Supplementary Material

Supplementary Table 1 - Standard Time-to-event Analysis Compared With Competing Risk Analysis.

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Supplementary Table 5 - The 2-Year Cumulative Incidence Of Major Amputation And Death Without Major Amputation In Patients Aged <75 And ≥75 Years Using Standard Time-to-event (Kaplan-Meier) And Competing Risk Analysis (Alaen-Johansen); And Unadjusted And Adjusted 2-Year Major Amputation Risk In Patients Aged <75 Vs. ≥75 Years, Derived From Standard Time-to-event (Hazard Ratio From Cox Proportional Hazard) And Competing Risk (Sub-Hazard Ratio From Fine-Gray) Regression Models, In Both Chronic Limb-Threatening Ischemia (CLTI) And Non-CLTI Cohorts.

Supplementary Table 1 - Standard Time-to-event Analysis Compared With Competing Risk Analysis.

	Standard Time-to-event	Competing Risk	Comparison
	Ignoring the competing all-cause mortality risk in the estimation of major amputation.	Taking the competing all-cause mortality risk into account in the estimation of major amputation.	
Cumulative Incidence Function			
Method	1 minus Kaplan-Meier	Aalen-Johansen	
Notations	CIF_{KM}	CIF_{AJ}	
Estimates	Cumulative incidence of the occurrence of primary event at time t. Sum of the cumulative incidence of events exceeds the cumulative incidence of the composite of events.	Cumulative incidence of the occurrence of the primary event at time t and before the occurrence of another event (competing event). Sum of the cumulative incidence of events equals the cumulative incidence of the composite of events.	Relative Difference $= \frac{CIF_{KM}-CIF_{AJ}}{CIF_{AJ}}$
Regression Model			
Method	Cox Proportional Hazard	Fine-Gray	
Notations	HR	sHR	
Estimates	Hazard Ratio: Measure of the association of covariates with the primary event ignoring competing event.	Sub-hazard Ratio: Measure of the association of covariates with both events, primary and competing events.	Relative Difference $= \frac{HR-sHR}{sHR}$
Prediction	Mean prediction of the major amputation risk	Mean prediction of the cumulation incidence major amputation	

Abbreviations: CIF, Cumulative Incidence Function; KM, Kaplan-Meier; AJ, Aalen-Johansen; HR, Hazard Ratio; sHR, Sub-hazard Ratio.

Supplementary Table 2 - Baseline Characteristics Of Patients Who Underwent A Peripheral Vascular Intervention (PVI) In The Chronic Limb-Threatening Ischemia (CLTI) And Non-CLTI Cohorts.

	CLTI (N=7,273)	Non-CLTI (N=5,095)
Age, years		
Mean (SD)	76.6 (7.6)	74.1 (6.3)
Median [Q1; Q3]	76.0 [70.0; 83.0]	73.0 [69.0; 78.0]
Female Sex	3,000 (41.2)	1,934 (38.0)
Hispanic or Latino	315 (4.3)	106 (2.1)
Race		
White	5,692 (78.3)	4,457 (87.5)
Black or African American	1,144 (15.7)	453 (8.9)
Other or Unknown	437 (6.0)	185 (3.6)
Primary insurer		
Medicare/Medicaid	7,001 (96.3)	4,883 (95.8)
Commercial/Other	272 (3.7)	212 (4.2)
Procedure urgency		
Elective	5,634 (77.5)	4,907 (96.3)
Urgent	1,454 (20.0)	161 (3.2)
Emergent	185 (2.5)	27 (0.5)
Preoperative location living at home	6,553 (90.1)	5,050 (99.1)
Functional status		
Full	2,345 (32.7)	2,824 (56.4)
Light work	1,809 (25.2)	1,315 (26.3)
Self-care	1,724 (24.1)	779 (15.6)
Ambulation category		
Independently	3,497 (48.8)	4,367 (87.3)
With assistance	2,724 (38.1)	588 (11.8)
BMI, kg.m-2		
Mean (SD)	27.3 (6.1)	27.7 (5.4)
Median [Q1; Q3]	26.6 [23.0; 30.8]	27.3 [24.1; 31.0]
Cerebrovascular disease	1,440 (19.8)	689 (13.5)
Coronary artery disease	2,788 (38.3)	1,955 (38.4)
Congestive heart failure	2,327 (32.0)	777 (15.3)
Dysrhythmia	2,439 (33.5)	944 (18.5)
Chronic lung disease	2,023 (27.8)	1,495 (29.3)
Diabetes	4,517 (62.1)	2,024 (39.7)
Stages of CKD		
Stage 1: ≥ 90	1,527 (21.0)	1,219 (23.9)
Stage 2: [60-90]	2,350 (32.3)	2,216 (43.5)
Stage 3: [30-60]	2,055 (28.3)	1,456 (28.6)
Stage 4: [15-30]	293 (4.0)	72 (1.4)
Stage 5: < 15	1,048 (14.4)	132 (2.6)
Hypertension	6,696 (92.1)	4,635 (91.0)
Smoking status		
Never	2,334 (32.1)	721 (14.2)

	CLTI (N=7,273)	Non-CLTI (N=5,095)
Prior	3,575 (49.2)	3,014 (59.2)
Current	1,364 (18.8)	1,360 (26.7)
Preoperative ASA	5,176 (71.2)	4,103 (80.5)
Preoperative Antiplatelet	2,891 (39.7)	2,447 (48.0)
Preoperative Statin	5,461 (75.1)	4,205 (82.5)
Preoperative ACEi/ARB ± HTN	4,094 (56.3)	3,435 (67.4)
Preoperative GDMT	2,726 (37.5)	2,655 (52.1)
Discharge GDMT	3,145 (44.0)	2,903 (57.1)
CABG	1,756 (24.1)	1,257 (24.7)
PCI	1,790 (24.6)	1,499 (29.4)
Carotid disease	660 (9.1)	717 (14.1)
No Prior major amputation	6,482 (89.1)	5,026 (98.6)
No Prior minor amputation	6,314 (86.8)	5,014 (98.4)
Prior inflow treatment PVI	861 (11.8)	1,043 (20.5)
Prior inflow treatment bypass	199 (2.7)	195 (3.8)
Prior infrainguinal PVI	2,283 (31.4)	1,724 (33.9)
Prior infrainguinal bypass	756 (10.4)	427 (8.4)
Prior femoral endarterectomy	419 (5.8)	345 (6.8)
CLTI laterality		
Unilateral	6,148 (84.5)	
Bilateral	1,125 (15.5)	
Number of access sites		
1	6,401 (88.1)	4,055 (79.7)
2	864 (11.9)	1,036 (20.3)
Number of artery treated (Mean (SD))	1.8 (0.9)	1.6 (0.8)
Plain balloon	5,831 (80.2)	3,461 (68.0)
Atherectomy	1,501 (20.6)	1,200 (23.6)
Stent	2,758 (37.9)	2,715 (53.3)

All values are presented as n (%), unless otherwise specified.
Abbreviations: CLTI, Chronic Limb-threatening Ischemia; SD, Standard Deviation; Q1;Q3, Interquartile Range; BMI, Body Mass Index; CKD, Chronic Kidney Disease; ASA, Aspirin; HTN, Hypertension; ACEi, Angiotensin-Converting Enzyme Inhibitor; ARB, Angiotensin Receptor Blocker; GDMT, Guideline-Directed Medical Therapy; CABG, Coronary Artery Bypass Grafting; PCI, Percutaneous Intervention; PVI, Peripheral Vascular Intervention.

Supplementary Table 3 - The Unadjusted And Adjusted 2-Year Risk Of Major Amputation In Patients Aged ≥75 Years Vs. <75 Year Derived From Standard Cox Proportional Hazard Regression Model And Compared With Competing Risk Fine-Gray Regression Model, In The Chronic Limb-Threatening Ischemia (CLTI) Cohort.

	Standard Time-to-event Cox Proportional Hazard HR (95%CI)	P-Value	Competing Risk Fine-Gray sHR (95%CI)	P-Value	Relative Difference (%)*
Unadjusted					
Aged ≥75 vs. <75 years	0.71 (0.62-0.81)	<0.001	0.66 (0.58-0.75)	<0.001	7.1
Adjusted					
Aged ≥75 vs. <75 years	0.85 (0.74-0.97)	0.015	0.79 (0.69-0.91)	0.001	7.0
Female Sex	0.68 (0.58-0.78)	<0.001	0.67 (0.57-0.77)	<0.001	1.7
Race					
Black/African American	1.57 (1.33-1.85)	<0.001	1.57 (1.33-1.85)	<0.001	-0.1
Other or Unknown	1.33 (1.02-1.73)	0.033	1.32 (1.01-1.72)	0.040	0.7
Ethnicity (Hispanic)	1.07 (0.79-1.45)	0.659	1.08 (0.79-1.47)	0.627	-0.8
Region ID	1.00 (0.98-1.01)	0.409	1.00 (0.98-1.01)	0.399	0.0
Commercial/Other	0.68 (0.47-1.00)	0.049	0.67 (0.46-0.97)	0.034	2.8
Living at Home	0.72 (0.59-0.87)	0.001	0.80 (0.65-0.97)	0.027	-9.9
Smoking (vs. Current)					
Never	1.33 (1.08-1.64)	0.006	1.34 (1.09-1.64)	0.006	-0.28
Prior	1.16 (0.95-1.41)	0.135	1.15 (0.95-1.39)	0.158	0.90
Preoperative GDMT	0.94 (0.82-1.08)	0.373	0.98 (0.86-1.13)	0.804	-4.3
Hypertension	0.86 (0.67-1.10)	0.232	0.89 (0.69-1.14)	0.350	-3.2
Congestive Heart Failure	1.13 (0.99-1.30)	0.078	1.04 (0.90-1.20)	0.577	8.9
Coronary Artery Disease	1.19 (1.02-1.38)	0.028	1.17 (1.01-1.37)	0.038	1.1
CABG	1.03 (0.88-1.21)	0.690	1.03 (0.88-1.20)	0.727	0.4
PCI	1.01 (0.87-1.18)	0.873	0.99 (0.84-1.15)	0.861	2.7
Diabetes	1.59 (1.35-1.88)	<0.001	1.58 (1.34-1.87)	<0.001	0.5
Stages of CKD 3 to 5 vs. 1/2	1.29 (1.12-1.47)	<0.001	1.18 (1.03-1.36)	0.016	8.6
Cerebrovascular Disease	1.04 (0.89-1.22)	0.618	1.02 (0.87-1.19)	0.814	2.1
Endarterectomy/Carotid stenting	1.22 (0.98-1.51)	0.069	1.23 (0.99-1.53)	0.056	-0.9
Prior amputation (vs. No)					
Major	2.11 (1.77-2.50)	<0.001	2.09 (1.76-2.49)	<0.001	0.7
Minor	1.63 (1.37-1.94)	<0.001	1.65 (1.38-1.97)	<0.001	-1.3
History of bypass, endarterectomy, or PVI	1.27 (1.11-1.46)	<0.001	1.30 (1.14-1.49)	<0.001	-2.0
Urgency					
Urgent	1.25 (1.08-1.46)	0.003	1.18 (1.01-1.37)	0.040	6.7
Emergent	1.24 (0.84-1.85)	0.284	1.07 (0.71-1.61)	0.737	15.8

Abbreviations: CLTI, Chronic Limb-threatening Ischemia; GDMT, Guideline-Directed Medical Therapy; CABG, Coronary Artery Bypass Grafting; PCI, Percutaneous Intervention; CKD, Chronic Kidney Disease; PVI, Peripheral Vascular Intervention.

*All relative differences were calculated before rounding the estimators

Supplementary Table 4 - The Unadjusted And Adjusted 2-Year Risk Of Major Amputation In Patients Aged ≥75 Years Vs. <75 Year Derived From Standard Cox Proportional Hazard Regression Model And Compared With Competing Risk Fine-Gray Regression Model, In The Non-Chronic Limb-Threatening Ischemia (Non-CLTI) Cohort.

	Standard Time-to-event Cox Proportional Hazard HR (95%CI)	P-Value	Competing Risk Fine-Gray sHR (95%CI)	P-Value	Relative Difference (%)*
Unadjusted					
Aged ≥75 vs. <75 years	1.14 (0.70-1.85)	0.607	1.11 (0.68-1.81)	0.676	2.4
Adjusted					
Aged ≥75 vs. <75 years	0.90 (0.53-1.51)	0.686	0.86 (0.51-1.43)	0.551	5.1
Female Sex	0.90 (0.51-1.57)	0.708	0.88 (0.49-1.59)	0.674	2.1
Race					
Black/African American	1.70 (0.86-3.36)	0.129	1.62 (0.76-3.47)	0.215	4.8
Other or Unknown	1.05 (0.28-3.87)	0.947	1.05 (0.27-4.06)	0.948	-0.1
Ethnicity (Hispanic)	2.65 (0.84-8.37)	0.097	2.80 (0.83-9.50)	0.098	-5.5
Region ID	0.98 (0.94-1.02)	0.312	0.98 (0.94-1.02)	0.318	-0.2
Commercial/Other	1.79 (0.64-5.00)	0.270	1.80 (0.65-4.98)	0.256	-0.9
Living at Home	0.18 (0.07-0.48)	0.001	0.23 (0.07-0.75)	0.015	-20.3
Smoking (vs. Current)					
Never	2.04 (0.85-4.91)	0.110	2.08 (0.84-5.11)	0.112	-1.6
Prior	1.72 (0.81-3.62)	0.156	1.77 (0.78-4.01)	0.172	-3.0
Preoperative GDMT	0.71 (0.42-1.19)	0.193	0.72 (0.43-1.19)	0.199	-1.0
Hypertension	0.68 (0.26-1.78)	0.436	0.70 (0.26-1.86)	0.474	-2.3
Congestive Heart Failure	1.50 (0.85-2.66)	0.163	1.44 (0.81-2.59)	0.217	3.9
Coronary Artery Disease	1.12 (0.62-2.02)	0.715	1.17 (0.61-2.23)	0.630	-4.7
CABG	1.19 (0.65-2.18)	0.577	1.15 (0.60-2.19)	0.670	3.3
PCI	0.61 (0.31-1.17)	0.137	0.56 (0.29-1.08)	0.086	7.5
Diabetes	1.60 (0.94-2.74)	0.085	1.54 (0.89-2.65)	0.120	4.1
Stages of CKD 3 to 5 vs. 1/2	2.05 (1.21-3.47)	0.008	1.96 (1.16-3.32)	0.012	4.4
Cerebrovascular Disease	1.48 (0.80-2.76)	0.214	1.47 (0.78-2.78)	0.231	0.6
Endarterectomy/Carotid stenting	0.67 (0.30-1.52)	0.341	0.70 (0.30-1.61)	0.397	-3.4
Prior amputation (vs. No)					
Major	7.08 (3.41-14.73)	<0.001	7.22 (3.39-15.41)	<0.001	-2.0
Minor	2.05 (0.71-5.95)	0.186	1.93 (0.57-6.54)	0.291	6.3
History of bypass, endarterectomy, or PVI	1.08 (0.64-1.82)	0.780	1.08 (0.63-1.84)	0.782	-0.1
Urgency					
Urgent	4.44 (2.12-9.26)	<0.001	3.92 (1.73-8.91)	<0.001	13.0
Emergent	1.42 (0.18-11.28)	0.742	1.46 (0.14-15.2)	0.752	-2.9

Abbreviations: CLTI, Chronic Limb-threatening Ischemia; GDMT, Guideline-Directed Medical Therapy; CABG, Coronary Artery Bypass Grafting; PCI, Percutaneous Intervention; CKD, Chronic Kidney Disease; PVI, Peripheral Vascular Intervention.

*All relative differences were calculated before rounding the estimators

Supplementary Table 5 - The 2-Year Cumulative Incidence Of Major Amputation And Death Without Major Amputation In Patients Aged <75 And ≥75 Years Using Standard Time-to-event (Kaplan-Meier) And Competing Risk Analysis (Alaen-Johansen); And Unadjusted And Adjusted 2-Year Major Amputation Risk In Patients Aged <75 Vs. ≥75 Years, Derived From Standard Time-to-event (Hazard Ratio From Cox Proportional Hazard) And Competing Risk (Sub-Hazard Ratio From Fine-Gray) Regression Models, In Both Chronic Limb-Threatening Ischemia (CLTI) And Non-CLTI Cohorts.

	Standard Time-to-event	Competing Risk	Relative Difference (%)*
CLTI			
2-Year Cumulative Incidence Function (CIF)	**Kaplan-Meier % (95%CI)**	**Aalen-Johansen % (95%CI)**	
Of Major Amputation			
In <75 years old	19.1 (17.6-20.7)	16.8 (15.5-18.2)	13.7
In ≥75 years old	13.5 (12.3-14.8)	11.2 (10.2-12.2)	20.5
Of Death Without Major Amputation			
In <75 years old	32.7 (30.8-34.8)	28.7 (27.0-30.5)	13.9
In ≥75 years old	47.7 (45.9-49.5)	43.5 (41.9-45.2)	9.7
2-Year Risk Major Amputation In Patients Aged ≥75 vs. <75 Years	**Cox Proportional Hazard Hazard Ratio (95%CI)**	**Fine-Gray Sub-Hazard Ratio (95%CI)**	
Unadjusted	0.71 (0.62-0.8)	0.66 (0.58-0.75)	7.0
Adjusted	0.85 (0.74-0.97)	0.79 (0.69-0.91)	7.1
Non-CLTI			
2-Year Cumulative Incidence Function (CIF)	**Kaplan-Meier % (95%CI)**	**Aalen-Johansen % (95%CI)**	
Of Major Amputation			
In <75 years old	1.4 (1.0-2.0)	1.4 (1.0-1.9)	0.0
In ≥75 years old	1.5 (1.1-2.2)	1.4 (1.0-2.0)	7.1
Of Death Without Major Amputation			
In <75 years old	8.6 (7.6-9.8)	9.6 (8.4-10.9)	-10.4
In ≥75 years old	15.6 (14.0-17.3)	17.1 (15.3-18.9)	-8.8
2-Year Risk Major Amputation In Patients Aged ≥75 vs. <75 Years	**Cox Proportional Hazard Hazard Ratio (95%CI)**	**Fine-Gray Sub-Hazard Ratio (95%CI)**	
Unadjusted	1.14 (0.70-1.85)	1.11 (0.68-1.81)	2.4
Adjusted	0.90 (0.53-1.51)	0.86 (0.51-1.43)	5.1

Abbreviations: CLTI, Chronic Limb-threatening Ischemia; CIF, Cumulative Incidence Function.

*All relative differences were calculated before rounding the estimators