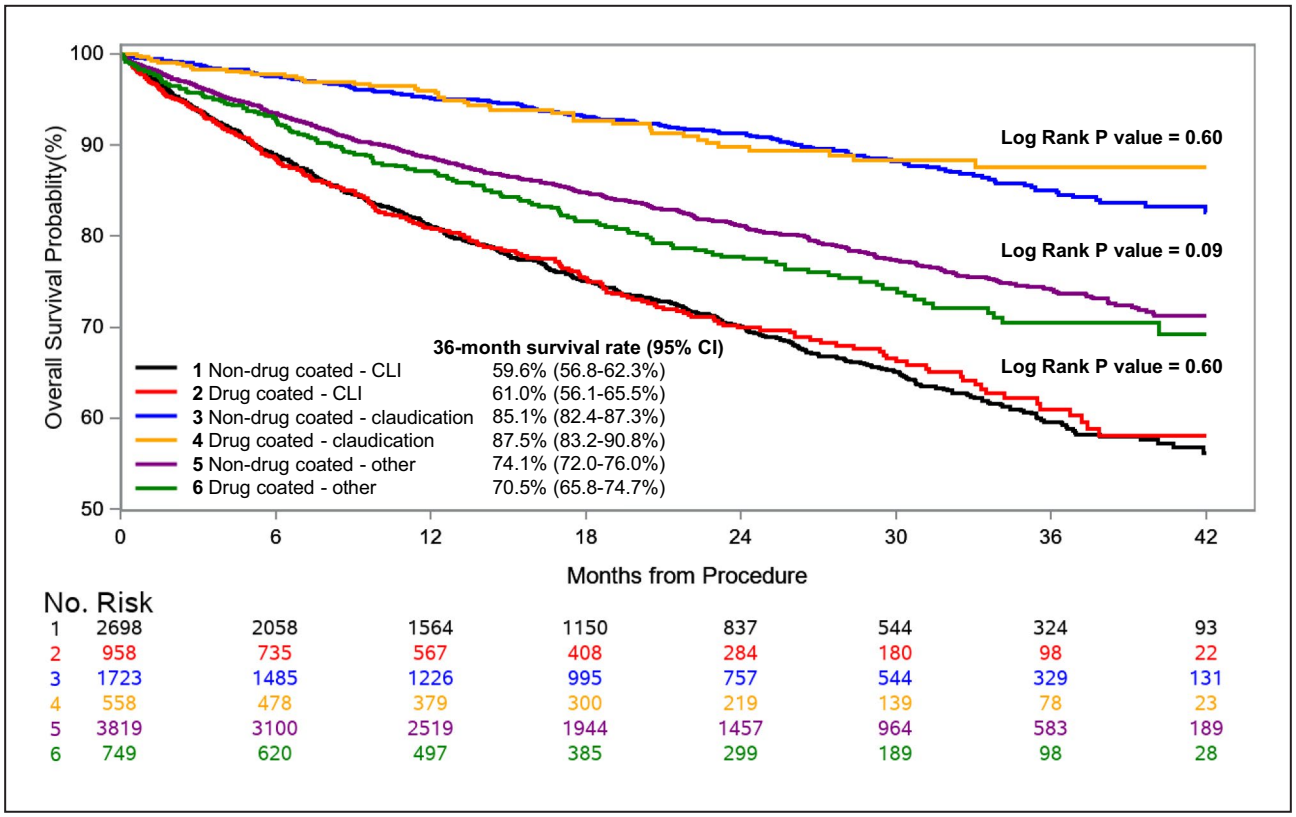

Figure 2. Kaplan–Meier curve for overall survival stratified by presentation (claudication and CLI).
CLI indicates critical limb ischemia.

Circulatory System Devices Panel and the US Food and Drug Administration acknowledge that additional clinical study data, particularly those evaluating long-term safety of PCDs, are needed.

To this end, a number of industry-sponsored, patient-level data studies have reported no mortality difference with the use of their respective drug-coated device.[15–18] Two prior large studies involving 16 560 (median 389-day follow-up) and 83 225 (365-day follow-up) Centers for Medicare and Medicaid Services beneficiaries undergoing PVI with drug-coated devices found no associated increased risk in all-cause mortality.[2,3] The present analysis reaffirms and adds to this literature by demonstrating no increased all-cause mortality risk through 3 to 4 years following the index procedure in a real-world US patient population that includes patients <65, who are not captured in the Medicare studies. Furthermore, our findings are consistent with a recent, large, real-world analysis using German health claims data among patients treated with PCDs and a median follow-up period of 7.7 years.[19]

Given the unique aspects of the VHA model of healthcare delivery, patients generally stay within the VHA for both follow-up medical care and pharmacy refills. A high patient retention rate combined with a detailed data collection system via the Computerized Patient Record System provided us with a study cohort not limited by age and without missing data during the study follow-up period. This was expected as aggregate patient-level data across the VHA have been found to have both high quality and interoperability, allowing for weekly updates to mirror acute changes in patient clinical status.[20] Furthermore, morality data within VA databases have been previously validated to be both complete (100%) and highly accurate (98%) when compared with the NDI, which is considered the "gold standard."[6] As such, a large patient sample, a complete data set, and no loss to follow-up are key strengths of the VA CDW that enhance the robustness of our findings.

Identifying modes of death in patients undergoing lower extremity PVI with PCDs is critical as there are currently no pathophysiologic mechanisms explaining paclitaxel's role in impacting late mortality. Concerns have been raised as to whether exposure to higher systemic doses of the cytotoxic agent seen with lower extremity devices may increase patient susceptibility to not only cardiovascular events but also malignancy or infection.[21,22] Another strength of the present analysis

Table 2. All-Cause Mortality HR Estimates From Cox Regression Models

Parameter	Unadjusted		Adjusted	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Drug coated vs. non–drug coated	1.05 (0.94–1.16)	0.4045	1.06 (0.95–1.18)	0.3013
Age	1.04 (1.04–1.05)	<0.0001	1.04 (1.03–1.05)	<0.0001
Sex (female vs. male)	0.83 (0.57–1.22)	0.3527	0.81 (0.55–1.21)	0.3051
Race (Black vs. White)	0.86 (0.77–0.97)	0.0142	0.87 (0.77–0.98)	0.0202
Race (other vs. White)	1.14 (0.95–1.36)	0.1655	1.16 (0.97–1.40)	0.1020
Comorbidity*				
Alcohol abuse	1.06 (0.91–1.23)	0.4896	1.04 (0.89–1.22)	0.5954
Anemia	1.03 (0.91–1.17)	0.6249	1.04 (0.91–1.18)	0.5550
Arrhythmia	1.13 (1.02–1.24)	0.0175	1.16 (1.05–1.28)	0.0048
Coagulopathy	1.15 (0.93–1.40)	0.1909	1.15 (0.94–1.42)	0.1828
Chronic kidney disease	1.40 (1.27–1.55)	<0.0001	1.40 (1.26–1.56)	<0.0001
Chronic obstructive pulmonary disease	1.14 (1.03–1.26)	0.0102	1.14 (1.03–1.26)	0.0093
Collagen vascular disease	0.84 (0.62–1.15)	0.2790	0.86 (0.63–1.17)	0.3349
Congestive heart failure	1.63 (1.47–1.80)	<0.0001	1.64 (1.48–1.82)	<0.0001
Current or prior tobacco use	0.80 (0.72–0.88)	<0.0001	0.81 (0.73–0.89)	<0.0001
Dementia	1.36 (1.16–1.60)	0.0001	1.38 (1.16–1.64)	0.0002
Depression	1.10 (0.99–1.23)	0.0715	1.11 (1.00–1.24)	0.0487
Diabetes mellitus	1.28 (1.15–1.42)	<0.0001	1.26 (1.14–1.40)	<0.0001
Fluid electrolyte	1.34 (1.19–1.50)	<0.0001	1.34 (1.19–1.51)	<0.0001
Hemiplegia or paraplegia	0.89 (0.81–0.99)	0.0309	0.90 (0.81–1.00)	0.0499
Hypertension	0.64 (0.57–0.72)	<0.0001	0.64 (0.57–0.72)	<0.0001
Hypothyroid	0.76 (0.64–0.90)	0.0012	0.76 (0.64–0.90)	0.0014
Liver disease	1.10 (0.94–1.29)	0.2183	1.12 (0.95–1.31)	0.1697
Malignancy	1.35 (1.21–1.51)	<0.0001	1.33 (1.19–1.49)	<0.0001
Myocardial infarction	1.45 (1.25–1.69)	<0.0001	1.39 (1.19–1.64)	<0.0001
Neurologic disorder	1.01 (0.87–1.17)	0.8663	1.00 (0.86–1.17)	0.9882
Obesity	0.69 (0.60–0.79)	<0.0001	0.69 (0.60–0.79)	<0.0001
Psychiatric	1.11 (0.82–1.52)	0.4885	1.10 (0.81–1.47)	0.5460
Substance abuse	1.06 (0.86–1.30)	0.5899	1.06 (0.87–1.29)	0.5737
Valvular heart disease	1.15 (1.00–1.33)	0.0460	1.14 (0.98–1.32)	0.0793
Weight loss	1.58 (1.38–1.82)	<0.0001	1.59 (1.38–1.84)	<0.0001
Procedural				
Adjuvant atherectomy	0.91 (0.82–1.02)	0.1013	0.91 (0.81–1.02)	0.0984
Claudication	0.57 (0.50–0.65)	<0.0001	0.58 (0.51–0.66)	<0.0001
Critical limb ischemia	1.47 (1.34–1.62)	<0.0001	1.48 (1.34–1.62)	<0.0001

HR indicates hazard ratio.
*Reference for comorbidities is "no condition."

is the ability to link VA administrative data with the NDI, which is housed as a subset of the VA Suicide Repository, for 3 years of our study period. All mortality events were both validated and linked to a cause of death. Rates of cause of death from cardiovascular, malignancy, and infection were no different among patients treated with PCD versus non-PCD and consistent across all other major causes of death explored. It is important to note that outside of randomized controlled trials where death events undergo a rigorous adjudication process, the NDI is widely considered the primary reliable source of identifiable death data and the "gold standard" for mortality determination.[6,23]

A more recent meta-analysis by Katsanos et al. evaluated PCD use in below-the-knee interventions for CLI and found significantly lower rates of 1-year amputation-free survival in paclitaxel-treated patients compared with uncoated balloon angioplasty (13.7% crude risk of death or limb loss versus 9.4%; HR, 1.52; 95% CI, 1.12–2.07; *P*=0.008).[24] The benefit of paclitaxel

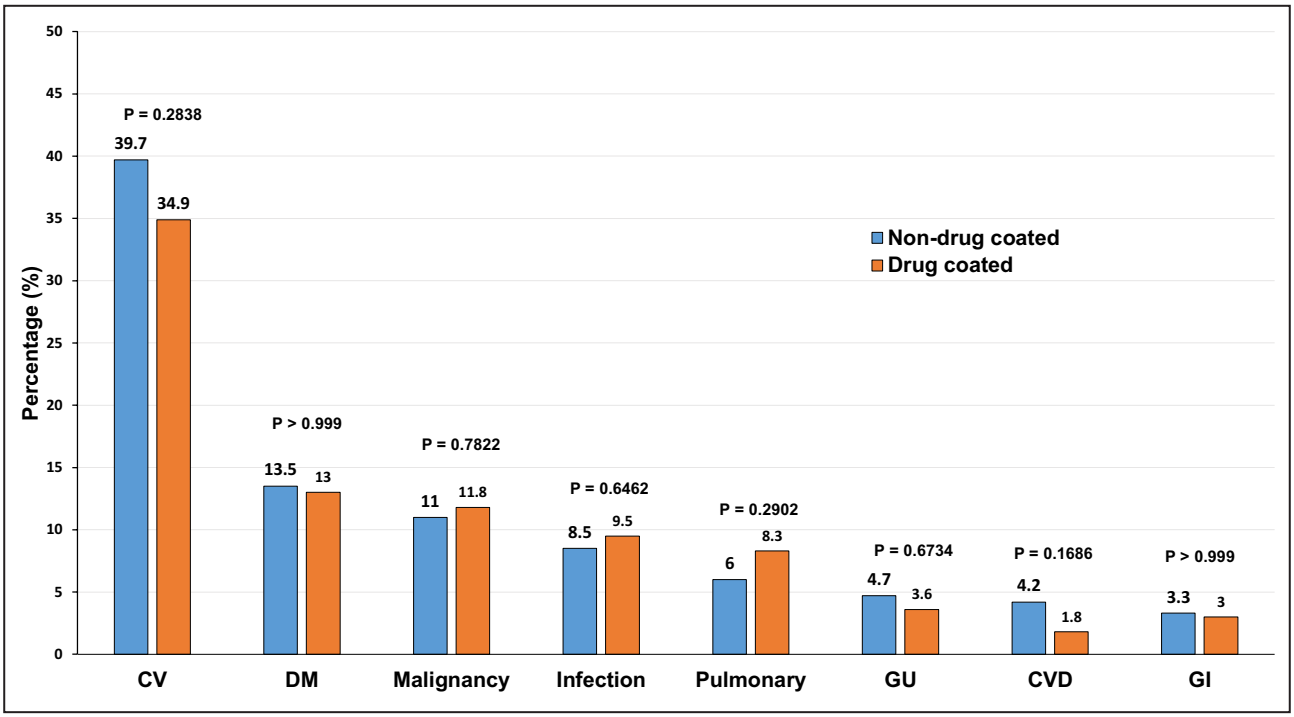

Figure 3. Specific-cause mortality: non–drug coated vs. drug coated.
CV indicates cardiovascular; CVD, cerebrovascular; DM, diabetes mellitus–related complication; GI, gastrointestinal; and GU, genitourinary.

treatment in below-the-knee arteries was evident by significant reductions in target lesion revascularization (11.8% crude risk versus 25.6% in controls; HR, 0.53; 95% CI, 0.35–0.81; *P*=0.004). Our analysis evaluated mortality by clinical presentations of claudication and CLI to draw comparable mortality rate comparisons with other data sets and to ensure that patients at higher risk of CLI with more comorbidities were not susceptible to paclitaxel exposure differentially. This subgroup analysis was performed knowing that PCD for below-the-knee use is not commercially available in the United States. Nevertheless, many patients with CLI are treated with PCDs for femoropopliteal revascularization and therefore sustain paclitaxel exposure. As expected, mortality in the CLI group was significantly higher than in patients with claudication at all time points; however, there was no within-group treatment effect of paclitaxel exposure on mortality throughout the 3-year to 4-year study period. Although this finding provides additional reassurance, further prospective data on combination therapies with below-the-knee PCD devices are warranted.

There are limitations to this analysis. First, the present study is observational with a nonrandomized treatment that cannot account for operator selection bias, and unmeasured confounders may be present. However, efforts were made to validate findings through sensitivity analyses such as the assessment of outcomes among cohorts with varying degrees of follow-up. Second, for patients undergoing PVI with a PCD, index procedure was defined as first incidence of PCD use despite the fact that they may have previously undergone PVI with a non-PCD device. Furthermore, subsequent PVI procedures were not taken into consideration. This methodology may introduce survival bias. Third, details of peripheral artery disease severity (such as Rutherford classification), lesion characteristics (eg, anatomy, atherosclerotic burden, and calcification), and specific brands of PCDs are unavailable. Fourth, diagnosis, procedural, and cause of death codes are subject to misclassification. Fifth, hospital-level and operator-level characteristics were not accounted for in the analysis. Lastly, CDW is a data set that is predominantly male, and therefore the findings may not be applicable to female patients.

CONCLUSIONS

In this large, contemporary cohort of patients undergoing femoropopliteal PVI within the VHA, there was no evidence of an associated increased risk of long-term, all-cause mortality among patients treated with PCDs when compared with those treated with non-PCDs. Cause-specific mortality rates were similar between both cohorts. This study also highlights the vast possibilities of using VHA CDW data with NDI for future postmarket safety surveillance of or safety signal discernment related to peripheral arterial devices.

ARTICLE INFORMATION

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Supplementary Material

Tables S1–S8
Figures S1–S4

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Supplemental Material

Table S1. ICD-10-CM Codes for cohort query and ICD-10-PCS, HCPCS, and CPT Codes of Femoropopliteal Peripheral Vascular Intervention.

Cohort query	E08.52, E09.52, E1051, E1051, E1052, E1059, E1151, E1152, E1159, E1351, E1352, E1359, I700, I70201, I70202, I70203, I70208, I70209, I70211, I70212, I70213, I70218, I70219, I70221, I70222, I70223, I70228, I70229, I70231, I70232, I70233, I70234, I70235, I70238, I70239, I70241, I70242, I70243, I70244, I70245, I70248, I70249, I7025, I70261, I70262, I70263, I70268, I70269, I70291, I70292, I70293, I70298, I70299, I70301, I70302, I70303, I70308, I70309, I70311, I70312, I70313, I70318, I70319, I70321, I70322, I70323, I70328, I70329, I70331, I70332, I70333, I70334, I70335, I70338, I70339, I70341, I70342, I70343, I70344, I70345, I70348, I70349, I7035, I70361, I70362, I70363, I70368, I70369, I70391, I70392, I70393, I70398, I70399, I70401, I70402, I70403, I70408, I70409, I70411, I70412, I70413, I70418, I70419, I70421, I70422, I70423, I70428, I70429, I70431, I70432, I70433, I70434, I70435, I70438, I70439, I70441, I70442, I70443, I70444, I70445, I70448, I70449, I7045, I70461, I70462, I70463, I70468, I70469, I70491, I70492, I70493, I70498, I70499, I70501, I70502, I70503, I70508, I70509, I70511, I70512, I70513, I70518, I70519, I70521, I70522, I70523, I70528, I70529, I70531, I70532, I70533, I70534, I70535, I70538, I70539, I70541, I70542, I70543, I70544, I70545, I70548, I70549, I7055, I70561, I70562, I70563, I70568, I70569, I70591, I70592, I70593, I70598, I70599, I70601, I70602, I70603, I70608, I70609, I70611, I70612, I70613, I70618, I70619, I70621, I70622, I70623, I70628, I70629, I70631, I70632, I70633, I70634, I70635, I70638, I70639, I70641, I70642, I70643, I70644, I70645, I70648, I70649, I7065, I70661, I70662, I70663, I70668, I70669, I70691, I70692, I70693, I70698, I70699, I70701, I70702, I70703, I70708, I70709, I70711, I70712, I70713, I70718, I70719, I70721, I70722, I70723, I70728, I70729, I70731, I70732, I70733, I70734, I70735, I70738, I70739, I70741, I70742, I70743, I70744, I70745, I70748, I70749, I7075, I70761, I70762, I70763, I70768, I70769, I70791, I70792, I70793, I70798, I70799, I7090, I7091, I7092, I739, I7401, I7409, I7410, I7419, I743, I744, I745, I748, I75021, I75022, I75023, I75029, I771, I96, L97101, L97102, L97103, L97104, L97109, L97111, L97112, L97113, L97114, L97119, L97121, L97122, L97123, L97124, L97129, L97201, L97202, L97203, L97204, L97209, L97211, L97212, L97213, L97214, L97219, L97221, L97222, L97223, L97224, L97229, L97301, L97302, L97303, L97304, L97309, L97311, L97312, L97313, L97314, L97319, L97321, L97322, L97323, L97324, L97329, L97401, L97402, L97403, L97404, L97409, L97411, L97412, L97413, L97414, L97419, L97421, L97422, L97423, L97424, L97429, L97501, L97502, L97503, L97504, L97509, L97511, L97512, L97513, L97514, L97519, L97521, L97522, L97523, L97524, L97529, L97801, L97802, L97803, L97804, L97809, L97811, L97812, L97813, L97814, L97819, L97821, L97822, L97823, L97824, L97829, L97901, L97902, L97903, L97904, L97909, L97911, L97912, L97913, L97914, L97919, L97921, L97922, L97923, L97924, L97929
Drug-coated balloon (DCB)	047K3Z1, 047L3Z1, 047M3Z1, 047N3Z1; C2623
Drug eluting stent (DES)	047K346, 047K34Z, 047K356, 047K35Z, 047K366, 047K36Z, 047K376, 047K37Z, 047L346, 047L34Z, 047L356, 047L35Z, 047L366, 047L36Z, 047L376, 047L37Z, 047M346, 047M34Z, 047M356, 047M35Z, 047M366, 047M36Z, 047M376, 047M37Z, 047N346, 047N34Z, 047N356, 047N35Z, 047N366, 047N36Z, 047N376, 047N37Z; C1874, C1875
Percutaneous transluminal angioplasty balloon (PTA)	047K3Z6, 047K3ZZ, 047L3ZZ, 047L3Z6, 047M3Z6, 047M3ZZ, 047N3Z6, 047N3ZZ; 37224; C1725
Bare metal stent (BMS)	047K3D6, 047K3DZ, 047K3E6, 047K3EZ, 047K3F6, 047K3FZ, 047K3G6, 047K3GZ, 047L3D6, 047L3DZ, 047L3E6, 047L3EZ, 047L3F6, 047L3FZ, 047L3G6, 047L3GZ, 047M3D6, 047M3DZ, 047M3E6, 047M3EZ, 047M3F6, 047M3FZ, 047M3G6, 047M3GZ, 047N3D6, 047N3DZ, 047N3E6, 047N3EZ, 047N3F6, 047N3FZ, 047N3G6, 047N3GZ; C1876, C1877

Drug-coated balloon (DCB) + bare metal stent (BMS)	047K3D1, 047L3D1, 047M3D1, 047N3D1
Drug-coated balloon (DCB) + drug eluting stent (DES)	047K341, 047L341, 047M341, 047N341

Table S2. ICD-10 Codes of Baseline and procedural characteristics.

Baseline	
Alcohol abuse	G621*, I426*, K292*, K700*, K703*, K709*, Z502*, Z714*, Z721*, F10*, E52*, T51*
Anemia	D50*, D508*, D509*, D51*, D52*, D53*
Arrythmia	I441*, I442*, I443*, I456*, I459*, R000*, R001*, R008*, T821*, Z450*, Z950*, I47*, I48*, I49*
Coagulopathy	D65*, D66*, D67*, D68*, D691*, D693*, D694*, D695*, D696*
Connective tissue disease	M05*, M32*, M33*, M34*, M06*, M315*, M351*, M353*, M360*
Congestive heart failure	I43*, I50*, I099*, I110*, I130*, I132*, I255*, I420*, I425*, I426*, I427*, I428*, I429*, P290*
Chronic kidney disease	N18*, N19*, N052*, N053*, N054*, N055*, N056*, N057*, N250*, I120*, I131*, N032*, N033*, N034*, N035*, N036*, N037*, Z490*, Z491*, Z492*, Z940*, Z992*
Chronic obstructive pulmonary disease	I278*, I279*, J684*, J701*, J703*, J40*, J41*, J42*, J43*, J44*, J45*, J46*, J47*, J60*, J61*, J62*, J63*, J64*, J65*, J66*, J67*
Current or prior tobacco use	F172*, F1720*, F17200*, F17201*, F17203*, F17208*, F1720*, F1721*, F17210*, F17211*, F17213*, F17218*, F17219*, F1722*, F17220*, F17221*, F17223*, F17228*, F17229*, F1729*, F17290*, F17291*, F17293*, F17298*, F17299*, Z720*, Z87891*
Dementia	F00*, F01*, F02*, F03*, G30*, F051*, G311*
Depression	F32*, F33*, F204*, F313*, F314*, F315*, F341*, F412*, F432*
Diabetes Mellitus	E110*, E111*, E116*, E118*, E119*, E120*, E121*, E126*, E128*, E100*, E101*, E106*, E108*, E109*, E129*, E130*, E131*, E136*, E138*, E139*, E140*, E141*, E146*, E148*, E149*, E143*, E144*, E145*, E147*, E127*, E132*, E133*, E134*, E135*, E137*, E142*, E113*, E114*, E115*, E117*, E122*, E123*, E124*, E125*, E102*, E103*, E104*, E105*, E107*, E112*
Fluid and electrolyte disorder	E86*, E87*, E222*
Hemiplegia or Paraplegia	H340*, I64*, I65*, I66*, I67*, I68*, I69*, G45*, G46*, I60*, I61*, I62*, I63*
Hypertension	I10*, I11*, I12*, I13*, I15*
Hypothyroidism	E00*, E01*, E02*, E03*, E890*
Liver disease	I850*, I859*, I864*, I982*, K704*, K711*, K721*, K729*, K765*, K766*, K767*, B18*, K73*, K74*, K700*, K701*, K702*, K703*, K709*, K713*, K714*, K715*, K717*, K760*, K762*, K763*, K764*, K768*, K769*, Z944*
Malignancy	C00*, C01*, C02*, C03*, C04*, C05*, C06*, C07*, C08*, C09*, C10*, C11*, C12*, C13*, C14*, C15*, C16*, C17*, C18*, C19*, C20*, C21*, C22*, C23*, C24*, C25*, C26*, C30*, C31*, C32*, C33*, C34*, C37*, C38*, C39*, C40*, C41*, C43*, C45*, C46*, C47*, C48*, C49*, C50*, C51*, C52*, C53*, C54*, C55*, C56*, C57*, C58*, C60*, C61*, C62*, C63*, C64*, C65*, C66*, C67*, C68*, C69*, C70*, C71*, C72*, C73*, C74*, C75*, C76*, C77*, C78*, C79*, C80*, C81*, C82*, C83*, C84*, C85*, C88*, C90*, C91*, C92*, C93*, C94*, C95*, C96*, C97*
Myocardial infarction	I21*
Neurologic disorder	G254*, G255*, G312*, G318*, G319*, G931*, G934*, R470*, G10*, G11*, G12*, G13*, G20*, G21*, G22*, G32*, G35*, G36*, G37*, G40*, G41*, R56*
Obesity	E66*
Psychiatric (not including depression)	F20*, F22*, F23*, F24*, F25*, F28*, F29*, F302*, F312*, F315*
Substance abuse	F11*, F12*, F13*, F14*, F15*, F16*, F18*, F19*, Z715*, Z722*
Valvular heart disease	A520*, I091*, I098*, Q230*, Q231*, Q232*, Q233*, Z952*, Z953*, Z954*, I05*, I06*, I07*, I08*, I34*, I35*, I36*, I37*, I38*, I39*
Weight Loss	E40*, E41*, E42*, E43*, E44*, E45*, E46*, R64*, R634*
Procedural	
Atherectomy	04CK3ZZ, 04CL3ZZ, 04CM3ZZ, 04CN3ZZ

Claudication	E0852, E0952, E105*, E115*, E135*, I700, I702*, I703*, I704*, I705*, I706*, I707*, I709*, I739, I740*, I7410, I7419, I743, I744, I745, I748, I7502*, I771, I96, L97*, E10621, E11621
Critical limb ischemia	I7022*, I7023*, I7024*, I7026*, I7032*, I7033*, I7034*, I7036*, I7042*, I7043*, I7044*, I7046*, I7052*, I7053*, I7054*, I7056*, I7062*, I7063*, I7064*, I7066*, I7072*, I7073*, I7074*, I7076*, E1052*, E10621*, E1152*, E11621*

* Wild card character (any sequence of characters after this will be included)

Table S3. ICD-10-CM Codes of Cause of Death.

Cardiovascular	I10, I110, I119, I120, I131, I132, I214, I219, I249, I250, I251, I255, I258, I259, I269, I272, I279, I429, I458, I469, I472, I48, I490, I498, I499, I500, I501, I509, I512, I516, I518, I519, I702, I709, I711, I714, I724, I739, I743, I772, I802, I99
Cerebrovascular	F019, I609, I613, I619, I620, I621, I629, I632, I634, I639, I64, I674, I679, I694
Complications of Diabetes Mellitus	E105, E107, E109, E111, E112, E115, E117, E119, E140, E141, E142, E145, E147, E149
Gastrointestinal	I850, K265, K274, K469, K550, K559, K566, K567, K629, K703, K720, K746, K767, K810, K811, K922
Genitourinary	N170, N179, N184, N185, N189, N19, N288, N390
Infection	A047, A099, A410, A419, A490, B020, B182, B238, I330, I350, I359, I38, J152, J159, J181, J189, K650, L031, L039, L089, M009, M726, M866, M869
Malignancy	C099, C139, C155, C159, C169, C170, C179, C189, C19, C210, C220, C259, C320, C329, C341, C349, C450, C499, C61, C64, C679, C719, C760, C762, C80, C833, C859, C900, C910, C911, C920, C959, C97, D380, D381, D469
Pulmonary	J439, J440, J441, J449, J690, J80, J841, J849, J90, J961, J969,

Table S4. Summary of Concordance Statistics for Overall Survival.

Statistics	Univariate Cox	Multivariate Cox
AIC	35026.977	33673.744
Harrell's C-statistic (SE)	0.5081 (0.0050)	0.7356 (0.0057)
Uno's C-statistic (SE)	0.5043 (0.0071)	0.7095 (0.0081)
Integrated AUC	0.5127	0.7621

AIC = Akaike information criterion; AUC = area under the receiver operating characteristic curve

Table S5. Baseline characteristics (subjects enrolled between 10/01/2015 and 07/09/2017).

N (%)	Non-Paclitaxel (N=3,824)	Paclitaxel (N=1,018)	Total (N=4,842)	P-value
Baseline				
Age				0.0351*
Mean (SD)	68.1 (8.3)	68.7 (8.3)	68.2 (8.3)	
Sex				0.8061†
M	3757 (98.2%)	999 (98.1%)	4756 (98.2%)	
Race				0.0218†
White	2836 (74.2%)	784 (77.0%)	3620 (74.8%)	
Black	800 (20.9%)	175 (17.2%)	975 (20.1%)	
Other	188 (4.9%)	59 (5.8%)	247 (5.1%)	
Alcohol abuse	452 (11.8%)	118 (11.6%)	570 (11.8%)	0.8405†
Anemia	410 (10.7%)	119 (11.7%)	529 (10.9%)	0.3790†
Arrhythmia	1060 (27.7%)	280 (27.5%)	1340 (27.7%)	0.8917†
Coagulopathy	118 (3.1%)	28 (2.8%)	146 (3.0%)	0.5783†
Chronic kidney disease	908 (23.7%)	235 (23.1%)	1143 (23.6%)	0.6593†
Chronic obstructive pulmonary disease	1059 (27.7%)	288 (28.3%)	1347 (27.8%)	0.7055†
Collagen vascular disease	94 (2.5%)	19 (1.9%)	113 (2.3%)	0.2664†
Congestive heart failure	916 (24.0%)	244 (24.0%)	1160 (24.0%)	0.9923†
Current or prior tobacco use	1612 (42.2%)	475 (46.7%)	2087 (43.1%)	0.0099†
Dementia	179 (4.7%)	39 (3.8%)	218 (4.5%)	0.2451†
Depression	862 (22.5%)	236 (23.2%)	1098 (22.7%)	0.6643†
Diabetes mellitus	2133 (55.8%)	575 (56.5%)	2708 (55.9%)	0.6876†
Fluid electrolyte disorder	471 (12.3%)	108 (10.6%)	579 (12.0%)	0.1356†
Hemiplegia or paraplegia	899 (23.5%)	253 (24.9%)	1152 (23.8%)	0.3711†
Hypertension	3046 (79.7%)	809 (79.5%)	3855 (79.6%)	0.8963†
Hypothyroid	276 (7.2%)	54 (5.3%)	330 (6.8%)	0.0314†
Liver disease	339 (8.9%)	73 (7.2%)	412 (8.5%)	0.0851†
Malignancy	530 (13.9%)	144 (14.1%)	674 (13.9%)	0.8151†
Myocardial infarction	177 (4.6%)	47 (4.6%)	224 (4.6%)	0.9873†
Neurologic disorder	281 (7.3%)	79 (7.8%)	360 (7.4%)	0.6561†
Obesity	477 (12.5%)	124 (12.2%)	601 (12.4%)	0.8010†
Psychiatric	64 (1.7%)	17 (1.7%)	81 (1.7%)	0.9935†
Substance abuse	247 (6.5%)	62 (6.1%)	309 (6.4%)	0.6688†
Valvular heart disease	246 (6.4%)	81 (8.0%)	327 (6.8%)	0.0851†
Weight loss	205 (5.4%)	63 (6.2%)	268 (5.5%)	0.3047†
Procedural				
Adjuvant atherectomy	817 (21.4%)	261 (25.6%)	1078 (22.3%)	0.0036†
Claudication	971 (25.4%)	306 (30.1%)	1277 (26.4%)	0.0027†
Critical limb ischemia	1190 (31.1%)	401 (39.4%)	1591 (32.9%)	<.0001†

* two sample t-test; † Chi-square test.

Table S6. Baseline characteristics (subjects enrolled between 10/01/2015 and 07/09/2016).

N (%)	Non-Paclitaxel (N=1,724)	Paclitaxel (N=396)	Total (N=4,120)	P-value
Baseline				
Age				0.2658*
Mean (SD)	67.9 (8.3)	68.4 (7.9)	67.9 (8.2)	
Sex				0.7547†
M	1694 (98.3%)	390 (98.5%)	2084 (98.3%)	
Race				0.1031†
White	1285 (74.5%)	306 (77.3%)	1591 (75.0%)	
Black	347 (20.1%)	63 (15.9%)	410 (19.3%)	
Other	92 (5.3%)	27 (6.8%)	119 (5.6%)	
Alcohol abuse	185 (10.7%)	33 (8.3%)	218 (10.3%)	0.1566†
Anemia	150 (8.7%)	35 (8.8%)	185 (8.7%)	0.9302†
Arrhythmia	456 (26.5%)	84 (21.2%)	540 (25.5%)	0.0310†
Coagulopathy	42 (2.4%)	11 (2.8%)	53 (2.5%)	0.6946†
Chronic kidney disease	389 (22.6%)	86 (21.7%)	475 (22.4%)	0.7156†
Chronic obstructive pulmonary disease	437 (25.3%)	103 (26.0%)	540 (25.5%)	0.7851†
Collagen vascular disease	37 (2.1%)	6 (1.5%)	43 (2.0%)	0.4218†
Congestive heart failure	387 (22.4%)	87 (22.0%)	474 (22.4%)	0.8369†
Current or prior tobacco use	644 (37.4%)	172 (43.4%)	816 (38.5%)	0.0250†
Dementia	65 (3.8%)	13 (3.3%)	78 (3.7%)	0.6422†
Depression	350 (20.3%)	73 (18.4%)	423 (20.0%)	0.4018†
Diabetes mellitus	927 (53.8%)	217 (54.8%)	1144 (54.0%)	0.7114†
Fluid electrolyte disorder	158 (9.2%)	27 (6.8%)	185 (8.7%)	0.1357†
Hemiplegia or paraplegia	359 (20.8%)	86 (21.7%)	445 (21.0%)	0.6938†
Hypertension	1299 (75.3%)	294 (74.2%)	1593 (75.1%)	0.6462†
Hypothyroid	120 (7.0%)	13 (3.3%)	133 (6.3%)	0.0065†
Liver disease	135 (7.8%)	20 (5.1%)	155 (7.3%)	0.0553†
Malignancy	239 (13.9%)	52 (13.1%)	291 (13.7%)	0.7027†
Myocardial infarction	55 (3.2%)	9 (2.3%)	64 (3.0%)	0.3359†
Neurologic disorder	107 (6.2%)	24 (6.1%)	131 (6.2%)	0.9134†
Obesity	181 (10.5%)	27 (6.8%)	208 (9.8%)	0.0264†
Psychiatric	25 (1.5%)	3 (0.8%)	28 (1.3%)	0.2763†
Substance abuse	92 (5.3%)	21 (5.3%)	113 (5.3%)	0.9787†
Valvular heart disease	90 (5.2%)	22 (5.6%)	112 (5.3%)	0.7880†
Weight loss	66 (3.8%)	18 (4.5%)	84 (4.0%)	0.5094†
Procedural				
Adjuvant atherectomy	366 (21.2%)	99 (25.0%)	465 (21.9%)	0.1020†
Claudication	445 (25.8%)	122 (30.8%)	567 (26.7%)	0.0428†
Critical limb ischemia	536 (31.1%)	167 (42.2%)	703 (33.2%)	<.0001†

* two sample t-test; † Chi-square test.

Table S7. All-Cause mortality hazard ratio estimates from Cox regression models (subjects enrolled between 10/01/2015 and 07/09/2017).

	Unadjusted		Adjusted	
Parameter	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
Drug coated vs non-drug coated	0.97 (0.85-1.11)	0.6665	0.98 (0.86-1.12)	0.7672
Age	1.04 (1.03-1.05)	<.0001	1.04 (1.03-1.05)	<.0001
Sex (female vs. male)	0.98 (0.61-1.58)	0.9489	0.95 (0.61-1.48)	0.8215
Race (AA vs. White)	1.00 (0.86-1.15)	0.9682	1.01 (0.87-1.16)	0.9432
Race (Other vs. White)	1.24 (1.00-1.55)	0.0500	1.27 (1.01-1.58)	0.0399
*Comorbidity**				
Alcohol abuse	1.21 (0.99-1.47)	0.0574	1.19 (0.98-1.44)	0.0823
Anemia	0.97 (0.82-1.15)	0.7607	0.99 (0.83-1.17)	0.8706
Arrhythmia	1.12 (.98-1.27)	0.0849	1.14 (1.00-1.29)	0.0495
Coagulopathy	1.02 (0.76-1.37)	0.8703	1.03 (0.76-1.38)	0.8645
Chronic kidney disease	1.33 (1.17-1.51)	<.0001	1.35 (1.18-1.54)	<.0001
Chronic obstructive pulmonary disease	1.15 (1.02-1.31)	0.0261	1.16 (1.03-1.32)	0.0181
Collagen vascular disease	0.87 (0.591.29)	0.4905	0.90 (0.601.33)	0.5896
Congestive heart failure	1.50 (1.32-1.70)	<.0001	1.50 (1.32-1.71)	<.0001
Current or prior tobacco use	0.78 (0.68-0.88)	<.0001	0.78 (0.69-0.89)	0.0001
Dementia	1.37 (1.12-1.69)	0.0029	1.40 (1.13-1.75)	0.0026
Depression	1.03 (0.90-1.18)	0.6689	1.04 (0.91-1.19)	0.6001
Diabetes mellitus	1.30 (1.15-1.48)	<.0001	1.28 (1.13-1.45)	0.0001
Fluid electrolyte	1.36 (1.17-1.59)	<.0001	1.35 (1.15-1.58)	0.0003
Hemiplegia or paraplegia	0.91 (0.80-1.04)	0.1734	0.91 (0.80-1.04)	0.1756
Hypertension	0.63 (0.55-0.72)	<.0001	0.63 (0.55-0.72)	<.0001
Hypothyroid	0.73 (0.59-0.91)	0.0047	0.74 (0.600.93)	0.0084
Liver disease	1.01 (0.82-1.24)	0.9484	1.01 (0.81-1.26)	0.9211
Malignancy	1.37 (1.19-1.58)	<.0001	1.35 (1.17-1.55)	<.0001
Myocardial infarction	1.50 (1.21-1.85)	0.0002	1.45 (1.17-1.80)	0.0006
Neurologic disorder	1.06 (0.87-1.28)	0.5596	1.06 (0.86-1.29)	0.5905
Obesity	0.68 (0.56-0.82)	<.0001	0.68 (0.57-0.83)	<.0001
Psychiatric	1.26 (0.84-1.90)	0.2648	1.22 (0.82-1.81)	0.3268
Substance abuse	1.00 (0.76-1.31)	0.9951	1.01 (0.78-1.32)	0.9273
Valvular heart disease	1.21 (1.00-1.45)	0.0471	1.20 (0.99-1.46)	0.0659
Weight loss	1.38 (1.13-1.69)	0.0014	1.38 (1.12- 1.69)	0.0020
Procedural				
Adjuvant atherectomy	0.94 (0.82-1.08)	0.3734	0.95 (0.83-1.09)	0.4427
Claudication	0.57 (0.48-0.67)	<.0001	0.58 (0.49-0.68)	<.0001
Critical limb ischemia	1.47 (1.31-1.65)	<.0001	1.48 (1.32-1.66)	<.0001

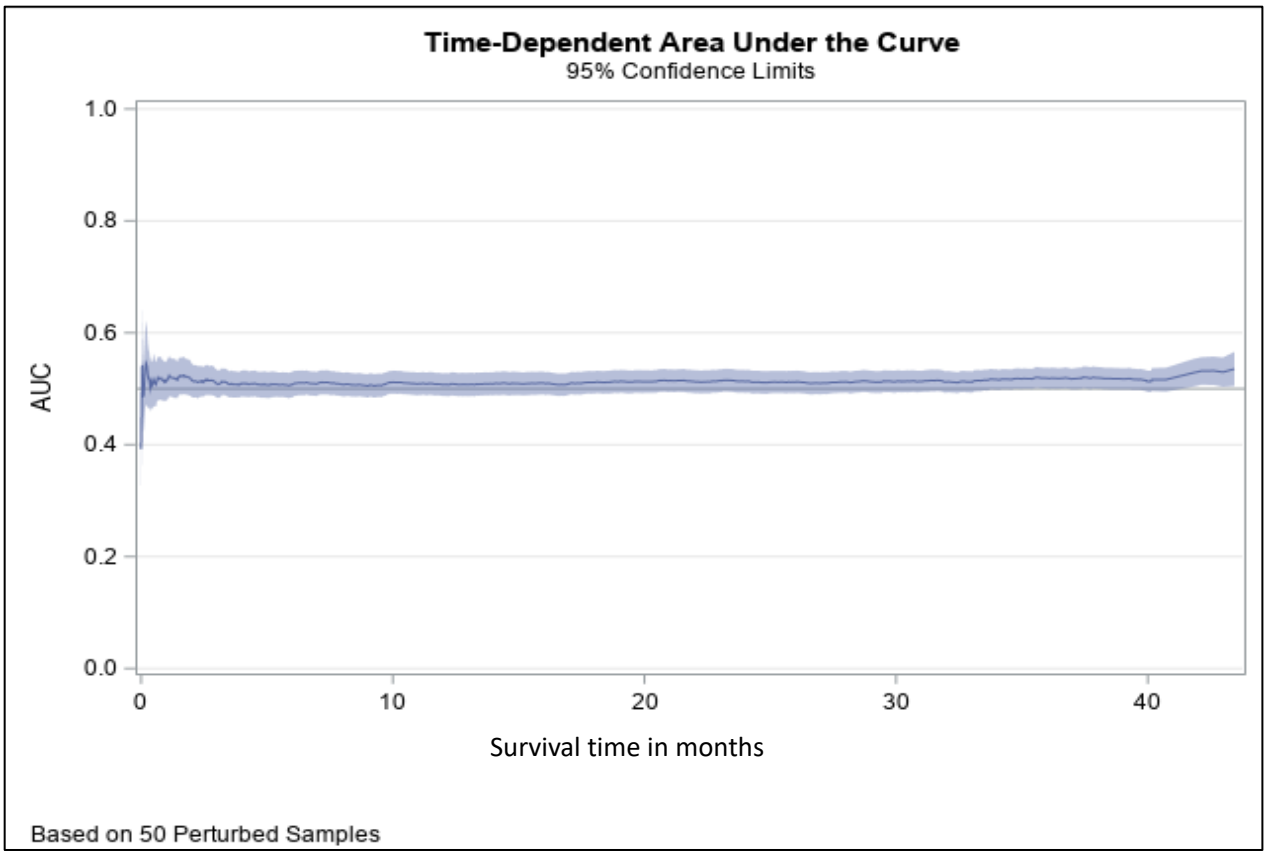
*Reference for comorbidities is “no condition”

Table S8. All-cause mortality hazard ratio estimates from Cox regression models (subjects enrolled between 10/01/2015 and 07/09/2016).

	Unadjusted		Adjusted	
Parameter	**HR (95% CI)**	**P value**	**HR (95% CI)**	**P value**
Drug coated vs non-drug coated	1.13 (0.92-1.38)	0.2417	1.11 (0.91-1.35)	0.3212
Age	1.04 (1.03-1.06)	<.0001	1.04 (1.03-1.06)	<.0001
Sex (female vs. male)	1.45 (0.77-2.73)	0.2516	1.42 (0.83-2.45)	0.2016
Race (AA vs. White)	1.05 (0.85-1.30)	0.6376	1.06 (0.86-1.32)	0.5842
Race (Other vs. White)	1.20 (0.87-1.65)	0.2584	1.25 (0.91-1.73)	0.1750
*Comorbidity**				
Alcohol abuse	1.24 (0.93- 1.66)	0.1438	1.24 (0.93-1.66)	0.1498
Anemia	0.76 (0.56-1.03)	0.0767	0.76 (0.54-1.05)	0.0970
Arrhythmia	1.23 (1.02-1.48)	0.0274	1.25 (1.04-1.51)	0.0205
Coagulopathy	1.04 (0.62- .72)	0.8880	1.01 (0.62-1.63)	0.9789
Chronic kidney disease	1.28 (1.06-1.55)	0.0104	1.32 (1.08-1.61)	0.0059
Chronic obstructive pulmonary disease	1.23 (1.02-.48)	0.0327	1.26 (1.04-1.52)	0.0159
Collagen vascular disease	0.71 (0.36- 1.39)	0.3198	0.72 (0.36-1.45)	0.3610
Congestive heart failure	1.38 (1.14-1.66)	0.0008	1.38 (1.15-1.67)	0.0007
Current or prior tobacco use	0.75 (0.62-0.91)	0.0031	0.75 (0.63-0.91)	0.0029
Dementia	1.00 (0.70-1.43)	0.9794	1.07 (0.73-1.57)	0.7128
Depression	1.01 (0.82-1.24)	0.9515	1.01 (0.82-1.24)	0.9265
Diabetes mellitus	1.27 (1.06-1.52)	0.0088	1.27 (1.06-1.52)	0.0097
Fluid electrolyte	1.35 (1.04-1.75)	0.0250	1.33 (1.00-1.76)	0.0463
Hemiplegia or paraplegia	0.80 (0.66-0.99)	0.0364	0.81 (0.66-1.00)	0.0530
Hypertension	0.56 (0.47-0.68)	<.0001	0.56 (0.46-0.67)	<.0001
Hypothyroid	0.85 (0.61-1.17)	0.3176	0.82 (0.59-1.15)	0.2495
Liver disease	0.98 (0.70-1.36)	0.8987	0.97 (0.69-1.37)	0.8631
Malignancy	1.41 (1.14-1.74)	0.0013	1.39 (1.12-1.72)	0.0024
Myocardial infarction	1.77 (1.22-2.55)	0.0024	1.75 (1.21-2.52)	0.0028
Neurologic disorder	0.98 (0.71-1.35)	0.9150	1.00 (0.72-1.38)	0.9901
Obesity	0.60 (0.44-0.83)	0.0021	0.60 (0.44-0.81)	0.0010
Psychiatric	1.11 (0.55-2.24)	0.7789	1.07 (0.55-2.09)	0.8359
Substance abuse	1.25 (0.82-1.91)	0.2986	1.30 (0.86-1.96)	0.2084
Valvular heart disease	1.15 (0.86-1.54)	0.3534	1.15 (0.84-1.58)	0.3681
Weight loss	1.39 (1.01-1.93)	0.0448	1.38 (1.00-1.91)	0.0529
Procedural				
Adjuvant atherectomy	0.79 (0.64-0.97)	0.0257	0.79 (0.64-0.98)	0.0331
Claudication	0.60 (0.48-0.75)	<.0001	0.61 (0.49-0.77)	<.0001
Critical limb ischemia	1.39 (1.17-1.64)	0.0001	1.39 (1.17-1.65)	0.0002

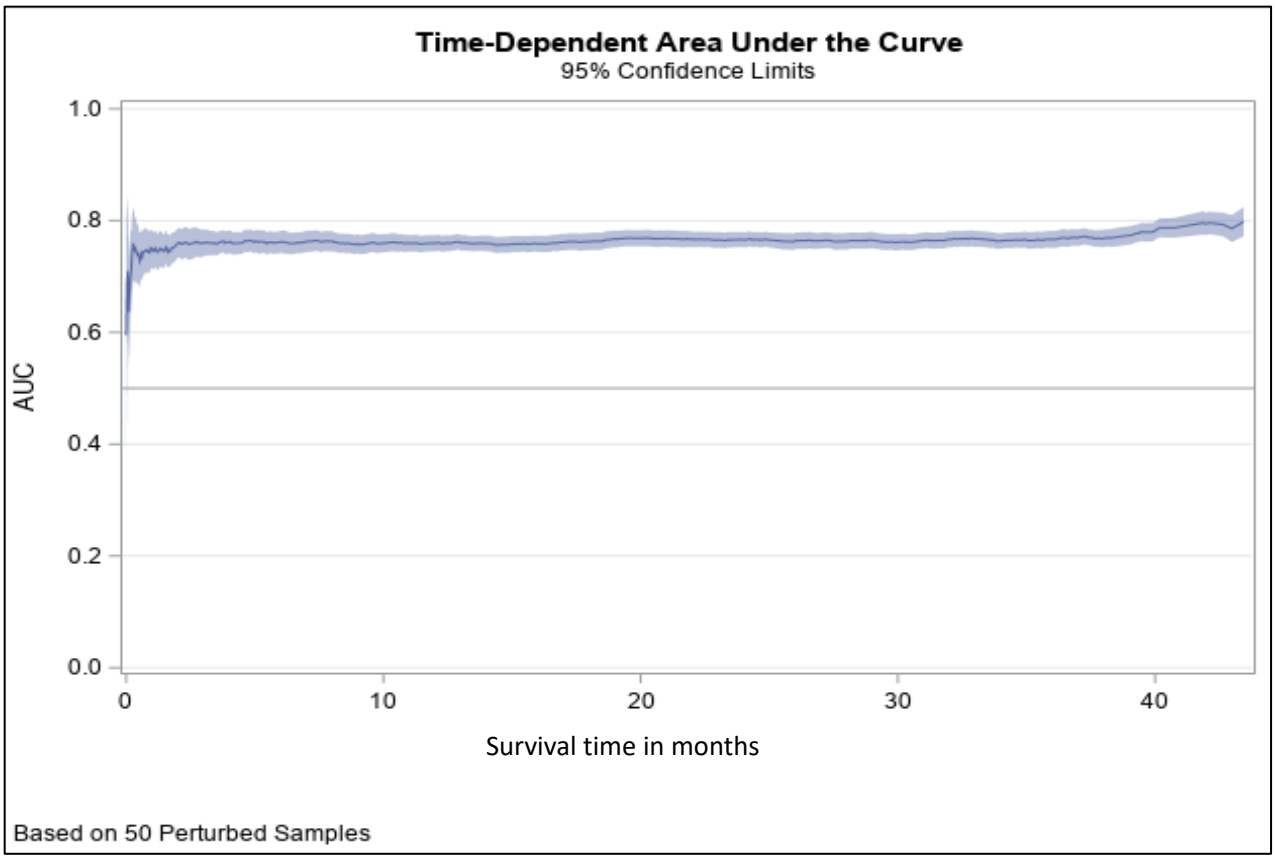
*Reference for comorbidities is “no condition”

Figure S1. Area under the curve plot and 95% confidence limits for univariate Cox regression model.



AUC = area under the curve

Figure S2. Area under the curve plot and 95% confidence limits for multivariate Cox regression model.



AUC = area under the curve

Figure S3. Receiver operator characteristic curves for univariate Cox regression model.

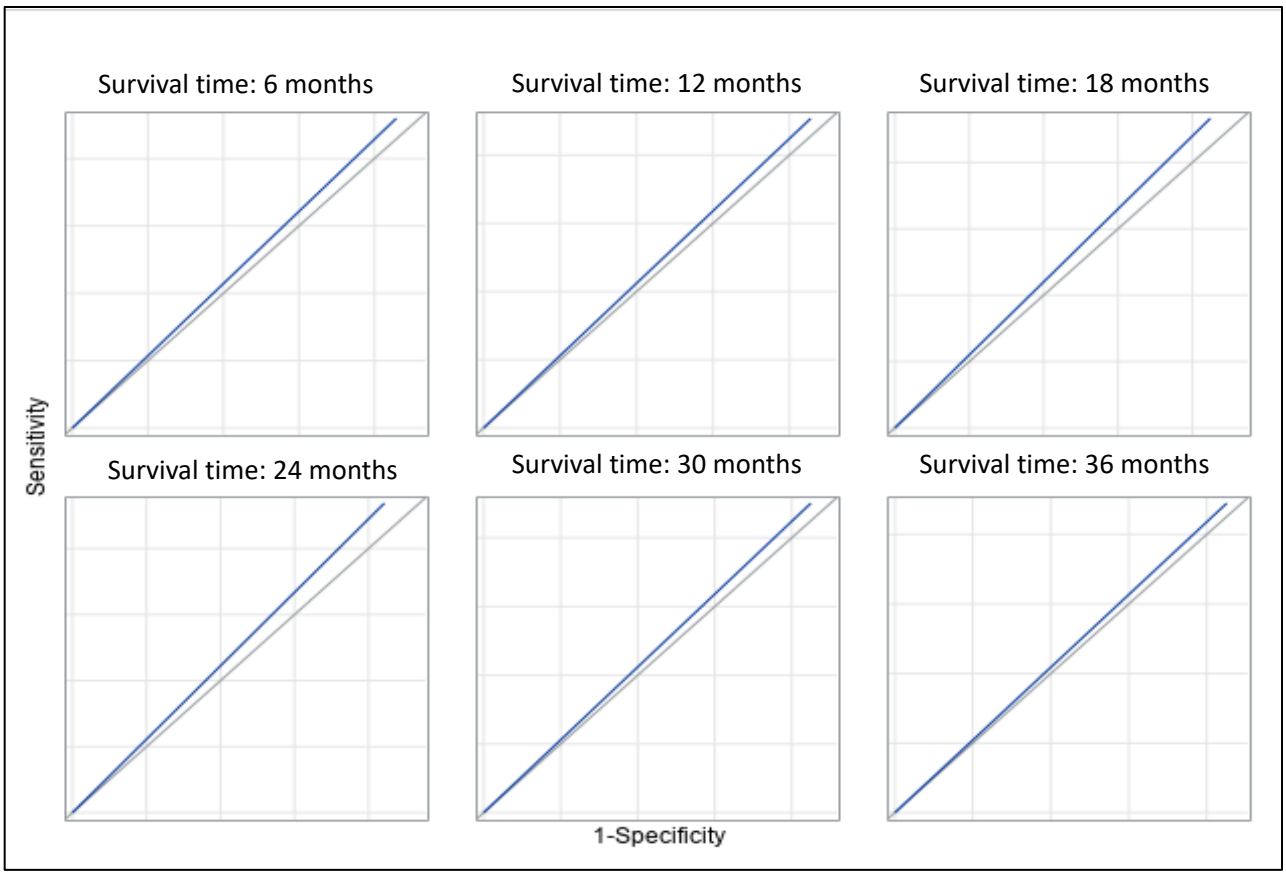


Figure S4. Receiver operator characteristic curves for multivariate Cox regression model.