



## Original Article

# Medical Therapy Following Urgent/Emergent Revascularization in Peripheral Artery Disease Patients (Canadian Acute Limb Ischemia Registry [CANALISE I])

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### ABSTRACT

**Background:** Following severe limb ischemia requiring urgent/emergent revascularization, peripheral arterial disease patients suffer a high risk of recurrent atherothrombosis.

**Methods:** Patients discharged from Hamilton General Hospital (Hamilton, Ontario) between April 2016 and September 2017 following severe limb ischemia requiring urgent/emergent revascularization were identified via the Local Health Integration Network CorHealth database, with supplemental information from chart review.

**Results:** A total of 158 patients admitted for urgent/emergent revascularization were identified (148 alive at discharge). Among patients without a pre-existing indication for anticoagulation, 38.8% ( $n = 47$ ) were discharged on single-antiplatelet therapy, 27.3% ( $n = 33$ ) on dual-antiplatelet therapy, 19.8% ( $n = 24$ ) on anticoagulants plus antiplatelet therapy, 6.6% ( $n = 8$ ) on anticoagulants alone, and 2.6% ( $n = 3$ ) on

### RÉSUMÉ

**Introduction :** Après une ischémie grave d'un membre ayant nécessité une revascularisation urgente/nouvelle revascularisation, les patients atteints d'une maladie artérielle périphérique ont un risque élevé de récurrence d'athérombose.

**Méthodes :** Nous avons recensé les patients qui ont obtenu leur sortie de la Hamilton General Hospital (Hamilton, Ontario) entre avril 2016 et septembre 2017 à la suite d'une ischémie grave d'un membre ayant nécessité une revascularisation urgente/nouvelle revascularisation via la base de données Local Health Integration Network CorHealth et grâce aux renseignements complémentaires issus de la revue des dossiers.

**Résultats :** Nous avons recensé un total de 158 patients admis pour une revascularisation urgente/nouvelle revascularisation (148 patients en vie à la sortie de l'hôpital). Parmi les patients chez lesquels

Peripheral arterial disease (PAD) affects an estimated 8 to 12 million Americans, with a worldwide prevalence affecting an excess of 200 million people.<sup>1</sup> PAD is associated with a significant increase in risk for both major adverse cardiac events

and major adverse limb events (MALE). Reduced perfusion to the lower limbs owing to flow-limiting atherosclerosis may result in development of ischemic tissue loss, chronic pain at rest, or motor sensory impairment, any one of which warrants revascularization.<sup>2</sup>

Among patients requiring revascularization for PAD, levels of cardiovascular risk can be further stratified based on the urgency of intervention.<sup>3</sup> Limb ischemia requiring urgent/emergent revascularization carries significantly elevated risk compared to elective intervention for subsequent cardiac and limb events. In outpatients with symptomatic PAD who do not have atrial fibrillation, urgent/emergent ischemic events occur at a rate of 1.0% per year, a percentage that doubles among patients presenting with critical limb ischemia

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**Ethics Statement:** Ethical approval was obtained for the Canadian Acute Limb Ischemia Registry (CANALISE) from the Hamilton Integrated Research Ethics Board (Hamilton, Ontario, Canada) on February 16, 2018.

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unknown therapy. Patients who received angioplasty with stenting were more likely be discharged on dual-antiplatelet therapy (hazard ratio [HR]: 7.14; 95% confidence interval [CI]: 2.87-17.76;  $P < 0.01$ ); patients who received an embolectomy/thrombectomy were more likely be discharged on an anticoagulant alone (HR: 2.61; 95% CI: 1.00-6.81;  $P = 0.049$ ); and patients who received peripheral bypass grafting were more likely be discharged on single-antiplatelet therapy (HR: 2.28; 95% CI: 1.11-4.69;  $P = 0.024$ ). Neither statins (60.8% vs 56.3%;  $P = 0.23$ ) nor renin-angiotensin-aldosterone system inhibitors (48.7% vs 50.6%;  $P = 0.58$ ) were prescribed at higher rates at discharge, compared with the rate at admission.

**Conclusions:** Substantial heterogeneity exists in antithrombotic prescription following urgent/emergent revascularization. No intensification of non-antithrombotic vascular protective medications occurred during hospitalization. Clinical trials and health system interventions to optimize medical therapy in peripheral arterial disease patients are urgently needed.

(CLI).<sup>4-6</sup> Despite evolving treatment options, 48% of these patients require amputation, and 42% die within 1 year of intervention; the rates are even higher for patients who present with acute limb ischemia (ALI).<sup>5</sup> These rates persist despite contemporary innovations and improvements in the surgical care available for these patients.<sup>7</sup> When amputation is required, the resultant disability and personal and societal costs are quite significant.<sup>8</sup>

The management of urgent/emergent limb ischemia requires an interventional procedure in the vast majority of cases. This treatment usually involves initiating a perioperative heparin infusion in combination with open, endovascular, or hybrid revascularization,<sup>9,10</sup> and less commonly, use of thrombolytic therapy. Outside of this immediate post-operative phase, and the time of discharge, however, significant heterogeneity in the use of antithrombotic agents persists.<sup>11,12</sup> In addition, although the period of hospitalization is an opportune time to optimize delivery of other evidenced-based medical therapies for PAD patients, the prescription of such medications has been shown to be suboptimal.<sup>13</sup>

The primary objective of this investigation was to characterize contemporary antithrombotic regimens used following urgent/emergent limb revascularization for severe limb ischemia in a single tertiary-care centre in Canada. The secondary objective was to report the use of vascular protective medications used among these patients requiring urgent/emergent revascularization during their hospital admission.

## Methods

This study was conducted at the Hamilton General Hospital (Hamilton, Ontario, Canada), a tertiary-level vascular referral centre. We assessed a retrospective cohort of

l'anticoagulation n'avait pas antérieurement été indiquée, 38,8 % ( $n = 47$ ) avaient reçu à leur sortie de l'hôpital un simple traitement antiplaquettaire; 27,3 % ( $n = 33$ ), une bithérapie antiplaquettaire; 19,8 % ( $n = 24$ ), des anticoagulants plus un traitement antiplaquettaire; 6,6 % ( $n = 8$ ), des anticoagulants seuls; 2,6 % ( $n = 3$ ), un traitement inconnu. Les patients qui avaient subi une angioplastie et une pose d'endoprothèse étaient plus susceptibles d'obtenir à leur sortie de l'hôpital une bithérapie antiplaquettaire (rapport de risque [RR] : 7,14; intervalle de confiance [IC] à 95 % : 2,87-17,76;  $P < 0,01$ ); les patients qui avaient subi une embolectomie, ou thrombectomie, étaient plus susceptibles d'obtenir à leur sortie de l'hôpital un anticoagulant seul (RR : 2,61; IC à 95 % : 1,00-6,81;  $P = 0,049$ ); les patients qui avaient subi un pontage périphérique étaient plus susceptibles d'obtenir à leur congé de l'hôpital un simple traitement antiplaquettaire (RR : 2,28; IC à 95 % : 1,11-4,69;  $P = 0,024$ ). Comparativement à l'admission, ni les statines (60,8 % vs 56,3 %;  $P = 0,23$ ) ni les inhibiteurs du système rénine-angiotensine-aldostérone (48,7 % vs 50,6 %;  $P = 0,58$ ) n'avaient été prescrits à des taux plus élevés à la sortie de l'hôpital. **Conclusions :** Nous observons une hétérogénéité substantielle de l'ordonnance des antithrombotiques après la revascularisation urgente/nouvelle revascularisation. L'hospitalisation n'a donné lieu à aucune augmentation des médicaments de protection vasculaire non antithrombotiques. Des essais cliniques et des interventions du système de santé qui permettent d'optimiser le traitement médical des patients atteints d'une maladie artérielle sont d'une urgente nécessité.

consecutive patients discharged from this hospital between April 2016 and September 2017, following admission for severe limb ischemia, defined as nontraumatic lower ALI or CLI requiring intervention.

## Ethics

Ethical approval was obtained for the **Canadian Acute Limb Ischemia Registry (CANALISE)** from the Hamilton Integrated Research Ethics Board (Hamilton, Ontario, Canada) on February 16, 2018.

## Data collection

All cases of severe limb ischemia requiring urgent/emergent revascularization between April 1, 2016 and September 1, 2017 were identified using the Local Health Integration Network (LHIN) CorHealth database.<sup>14</sup> These data were then uploaded to an online secure server (**Research Electronic Data Capture [REDCap]**).<sup>15</sup>

We included adult patients aged  $\geq 18$  years who were admitted to the hospital for lower-extremity revascularization for limb ischemia requiring urgent/emergent revascularization, defined as limb-threatening ischemia, confirmed by limb hemodynamics or imaging, that led to an acute vascular intervention within 30 days of symptom onset. In the absence of confirmation by limb hemodynamics or imaging, absent pedal pulses were acceptable as a hemodynamic criterion for ALI. CLI was defined as severe limb ischemia leading to an intervention, with symptom onset occurring  $> 30$  days prior to revascularization. We excluded cases of lower-extremity intervention secondary to trauma, infection, or pseudoaneurysm.

Patient and hospital care information was extracted from the electronic medical records using a standardized case-record

form. This included preadmission information, hospitalization details (including intervention type), and data at 30 days and 1 year following discharge from the hospital.

### Study outcomes

The primary outcome was antithrombotic therapy following intervention for urgent/emergent limb ischemia or CLI. This therapy was categorized as either: (i) single antiplatelet therapy (SAPT); (ii) dual antiplatelet therapy (DAPT); (iii) full-dose oral anticoagulant (AC); (iv) full- or reduced-dose oral AC + antiplatelet therapy (APT); (v) none; or (vi) unknown. These data were collected at the time of discharge following intervention.

The secondary outcome was use of other established vascular protective medications (ie, statin, angiotensin-converting enzyme inhibition/angiotensin receptor blocker) following intervention for urgent/emergent limb ischemia or CLI.

### Statistical analysis

Baseline characteristics are reported using either means and standard deviations, counts and proportions, or medians and interquartile ranges, depending on the type of variable and its distribution. We report odds ratios, adjusted odds ratios (aORs) their 95% confidence intervals (CIs) and associated *P* value.

To investigate the relationship between type of surgical intervention type and antithrombotic therapy choice, we developed univariate and multivariate ordinal logistic regression models. Ordinal categorization of antithrombotic therapy intensity was adjusted for age and according to a comorbidity index that included presence of diabetes, hypertension, dyslipidemia, coronary artery disease, stroke, and chronic kidney disease.

To assess changes in preventative therapy prescription rates before and after limb-related events, McNemar repeated-measure proportion tests of marginal homogeneity were utilized. We report the associated  $\chi^2$  scores ( $\chi^2_{MN2}$ ) and *P* values. The data analysis for this paper was performed using SAS software, version 8, of the SAS System for Windows SAS Institute, Inc. (Cary, N.C.).

### Results

A total of 158 patients were identified as hospitalized with ALI or CLI. (Supplemental Fig. S1). Of these patients, 148 (93.6%) were alive at discharge. Modifiable risk factors for vascular disease were common, including previous or current smoking (79.7%; *n* = 126), hypertension (77.8%; *n* = 123), dyslipidemia (64.6%; *n* = 102), and diabetes (41.8%; *n* = 66). The majority of patients had a history of vascular intervention for PAD, namely previous aorta–femoral or lower-extremity bypass surgery (48.1%; *n* = 76), previous endovascular intervention for indication of PAD (22.8%; *n* = 36), or previous limb or foot amputation (3.8%; *n* = 6). In all, 38.0% of patients (*n* = 60) had coronary artery disease, and 10.1% (*n* = 16) had renal insufficiency defined by a low estimated glomerular filtration rate. Despite these histories, established secondary vascular protective medications were comparatively less common.  $\beta$ -hydroxy  $\beta$ -methylglutaryl (HMG)-CoA reductase (statin) therapy was utilized in 56.3%

**Table 1. Patient demographics**

Variable	Value
Total number of patients (N)	158
Age, y, mean (SD)	67.0 (11.3)
Gender, male	102 (64.6)
Body mass index, mean (SD)	27.9 (5.7)
Smoking history (current or former)	126 (79.7)
History of PAD	118 (74.7)
Diabetes	66 (41.8)
Hypertension	123 (77.8)
Dyslipidemia	102 (64.6)
History of CAD	60 (38.0)
History of stroke or TIA	25 (15.8)
Chronic kidney disease (eGFR < 60)	16 (10.1)
Atrial fibrillation	26 (16.6)
Atrial fibrillation (on anticoagulation)	22 (13.9)
Mechanical heart valve	2 (1.3)
Previous VTE	13 (8.2)
Admission medications	
Statin	87 (55.3)
ACE /ARB	80 (50.3)
$\beta$ -blocker	55 (34.8)
Other antihypertensive	71 (44.7)
Insulin	23 (14.3)
Oral hypoglycemic	47 (29.8)
Proton pump inhibitor	46 (29.2)
Previous intervention for PAD	
Aorta–femoral or lower-extremity bypass	76 (48.1)
Endovascular intervention	36 (22.8)
Limb or foot amputation	6 (3.8)

Values are n (%), unless otherwise indicated.

ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; PAD, peripheral arterial disease; SD, standard deviation; TIA, transient ischemic attack; VTE, venous thromboembolism.

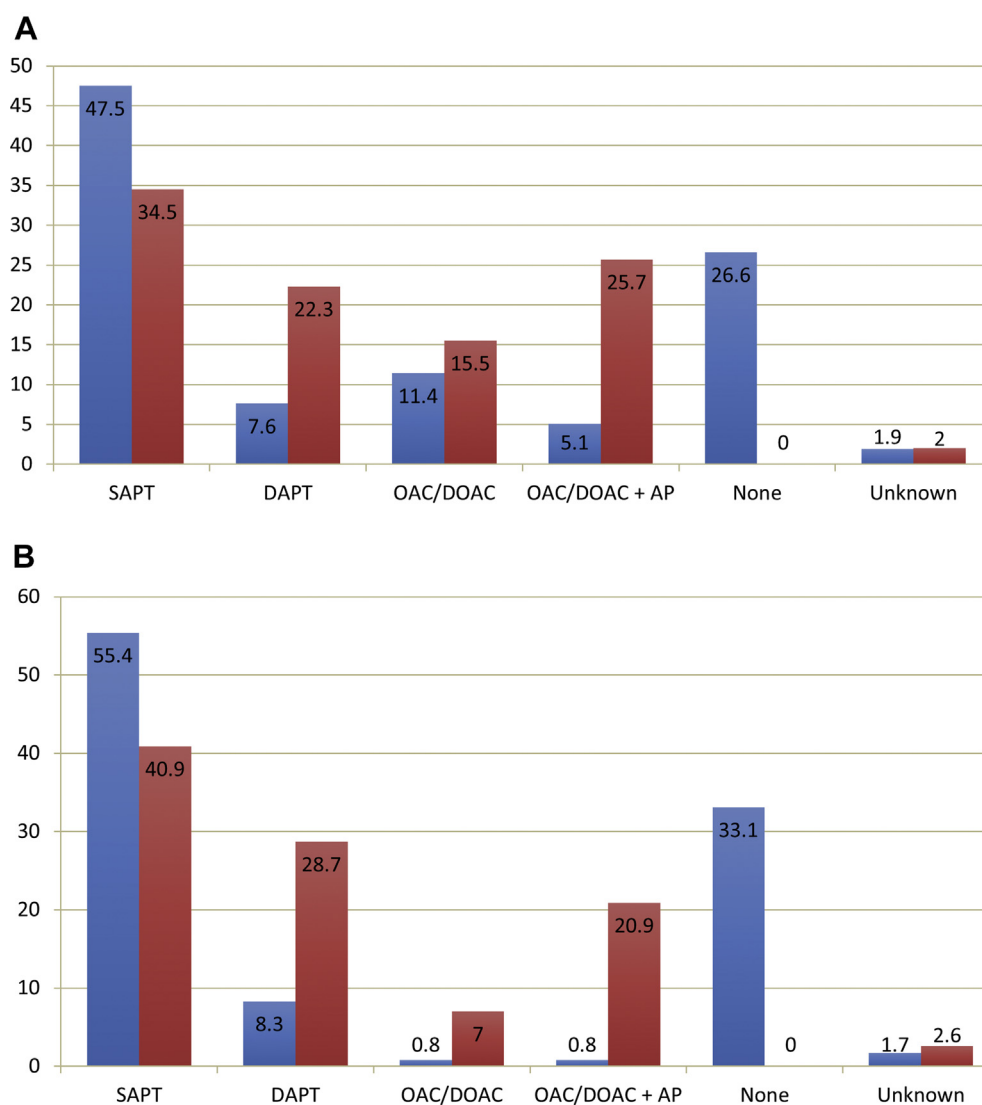
of patients (*n* = 89) at baseline, and renin–angiotensin–aldosterone system modifiers were used in 50.6% of patients (*n* = 80; Table 1).

A pre-existing indication for full-dose oral anticoagulation was present in 23.4% of patients (*n* = 37) admitted for severe limb ischemia, 16.6% (*n* = 26) with atrial fibrillation, 1.3% (*n* = 2) with a mechanical valve, and 8.2% (*n* = 13) with previous venous thromboembolic disease. Among the 121 patients without a pre-existing indication for anticoagulation therapy, the antithrombotic strategies at admission included SAPT (55.4%; *n* = 67), DAPT (8.3%; *n* = 10), an AC with an antiplatelet agent (0.8%; *n* = 1), and AC treatment alone (0.8%; *n* = 1); in 2 patients (1.7%), the treatment strategy was not recorded. Surprisingly, 33.1% of patients (*n* = 40) were on neither an antiplatelet agent nor an AC (Fig. 1A; Table 2).

### Surgical strategies during hospitalization

Surgical bypass was the most commonly utilized surgical strategy (57.0%; *n* = 90), followed by embolectomy/thrombectomy (50.6%; *n* = 80), endarterectomy (36.7%; *n* = 58), angioplasty (with stent: 20.9% [*n* = 33]; without stent: 5.1% [*n* = 8]), and amputation (3.2%; *n* = 5). Thrombolysis was utilized in a small number of patients, (1.3%; *n* = 2). These surgical strategies were not mutually exclusive.

Patients undergoing angioplasty with stenting were 7.14 times (95% CI: 2.87-17.76; *P* < 0.001) more likely to be



**Figure 1.** Antithrombotic medications(s) (% patients) at time of admission (blue) and discharge (red). (A) Total patient population. (B) No indication for full oral anticoagulant (OAC). AP, antiplatelet; DAPT, dual-antiplatelet therapy; DOAC, direct oral anticoagulant; SAPT, single-antiplatelet therapy.

prescribed DAPT at discharge, compared with those undergoing other vascular procedures. Patients undergoing embolectomy/thrombectomy were 2.61 times (95% CI: 1.00-6.81;  $P = 0.049$ ) as likely to be prescribed anticoagulation alone at discharge. Conversely, patients undergoing embolectomy/thrombectomy were less likely to receive DAPT (aOR:0.38; 95% CI: 0.17-0.89;  $P = 0.026$ ). Finally, patients undergoing bypass grafting alone were 2.28 times (95% CI: 1.11-4.69;  $P = 0.024$ ) more likely to be discharged on SAPT, compared with those undergoing other vascular procedures, and they had lower rates of DAPT at discharge as well (aOR: 0.34; 95% CI: 0.15-0.79;  $P = 0.011$ ). No other operative procedures were associated with particular antithrombotic regimens (Table 3).

### Therapies at discharge

Among patients who survived to discharge, and without a pre-existing indication for anticoagulation treatment, SAPT (38.8%;  $n = 47$ ); DAPT (27.3%;  $n = 33$ ), anticoagulation and antiplatelet treatment in combination (19.8%;  $n = 24$ ),

and anticoagulation treatment alone (6.6%;  $n = 8$ ) were prescribed in descending frequency, with 2.5% ( $n = 3$ ) being prescribed unknown antithrombotics (Fig. 1, A and B).

### Vascular protective medications

Comparing discharge rates to admission rates, neither statins (60.8% vs 56.3%;  $\chi^2_{MN2} \geq 1.45$  (degrees of freedom = 1);  $P = 0.23$ ) nor renin-angiotensin-aldosterone system - inhibitor (48.7% vs 50.6%;  $\chi^2_{MN2} \geq 0.31$ ;  $P = 0.58$ ) prescriptions were increased. Of other medications, only use of the hypertensive category of beta-blockers increased significantly at discharge compared to baseline (44.6% vs 34.38%;  $\chi^2_{MN2} \geq 5.57$  (degrees of freedom = 1);  $P = 0.018$ ; Fig. 2).

### Discussion

CANALISE I demonstrates that, among PAD patients hospitalized for severe limb ischemia, there is heterogeneity in the use of antithrombotic regimens following peripheral

**Table 2. Antithrombotic medications at time of discharge**

Antithrombotic therapy	Total	No indication for AC	Indication for AC
SAPT	51 (34.5)	47 (40.9)	4 (12.1)
DAPT	33 (22.3)	33 (28.7)	0 (0.0)
OAC/DOAC	23 (15.5)	8 (7.0)	15 (45.5)
OAC/DOAC + AP	38 (25.7)	24 (20.9)	14 (42.4)
None	0 (0.0)	0 (0.0)	0 (0.0)
Unknown	3 (2.0)	3 (2.6)	0 (0.0)

Values are n (%).

AC, anticoagulant; AP, antiplatelet; DAPT, dual-antiplatelet therapy; DOAC, direct oral anticoagulant; OAC, oral anticoagulant; SAPT, single-antiplatelet therapy.

vascular interventions. No antithrombotic regimens were utilized predominantly, although a pre-existing need for anticoagulation, along with procedure type, influenced antithrombotic therapy choices. Although antithrombotic therapy was prescribed to the vast majority of patients upon discharge, the use of other vascular protection medications did not significantly increase at discharge.

Patients with PAD have a high risk of both major adverse cardiac events and MALE.<sup>16</sup> This risk is substantially higher in the first year following an ischemic limb event.<sup>11</sup> Antithrombotics are among the most effective medical therapies to reduce this ischemic risk.<sup>10,16</sup> In the **Effects of Ticagrelor and Clopidogrel** in patients with Pad (EUCLID) trial, which compared use of ticagrelor to use of clopidogrel in patients with stable PAD, a subgroup analysis showed that in patients discharged from the hospital after suffering ALI, 41.3% required subsequent revascularization, and 19.4% had a subsequent amputation. Furthermore, approximately half of all deaths following ALI were secondary to cardiovascular causes.<sup>17</sup> Patients in the **Cardiovascular Outcomes for People Using Anticoagulation Strategies** (COMPASS) trial who suffered MALE, such as the need for urgent/emergent revascularization, had a 200-fold increased risk of vascular amputation and a 3-fold increase in death, compared with

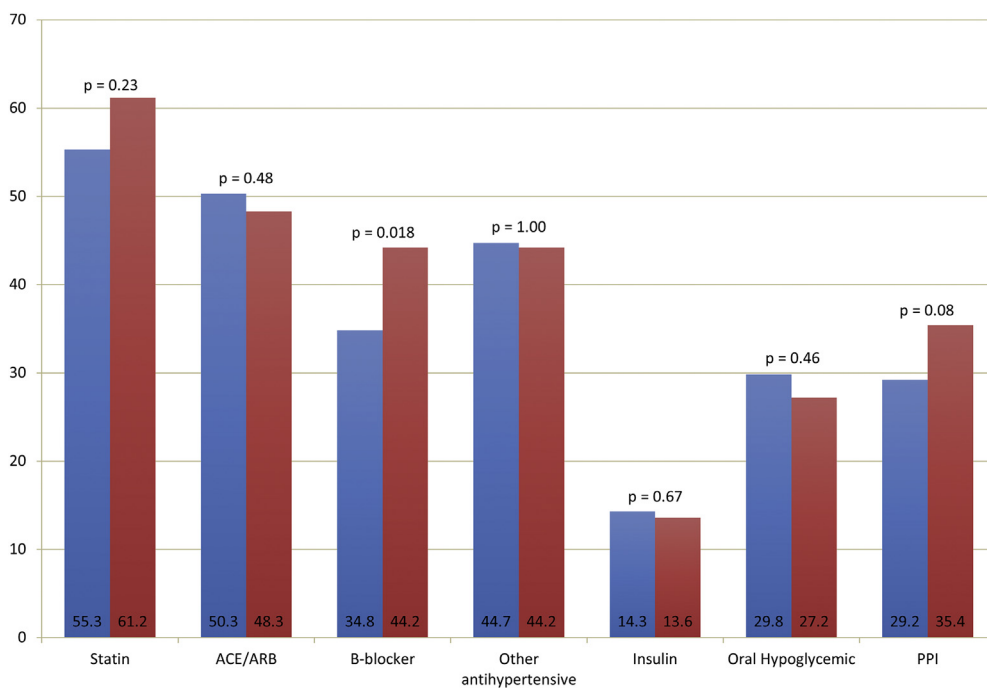
PAD patients who did not suffer MALE.<sup>11</sup> Despite the high risks for these patients, uncertainty remains regarding the optimal antithrombotic strategy. Following MALE in the COMPASS trial, there was enough uncertainty regarding the optimal antithrombotic to use that 63% remained on their blinded randomized drug therapy; 13% were transitioned to SAPT, 10% received DAPT, 2% received an oral AC, and 12% had all antithrombotic therapy discontinued.<sup>11</sup> These findings highlight the lack of evidence guiding clinician decision-making regarding antithrombotics following urgent/emergent revascularization for limb ischemia. This uncertainty is particularly significant given that the choice of antithrombotic therapy is not a benign one, with oral AC and DAPT regimens conferring significant risks of bleeding that must be balanced against their potential benefit.<sup>10</sup> Vascular surgeons echo this need for more robust evidence, as in a recent survey conducted in Canada, in which 91% were found to believe that significant uncertainty still exists in antithrombotic decision-making following urgent/emergent revascularization.<sup>12</sup>

In this analysis, only angioplasty with stenting demonstrated a strong and significant signal favoring a particular antithrombotic regimen, namely DAPT. This result is likely a reflection of ambient American Heart Association and European Society of Cardiology guidelines at that time, although even so, 46.4% of patients who received stenting were discharged on antithrombotic therapy other than DAPT. The use of DAPT after endovascular intervention has largely been extrapolated from the coronary trials, and it has been influenced by the manufacturer package insert. The duration of DAPT after an endovascular procedure ranges from 1 month to 6 months.<sup>18</sup> The guidelines support the use of DAPT in patients undergoing endovascular procedures, but they do not stratify by elective vs urgent scenarios. The recently published **Vascular Outcomes Study of ASA Along with Rivaroxaban in Endovascular or Surgical Limb Revascularization for PAD** (VOYAGER PAD) trial has the potential to change antithrombotic practice post-lower limb revascularization. This

**Table 3. Antithrombotic medication at discharge, stratified by intervention**

Intervention type	Antithrombotic therapy at discharge	Univariate analysis OR (95% CI)	P
Endarterectomy	SAPT	1.02 (0.50 to 2.09)	0.95
	DAPT	0.86 (0.37 to 2.00)	0.72
	OAC/DOAC	1.54 (0.62 to 3.81)	0.35
	OAC/DOAC + AP	0.81 (0.37 to 1.80)	0.61
Bypass	SAPT	2.28 (1.11 to 4.69)	0.024
	DAPT	0.34 (0.15 to 0.79)	0.011
	OAC/DOAC	0.44 (0.18 to 1.10)	0.08
	OAC/DOAC + AP	1.75 (0.81 to 3.78)	0.16
Embolectomy/thrombectomy	SAPT	0.92 (0.46 to 1.83)	0.81
	DAPT	0.38 (0.17 to 0.89)	0.026
	OAC/DOAC	2.61 (1.002 to 6.81)	0.049
	OAC/DOAC + AP	1.31 (0.62 to 2.76)	0.48
Angioplasty (without stent)	SAPT	0.59 (0.11 to 3.01)	0.52
	DAPT	1.22 (0.23 to 6.36)	0.81
	OAC/DOAC	1.81 (0.34 to 9.58)	0.49
	OAC/DOAC + AP	0.92 (0.18 to 4.75)	0.92
Angioplasty (with stent)	SAPT	0.54 (0.21 to 1.37)	0.19
	DAPT	7.14 (2.87 to 17.76)	0.00024
	OAC/DOAC	N/A	N/A
	OAC/DOAC + AP	0.71 (0.26 to 1.91)	0.49

AP, antiplatelet; CI, confidence interval; DAPT, dual-antiplatelet therapy; DOAC, direct oral anticoagulant; OAC, oral anticoagulant; N/A, not available; OR, odds ratio; SAPT, single-antiplatelet therapy.



**Figure 2.** Vascular protective medications (% patients) at admission (**blue**) compared to discharge (**red**). ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blockers; PPI, proton-pump inhibitor.

trial enrolled patients undergoing infrainguinal revascularization, including 20% of patients with critical limb ischemia, and tested the effectiveness of the combination of low-dose rivaroxaban and aspirin, compared with that of aspirin alone. In addition, investigators could use, at their discretion, short-term clopidogrel, as two-thirds of trial patients underwent endovascular therapy.<sup>6</sup> The VOYAGER PAD trial showed that the combination of low-dose rivaroxaban and aspirin, compared with aspirin alone, reduced rates of incident ALI, major amputation for vascular causes, myocardial infarction, ischemic stroke, and death from cardiovascular causes (hazard ratio 0.85, 95% CI: 0.76-0.96), as well as rates of unplanned index limb revascularization for recurrent ischemia (hazard ratio 0.88; 95% CI 0.79 -0.99). Interestingly, although 50% of patients in the trial also used concomitant short-term clopidogrel (median: 30 days), there was no additional benefit in reduction of ischemic events among patients who received clopidogrel.<sup>6</sup> Therefore, although the evidence from the COMPASS and VOYAGER PAD trials indicates that a reasonable antithrombotic option would be to use low-dose rivaroxaban and aspirin in stable PAD patients, including those undergoing lower-extremity revascularization, it cannot be extrapolated to patients with ALI. Guidelines from the American Heart Association and the European Society of Cardiology do not explicitly address antithrombotic use in this setting, save for the need for intravenous heparin until successful revascularization can be performed. Randomized controlled trials investigating optimal antithrombotic treatments following urgent/emergent limb revascularization, such as comparing full-dose anticoagulation to COMPASS therapy, are urgently needed.

Hospitalization for PAD intervention serves as an opportunity to optimize vascular protective therapies in this accessible population. The importance of vascular protective medications

following urgent/emergent revascularization is recognized by the practitioners taking care of these patients; we note in our study that all patients were discharged on some form of antithrombotic therapy, compared with 33.1% of patients who were not administered any antithrombotic leading up to admission. However, we demonstrate that this has not translated into increased use of other vascular protective medications, with no significant increase in the prescription of statins or renin-angiotensin-aldosterone system -inhibitors upon discharge from the hospital.

Our findings challenge the long-term management strategies for PAD patients and demonstrate a missed opportunity for vascular optimization in PAD patients admitted for limb ischemia. Patients with PAD are undertreated for their comorbidities,<sup>19</sup> with utilization of antithrombotics, statins, and renin-angiotensin-aldosterone system -inhibitors at a rate approximately half that for their counterparts with coronary artery disease.<sup>20</sup> On a population basis, treating the risk factors for PAD is the most effective strategy to reduce the global burden of disease. Simple guideline-based treatment of comorbidities can reduce major adverse cardiac events, MALE, and even overall mortality by 65% with the use of antiplatelet, statin, and angiotensin-converting enzyme/angiotensin receptor blocker, as estimated in the National Health and Nutrition Examination Survey (NHANES) cohort.<sup>21</sup> Beyond randomized trials investigating optimal antithrombotic therapy, systematic innovations are critical in improving outcomes in PAD patients. Although digital or process-based solutions are prudent, the roles of vascular medicine, vascular surgery, vascular rehabilitation, and primary care must expand, in order to address the medical and lifestyle gaps contributing to the poor outcomes in PAD patients.

This investigation is limited by the fact that it includes only one academic health system in Canada. However, the

large catchment area of Hamilton Health Sciences, and the tertiary nature of the care provided likely enhances the generalizability of the study. The fact that this sample is drawn from a large academic centre may also have led to different results, based on the availability of consultation services, such as those for thrombosis and vascular medicine, compared to what might have been found with community practices where these specialists may not exist. Thus, the study may overestimate the rate of antithrombotic intensification and the degree of risk-factor reduction pursued, as compared to those for typical care after urgent/emergent limb revascularization. Our results indicating suboptimal use of vascular protective medications are also congruent with other Canadian and US studies that collectively show no increase in use of vascular protective medications over time.<sup>18,22,23</sup>

### Conclusion

Patients requiring urgent and emergent limb revascularization for severe PAD face significant morbidity and mortality despite advances in peripheral interventions and medical therapy.<sup>11,24</sup> This investigation demonstrates the large heterogeneity in prescribing practices following these vascular interventions, which are only partially influenced by pre-existing need for anticoagulation and procedure type. Significant uncertainty regarding the optimal antithrombotic regimen after intervention for severe limb ischemia remains. This investigation also shows, using contemporary data, that even those at highest risk for ischemic events are not receiving adequate, proven, preventative medications, and it identifies a missed opportunity for such optimization during hospital admission. Randomized controlled trials informing antithrombotic therapy following urgent/emergent revascularization, as well as large-scale quality improvement measures to optimize proven secondary prevention therapies in PAD patients, are urgently needed for this high-risk patient population.

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### Disclosures

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### **Supplementary Material**

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