

Predictors of Major Adverse Limb Events After Infrainguinal Bypass in Patients with Diabetes



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OBJECTIVES:

- Diabetes mellitus (DM) is a major risk factor for peripheral artery disease (PAD).
- It is associated with an increase in the risk of disease severity, leading to lower limb amputation.
- The association of diabetes with major adverse limb events (MALE) after lower extremity revascularization (LER) remains controversial, as patients with diabetes are often analyzed as a homogenous group.
- Insulin is a marker of more long-standing diabetes in T1DM or greater disease duration and severity in T2DM.
- This study examines the impact of insulin use and glucose control on the outcomes of infrainguinal bypass.
- Our hypothesis is that insulin therapy and hemoglobin A1c (HbA1c) are associated with increased risk of MALEs after infrainguinal bypass in patients with DM and can be used to predict outcomes.

METHODS:

- The Vascular Quality Initiative database for infrainguinal bypass (2007-2021) was reviewed.
- Patients with diabetes undergoing infrainguinal bypass for PAD were included.
- Patients on dialysis or with kidney transplant were excluded.
- The characteristics and outcomes of patients with insulin requiring diabetes mellitus (IRDM) were compared to those of patients not requiring insulin (NIRDM).

RESULTS:

Tables 1,2 : Comparison of the characteristics and outcomes of patients with NIRDM to patients with IRDM

| Characteristics | | NIRDM (N=4,240) | IRDM (N=5,446) | P-value |
|---|-----------------------|-----------------|----------------|---------|
| Demographics | | | | |
| Age | (mean ± st dev) | 67.9±10.1 | 65±10.4 | <.001* |
| Male | | 2,894 (68.3) | 3,490 (64.1) | <.001* |
| Hispanic | | 245 (5.8) | 374 (6.9) | 0.031* |
| Race | White | 3,245 (76.6) | 3,998 (73.4) | <.001* |
| | African American | 691 (16.3) | 1,082 (19.9) | |
| | Other | 303 (7.2) | 366 (6.7) | |
| BMI | (mean ± st dev) | 28.4±5.7 | 29.5±6 | <.001* |
| Living status | Home | 4,138 (97.9) | 5,202 (95.7) | <.001* |
| Independent ambulation | | 4,073 (96.3) | 5,042 (92.7) | <.001* |
| Comorbidities | | | | |
| Hypertension | | 3,941 (93.1) | 5,123 (94.3) | 0.011* |
| CAD | | 1,500 (35.4) | 2,215 (40.7) | <.001* |
| COPD | | 1,050 (24.8) | 1,444 (26.5) | 0.05* |
| Smoking | | 3,609 (85.1) | 4,461 (81.9) | <.001* |
| Prior lower extremity revascularization | | 2,543 (60) | 3,393 (62.3) | 0.019* |
| Prior Carotid endarterectomy / stenting | | 461 (10.9) | 472 (8.7) | 0.003* |
| Cardiac Surgery/ stenting | | 1,692 (39.9) | 2,521 (46.3) | <.001* |
| Medications | | | | |
| Aspirin | | 3,276 (77.3) | 4,244 (78) | 0.441 |
| P2Y12 Inhibitors | | 1,482 (35) | 2,147 (39.5) | <.001* |
| Anticoagulation | | 715 (16.9) | 1,001 (18.4) | 0.051 |
| Statin | | 3,483 (82.2) | 4,561 (83.8) | 0.04* |
| Beta blockers | | 2,547 (60.1) | 3,530 (64.9) | <.001* |
| ACE inhibitors | | 2,726 (64.4) | 3,385 (62.2) | 0.03* |
| Laboratory Tests | | | | |
| Creatinine | (mean ± st dev) mg/dL | 1.1± 0.5 | 1.2± 0.6 | <.001* |
| HbA1c | (mean ± st dev) mg/dL | 7.2± 1.6 | 8.5± 2 | <.001* |
| Hemoglobin | (mean ± st dev) mg/dL | 12.3± 2.2 | 11.8± 2.1 | <.001* |

- A total of 9,686 patients with diabetes (56% IRDM) underwent infrainguinal bypass.
- Patients with IRDM were significantly younger than patients with NIRDM, and more likely to be female, African American, Hispanic, and had a higher mean BMI.
- Patients with IRDM were more likely to stay at a care facility and less likely to ambulate independently.
- Patients with IRDM were more likely to have comorbidities, prior LER, prior carotid procedure, and cardiac procedure, and were more likely to be on P2Y12 inhibitors, statins, beta blockers, and ACE inhibitors.
- The mean Creatinine (1.2± 0.6 mg/dL) and HbA1c (8.5± 2 mg/dL) were more likely to be higher in patients with IRDM compared to NIRDM

| Characteristics | | NIRDM (N=4,240) | IRDM (N=5,446) | P-value |
|--|-------------------------|-----------------|----------------|---------|
| Procedural Characteristics | | | | |
| Ankle-Brachial Index | (mean ± st dev) | 0.57± 0.45 | 0.62± 0.48 | <.001* |
| Indication | Claudication | 1,697 (40) | 2,052 (37.7) | 0.019* |
| | CLTI | 2,543 (60) | 3,393 (62.3) | |
| ASA Classification | ASA I-III | 3,372 (79.6) | 4,002 (73.6) | <.001* |
| | ASA IV-V | 867 (20.5) | 1,439 (26.5) | |
| Urgency | Urgent/Emergent | 704 (16.6) | 1,126 (20.7) | <.001* |
| Total procedure time | (mean ± st dev) minutes | 252.8±123.9 | 258.6±117.9 | 0.019* |
| Type of bypass | Femoropopliteal | 2,265 (54.6) | 2,811 (52.4) | 0.033* |
| | Tibial | 1,883 (45.4) | 2,553 (47.6) | |
| Vascular conduit | GSV- Single segment | 2,237 (90.2) | 2,959 (89.9) | 0.666 |
| | Alternative | 243 (9.8) | 334 (10.1) | |
| Perioperative Complications (30 days) | | | | |
| Surgical site infection | | 118 (2.8) | 187 (3.4) | 0.067 |
| Graft infection | | 12 (0.3) | 22 (0.4) | 0.318 |
| Cardiac complication | | 125 (3) | 165 (3) | 0.814 |
| Respiratory complication | | 54 (1.3) | 101 (1.9) | 0.024* |
| Renal complication | | 178 (4.2) | 397 (7.3) | <.001* |
| Neurological complication | | 24 (0.6) | 31 (0.6) | 0.982 |
| Transfusion | | 1,252 (29.6) | 1,865 (34.4) | <.001* |
| Number of Packed RBC Units transfused | (mean ± st dev) | 0.8±1.8 | 1±1.9 | 0.004* |
| Major Amputation | | 49 (1.2) | 91 (1.7) | 0.035* |
| Return to OR | | 453 (10.7) | 796 (14.6) | <.001* |
| Mortality | | 28 (0.7) | 35 (0.6) | 0.914 |
| Any complication | | 1,611 (38.0) | 2,477 (45.5) | <.001* |
| Discharge to home | | 1,192 (28.4) | 1,876 (34.9) | <.001* |
| Hospital length of stay | (mean ± st dev) days | 8.1±15.8 | 9.8±15.2 | <.001* |
| Long-term Outcomes | | | | |
| Mean follow-up time | (mean ± st dev) | 430.8±353 | 423.8±322.9 | 0.319 |
| Primary Patency | | 2,026 (70.8) | 2,417 (68.5) | 0.043* |
| Reintervention | | 653 (20.7) | 897 (22.5) | 0.066 |
| Any Amputation (Minor + Major) | | 455 (14.4) | 835 (20.9) | <.001* |
| Major Amputation | | 292 (9.2) | 502 (12.6) | <.001* |
| MALEs | | 873 (27.6) | 1,302 (32.6) | <.001* |
| Mortality | | 670 (15.8) | 1,019 (18.7) | 0.002* |

- Patients with IRDM were more likely to be categorized into American Society of Anesthesiologist (ASA) classes IV-V.
- The infrainguinal bypass for patients with IRDM was more likely to be urgent/emergent and the total procedure time was higher compared to NIRDM.
- Patients with IRDM had significantly higher perioperative complications including major amputation, but there was no difference in perioperative mortality.
- Patients with NIRDM were less likely to be treated with tibial bypass for chronic limb-threatening ischemia (CLTI), an advanced stage of PAD that may present with ischemic rest pain, arterial insufficiency ulcers, and gangrene (tissue necrosis).
- After a mean follow up of 424 days, patients with IRDM had significantly lower primary patency and higher major amputation, MALE, and mortality.

Table 3: Multivariate regression for factors associated with long-term mortality

| Characteristics | | Hazard Ratio | 95% CI |
|--------------------|----------------------|--------------|-----------|
| Ambulation | | 1.31 | 1.09-1.57 |
| CAD | | 1.19 | 1.07-1.31 |
| COPD | | 1.25 | 1.12-1.39 |
| Medications | Insulin | 1.28 | 1.16-1.43 |
| | Anticoagulation | 1.18 | 1.05-1.33 |
| Prior LER | | 0.89 | 0.81-0.99 |
| Indication | CLTI vs claudication | 1.73 | 1.48-2.02 |
| ASA Classification | ASA IV, V vs I-III | 1.3 | 1.17-1.45 |
| Laboratory | Hemoglobin | 0.93 | 0.91-0.96 |
| | Creatinine | 1.17 | 1.09-1.26 |

Table 4: Multivariate regression for factors associated with MALEs

| Characteristics | | Hazard Ratio | 95% CI |
|----------------------|----------------------|--------------|-----------|
| Hispanic ethnicity | | 1.28 | 1.07-1.53 |
| Insulin | | 1.17 | 1.06-1.29 |
| Prior LER | | 1.22 | 1.11-1.35 |
| Indication | CLTI vs Claudication | 1.59 | 1.39-1.82 |
| Type of Bypass | Alternative vs GSV | 1.55 | 1.4-1.71 |
| Ankle-Brachial Index | | 0.89 | 0.81-0.99 |

- Regression analyses demonstrated that insulin requirement, but not A1c, was independently associated with higher risk of MALE and mortality

CONCLUSION:

Insulin requirement is a significant predictor of MALEs and survival after infrainguinal bypass and should be used to stratify the outcomes of LER in patients with diabetes.

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