


Veithsymposium 2024 | November 19, 2024 | NYC, USA

### Why Are Patients Who Undergo Lower Extremity Revascularization At Risk For Major Bleeding: How To Estimate That Risk

Assoc. Prof. Dr. Christian-Alexander Behrendt, FESVS  
 Chief & Head, Department of Vascular & Endovascular Surgery, Asklepios Clinic Wandsbek, Asklepios Medical School, Hamburg  
 Section Editor, European Journal of Vascular & Endovascular Surgery  
 Medical & Scientific Director, German Institute for Vascular Research, Berlin



Behrendt CA | christianbehrendt.net | @VAScevidence | behrendt@hamburg.de

## Disclosures

- I have the following potential conflicts of interest to report:
  - Receipt of grants/research support
  - Receipt of honoraria and travel support
  - Participation in a company sponsored speakers' bureau
  - Employment in industry
  - Shareholder in a healthcare company
  - Owner of a healthcare company
- I do not have any potential conflict of interest

**No competing interests & nothing to disclose!**


Behrendt CA | christianbehrendt.net | @VAScevidence | behrendt@hamburg.de

**A lot of updated and new guidelines, and numerous debates on antithrombotics...**

- ESVS Guidelines on antithrombotics in vascular disease 2023**
- IWGDF/ESVS/SVS Guidelines on diabetic foot ulcer 2023**
- ESVS/SVS/WFVS Global Vascular Guidelines To be updated! 2019**
- ESVS Guidelines on asymptomatic PAD and intermittent claudication 2024**
- ESC Guidelines on peripheral arterial & aortic disease 2024**
- German Multisocietal Guidelines on PAD 2024**

**...how does this work in everyday clinical practice?**

# PAD

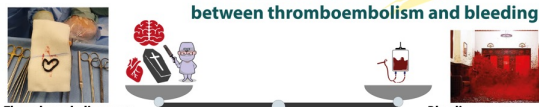


Behrendt CA | christianbehrendt.net | @VAScevidence | behrendt@hamburg.de

Twine CP et al.  
**Editor's Choice – European Society for Vascular Surgery (ESVS) 2023 Clinical Practice Guidelines on Antithrombotic Therapy for Vascular Diseases** <https://doi.org/10.1016/j.ejvs.2023.03.042>

**The ESVS issued completely new clinical practice guidelines on antithrombotic therapy for vascular disease!**

**...how can we master the thin line between thromboembolism and bleeding?!**



Thromboembolic events...      Bleeding events...


Behrendt CA | christianbehrendt.net | @VAScevidence | behrendt@hamburg.de

### No benefit over placebo in RCTs (but comparable bleeding risk)

**Asymptomatic Disease**

- Aspirin for Asymptomatic Atherosclerosis Trial (Fowkes et al. 2010)**
- 1998-2008 Scotland N = 28 980**
- Prevention of Progression of Arterial Disease and Diabetes (POPAPAD) Trial**
- 1997-2001 Scotland N = 1 276**

**Patients with isolated asymptomatic lower extremity artery disease are not recommended to have aspirin for cardiovascular prevention.**

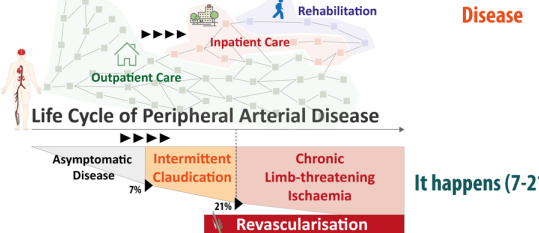


Behrendt CA | christianbehrendt.net | @VAScevidence | behrendt@hamburg.de

### ...but what if the patient approaches the next stage?

**Symptomatic Disease**

**Life Cycle of Peripheral Arterial Disease**



Asymptomatic Disease 7% → Intermittent Claudication 21% → Chronic Limb-threatening Ischaemia

It happens (7-21%)!

Behrendt CA | christianbehrendt.net | @VAScevidence | behrendt@hamburg.de

### Optimal pharmacological therapy of symptomatic PAD

...only few studies!

Different strategies are available...  
SAPT, DAPT, VKA, DOAC, NOAC, DPI

...???

It is all about weighting the individual benefits and risks!

Freedom from MALE & MACE vs Bleeding

CAPRIE, COMPASS, VOYAGER PAD, WAVE

Behrendt CA | christianbehrendt.net | @VAScevidence | behrendt@hamburg.de

### Due to exclusion bias... People with heightened risk for bleeding are not covered by trials

Exclusion criteria associated with bleeding risk

- End stage kidney disease
- Hepatic disease associated with bleeding
- History of bleeding & significant risk of bleeding
- History of haemorrhage, stroke, or TIA
- Vascular aneurysms of large arteries
- Poorly controlled diabetes or severe uncontrolled hypertension

Achilles heel?

Behrendt CA | christianbehrendt.net | @VAScevidence | behrendt@hamburg.de

Peters F, Kuchenbecker J, Acar L, Marschall U, L'Hoest H, Lanyro F, Spanos K, Behrendt CA. Antithrombotic Treatment Patterns of Patients with Symptomatic Peripheral Arterial Occlusive Disease in Germany: Evidence from Health Insurance Claims Data. J Clin Med. 2022;11(18):5455. DOI: 10.3390/jcm11185455

### Do clinicians find a way through these pitfalls in practice?

	IC n=40 004	CLTI n=40 422
Complicated diabetes	16%	41%
Prior stroke or TIA	7%	13%
History of bleeding	16%	34%
Kidney failure	22%	43%

No antithrombotics after discharge: 28%

No! One third does not get any antithrombotic agent!

Behrendt CA | christianbehrendt.net | @VAScevidence | behrendt@hamburg.de

### Bleeding risk assessment and risk reduction

...but how can we predict the individual risk of bleeding in an everyday clinical practice setting?

Available scores are not well validated (if at all) ...only on cardiac populations (e.g., atrial fibrillation)

Lower Extremity PAD

HEMOR<sup>2</sup>RHAGES, ACCP, HAS-BLED, REACH, ARC-HBR, ATRIA, PE-CH, NSAIDs, RIEE, Antithrombotics

Behrendt CA, Kreutzburg T, Nordanstig J, Twine CP, Marschall U, Kakkos S, Aboyns V, Peters F. The OAC3-PAD Risk Score Predicts Major Bleeding Events one Year after Hospitalisation for Peripheral Artery Disease. Eur J Vas Endovasc Surg. 2022;63:503-510. DOI: 10.1016/j.ejvs.2021.12.019

### Together with the guideline writing committee...

81 930 patients with index treatment of PAD

47% females, 72 years

inpatient, outpatient, prescriptions

2005 Lookback, 2010-2018, 12m follow-up, 2020

...we developed a PAD-specific risk score on German claims data

Behrendt CA | christianbehrendt.net | @VAScevidence | behrendt@hamburg.de

### OAC3-PAD

- Oral anticoagulation
- Age >80 years
- Chronic limb-threatening ischaemia
- Congestive heart failure
- Chronic kidney disease
- Prior bleeding event
- Anaemia
- Dementia

Sum: 1-Year Risk of Major Bleeding

Risk Group	Score	Points
High-risk group	6-9	3 points
Moderate to high risk group	3-5	0 points
Low to moderate risk group	1-2	1 point
Low-risk group	0	0 points

Harrell's C-Index = 0.69 (internal)

20% have high risk!

Behrendt CA | christian.behrendt.net | @VAScevidence | behrendt@hamburg.de

## The first and only externally validated PAD-specific risk score!

### OAC3-PAD

- Oral anticoagulation
- Age >80 years
- Chronic limb-threatening ischaemia
- Congestive heart failure
- Chronic kidney disease
- Prior bleeding event
- Anaemia
- Dementia

Sum:

High-risk group	4-62%	03-33 points
Moderate to high risk group	2-62%	01-8 points
Low to moderate risk group	1-26%	01-4 points
Low risk group	1-26%	00 points

**Externally validated!**

- Internal validation: C-index 0.69
- External validation: C-index 0.61
- External validation: C-index 0.65
- External validation: C-index 0.71
- External validation: C-index 0.65
- External validation: C-index 0.66
- External validation: **moderate!**

Behrendt CA | christian.behrendt.net | @VAScevidence | behrendt@hamburg.de

Twine CP, Kakkos SK, Aboyans V, Baumgartner I, Behrendt CA, Bellmunt-Montoya S, Jilma B, Nordanstig J, Saratzis A, Reekers JA, Zlatanovic P. European Society for Vascular Surgery (ESVS) 2023 Clinical Practice Guidelines on Antithrombotic Therapy for Vascular Diseases. <https://doi.org/10.1016/j.ejvs.2023.03.042>

### Symptomatic PAD

Single antiplatelet therapy

Clpidogrel

#### ...Scenario #1: The „BEST-CLI“-Patient

**Bleeding risk assessment and treat risk factors**

- not at high risk of bleeding
- high risk of bleeding
- Consider **SAPT**
- Patients should be considered for **DPI**
- Or (vein): Consider **Vitamin K antagonist**
- Or (prosthetic): Consider **SAPT**

#### ...Scenario #2: The „BASIL-2“-Patient

**Bleeding risk assessment and treat risk factors**

- not at high risk of bleeding
- Patients should be considered for **DPI**
- Patients may be considered for **short course DAPT**

Behrendt CA | christian.behrendt.net | @VAScevidence | behrendt@hamburg.de

## Conclusions

- Nothing is without risks: We must take bleeding complications into account!
- Approximately 20% have heightened bleeding risk and we must take this fact into consideration!
- The OAC3-PAD is the first disease-specific (#PAD) and both internally & externally validated risk prediction score!
- Real world data can help to closing gaps & guide decisions!
- The first clinical practice guidelines on antithrombotics: **ESVS!**

behrendt@hamburg.de

Assoc. Prof. Dr. Christian-Alexander Behrendt, FESVS  
 Chief & Head, Department of Vascular & Endovascular Surgery, Asklepios Clinic Wandsbek, Asklepios Medical School, Hamburg  
 Section Editor, European Journal of Vascular & Endovascular Surgery  
 Medical & Scientific Director, German Institute for Vascular Research, Berlin  
 Co-Chair, ESVS 2024 Clinical Practice Guidelines on PAD