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Patientenberichteter Therapieerfolg in Registern und Studien zur Peripher Arteriellen Verschlusskrankheit – ein Delphi-Konsens über Ergebnisqualitätsindikatoren

Publikationspromotion

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1. Manuskript mit Letter of Acceptance

A Delphi Consensus on Patient-reported Outcomes for Registries and Trials including Patients with Intermittent Claudication: Recommendations and Reporting Standard

--Manuscript Draft--

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Abstract:	<p>Objective</p> <p>This study aimed to develop a core set of patient-reported outcome quality indicators (QIs) for the treatment of patients with intermittent claudication (IC), that allow a broad international implementation across different vascular registries and within trials.</p> <p>Methods</p> <p>We utilized a rigorous modified two-stage Delphi technique to promote consensus building on patient-reported outcome QIs among an expert panel consisting of international vascular specialists, patient representatives and registry members of the VASCUNET and the International Consortium of Vascular Registries. Potential QIs identified through an extensive literature search or additionally proposed by the panel</p>

were validated by the experts in a preliminary survey and included for evaluation. Consensus was reached if $\geq 80\%$ of participants agreed that an item was both clinically relevant and practical.

Results

Participation rates in two Delphi rounds were 66% (31 participants out of 47 invited) and 90% (54 out of 60), respectively. Initially, 145 patient-reported outcome QI were documented. Following the two Delphi rounds, 18 quality indicators remained, all of which reached consensus regarding clinical relevance and practicability. The VascuQoL questionnaire (VascuQoL-6), currently the most common patient-reported outcome measurement (PROM) used within vascular registries, includes a total of six items. Five of these six items also matched with high rated indicators identified in the Delphi study. Consequently, the panel recommends the use of the VascuQoL-6 survey as a preferred core PROM QI set as well as an optional extension of 12 additional patient-reported QI that were also identified in the study.

Conclusion

The current recommendation based on the Delphi consensus building approach strengthens the international harmonisation of registry data collection in relation to patient-reported outcome quality. Continuous and standardized quality assurance will ensure that registry data may be used for future quality benchmarking studies and ultimately positively impact the overall quality of care provided to PAOD patients.

Dear Dr. Behrendt,

We are pleased to inform you that your manuscript EJVES17913R entitled A Delphi Consensus on Patient-reported Outcomes for Registries and Trials including Patients with Intermittent Claudication: Recommendations and Reporting Standard has been accepted for publication in the European Journal of Vascular & Endovascular Surgery.

Further comments from Editors and Reviewers (if any):

Dr. Behrendt: Thank you for your attentive and thorough revisions. We are pleased to inform you and your co-authors that we have made the editorial decision to ACCEPT this revised manuscript for publication in the EJVES.

The accepted version of your manuscript will be shortly available as uncorrected pre-proofs online. The manuscript will undergo additional style and copyediting and will be forwarded to the publisher for typesetting. The publisher will send galley proofs to you shortly afterwards via email in PDF format. Please return proofs immediately and limit your changes to minor editorial or typesetting corrections only.

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Congratulations!

Joe

Joseph L. Mills, MD
Associate Editor, Peripheral Arteries
EJVES

A Delphi Consensus on Patient-reported Outcomes for Registries and Trials including Patients with Intermittent Claudication: Recommendations and Reporting Standard

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Short title: Patient reported outcomes in the treatment of intermittent claudication

What does this study/review add to the existing literature and how will it influence future clinical practice

After two rounds in this modified Delphi study, a total of 145 patient reported outcome variables from the literature and established registries were evaluated by an international panel of medical specialists, registry experts, and patient representatives to ultimately generate a recommendation for both registries and trials on patients with intermittent claudication. For the first time, the collection of Vascu-QoL-6 as core outcomes along with 12 additional items was recommended by this panel. This may help to further harmonise real world data research as well as clinical practice in the future.

Abstract

Objective: This study aimed to develop a core set of patient-reported outcome quality indicators (QIs) for the treatment of patients with intermittent claudication (IC), that allow a broad international implementation across different vascular registries and within trials.

Methods: We utilized a rigorous modified two-stage Delphi technique to promote consensus building on patient-reported outcome QIs among an expert panel consisting of international vascular specialists, patient representatives and registry members of the VASCUNET and the International Consortium of Vascular Registries. Potential QIs identified through an extensive literature search or additionally proposed by the panel were validated by the experts in a preliminary survey and included for evaluation. Consensus was reached if $\geq 80\%$ of participants agreed that an item was both clinically relevant and practical.

Results: Participation rates in two Delphi rounds were 66% (31 participants out of 47 invited) and 90% (54 out of 60), respectively. Initially, 145 patient-reported outcome QI were documented. Following the two Delphi rounds, 18 quality indicators remained, all of which reached consensus regarding clinical relevance and practicability. The VascuQoL questionnaire (VascuQoL-6), currently the most common patient-reported outcome measurement (PROM) used

within vascular registries, includes a total of six items. Five of these six items also matched with high rated indicators identified in the Delphi study. Consequently, the panel recommends the use of the VascuQoL-6 survey as a preferred core PROM QI set as well as an optional extension of 12 additional patient-reported QI that were also identified in the study.

Conclusion: The current recommendation based on the Delphi consensus building approach, strengthens the international harmonisation of registry data collection in relation to patient-reported outcome quality. Continuous and standardized quality assurance will ensure that registry data may be used for future quality benchmarking studies and ultimately positively impact the overall quality of care provided to PAOD patients.

Introduction

Peripheral arterial occlusive disease (PAOD) is a widespread health burden worldwide. The number of PAOD-related interventions is continuously increasing^{1, 2} and PAOD is considered an important marker of risk for subsequent cardiovascular events and mortality.³ In 2015, approximately 237 million patients were affected globally.⁴ A number of valid guidelines on the treatment of patients with PAOD define the increase of patients' functional status and health-related quality of life (HRQoL) as primary treatment goals in patients with intermittent claudication (IC).⁵⁻⁷ WHO defines quality of life "as an individual's perception of their position in life (...) It is a broad ranging concept affected in a complex way by the persons' physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of the environment" (source: <https://www.who.int/healthinfo/survey/whoqol-qualityoflife/en/>). An abundance of studies has demonstrated that PAOD is associated with markedly reduced HRQoL⁸⁻¹⁰ and can lead to depression and substantial social isolation.^{11, 12}

As demonstrated by Pell et al.,⁸ the precision with which vascular specialists assess the HRQoL in their patients is ‘only moderately good’. Overall, surgeons estimate their patients’ HRQoL lower than patients assess themselves, and the authors emphasize the necessity of more accurate outcome measurements in situations when clinical decision-making is influenced by the patients’ HRQoL status. This discrepancy between surgeons’ and patients’ HRQoL assessments could also potentially explain why registry data show that approximately fifty percent of invasive procedures targeting PAOD are undertaken for intermittent claudication, even though supervised exercise and lifestyle changes are the first line treatment at this PAOD stage, since the reduction of major adverse cardiovascular event rates is the primary aim of intervention.^{1, 13} Modern evidence-based health care of PAOD patients recommends the creation of patient-centred treatment pathways, where patient-reported outcomes (PROs) have a key role⁸ by providing longitudinal information about limitations and changes in HRQoL status. Many clinical trials also use a variety of patient-reported outcome measurements (PROMs) to indicate treatment success and to allow comparison between chronic conditions and health economic analysis. PROMs capture diverse facets of self-reported outcomes¹⁴ by using either generic (e.g., short form health 36, SF-36) or disease-specific questionnaires (e.g., VascuQoL-6).¹⁵⁻¹⁷ While the former are particularly useful when comparing HRQoL impact across different diseases and therapeutic areas, disease-specific instruments are more sensitive in revealing smaller but clinically important changes, because they do focus on the specific problems experienced by PAOD patients.¹⁸

When measuring and comparing the quality in health care, three types of quality indicators (Qis) can be employed to capture either the structure, process, or outcome¹⁹ and can be utilized to document the overall quality of care, for benchmarking, and in research projects.²⁰ An important requirement for standardised integration and analysis of PROMs in everyday clinical practice is that the outcome indicators included in the questionnaires are objective, measurable and comparable, as well as precisely defined in advance. These indicators are intended to measure the quality of the outcome exclusively based on patient self-reporting. The availability of multiple

varying PROMs for the measurement of HRQoL makes the comparability and validation of results difficult.^{22, 23} To date, there is neither a widely accepted standard for disease-specific PROMs in general¹⁰ nor an existing consensus concerning data collection of PROMs in PAOD registries.

Accordingly, this study aimed to build consensus among international experts in the field of vascular medicine on a set of core indicators for IC regarding PRO data collection in vascular registries. The use of the Delphi method for consensus building is widely accepted and can be found in recent publications of various specialties, including vascular medicine.²⁵⁻²⁹

Methods

The study comprised a two-stage methodology, in which a comprehensive literature search for the compilation of an indicator index preceded the evaluation of the index by an international expert panel through the Delphi method.

To identify outcome QIs, a detailed literature search (**Electronic Supplemental eTable 1**) was conducted including meta-analyses, systematic reviews, and guidelines for the treatment of PAOD. The search was conducted between July and December 2020, and was restricted to online sources available in English and German language and included the bibliographic database PubMed/Medline, as well as websites of medical institutions, available guidelines, and databases and of vascular medical organizations (**Electronic Supplement eTable 2**). The first (HA) and last (CAB) author of the manuscript conducted the literature review. In addition, a grey literature search was conducted, to generate data from narrative literature of patient organisations published in non-commercial form (e.g., patient associations of vascular societies or PAOD self-help groups) The selected literature was based exclusively on outcome QIs, that can be derived from patient reports. Outcome was defined as patient-reported therapy results after a conservative or invasive PAOD treatment of patients suffering from IC. All items identified in the literature were

precisely defined and uniformly documented in a structured indicator index of PRO QI **(Electronic Supplement eTable 3)**.

Thereafter, the individual items were presented to an expert panel for approval and additional suggestions by providing a free text option in a preliminary survey. Subsequently the items were included for evaluation and consensus building in a modified Delphi approach. The Delphi method is a structured interactive communication technique that serves to find consensus on a specific topic or question among a group of experts. The goal of the Delphi method is to achieve agreement on specific questions by relying on the expertise of the participants, structured reports of the voting results, as well as discussions among the experts.²⁸

Expert panel

A wide range of experts was invited to participate with the goal of including representatives from different countries, institutions, and medical specialties. The expert panel included international vascular specialists, patient representatives, and registry members of the VASCUNET committee of the European Society for Vascular Surgery (ESVS),³⁰ the International Consortium of Vascular Registries (ICVR), and the Medical Device Epidemiology Network (MDEpiNet). During the more cumbersome preliminary and first rounds the survey leaned primarily on vascular specialists with membership in the largest international collaborations on vascular registries. Participation in the evaluation process was online and anonymous. Open-source software was utilized to create the questionnaire (LimeSurvey GmbH, Hamburg, Germany, www.limesurvey.org). Invitations with a link to the survey as well as reminders were sent electronically before and during each round via mail.

This study made use of a modified two-stage Delphi technique to accomplish consensus. Items were rated on a 5-point Likert scale (strongly disagree/disagree/neutral/agree/strongly agree) in the first round. Participants were asked to rate each item independently in relation to the parameters “clinical relevance” and “practicability”. If at least 80% of the participants rated an item as "strongly agree" or "agree", the item reached consensus and was included for evaluation

in the second round. In addition, items that almost formed consensus ($\geq 70\%$ of agreement) were also included for re-evaluation in the modified second Delphi round which included an extended expert group and a rating on a 4-point forced-choice Likert scale (strongly disagree/disagree/agree/strongly agree). Following both rounds, a structured anonymized report of the results using graphical diagrams was compiled and distributed to the experts electronically (**Electronic Supplement eTable 4**). Subsequently, after both the preliminary and first round, the results were meticulously discussed at two online video meetings resulting in the decision to expand the panel in the second round to introduce greater diversity. Voting results for each item were explained with respect to clinical relevance and practicability. An online discussion of the results was held to review and approve the final recommendations for data collection of PROMs of IC in vascular registries and trials. The discussion included the research team as well as all Delphi panel members with membership in international vascular registries.

Results

Thirty of the 46 (65%) invited experts participated in the preliminary survey. The panel represented 29 different countries and was expanded by 13 experts including 2 senior vascular nurses who represented the patients' perspective in the second round. Out of 47 invited experts, thirty-one (66%) completed the first round, and 53 out of 60 (90%) participated in the second and final round (**Figure 1**).

The preliminary survey results affirmed all 118 items compiled during literature search and included 27 new items suggested by the panel and added to the evaluation process as potentially useful patient-reported outcome QI. Subsequently, the items were added to the structured indicator index, which finally consisted of 8 domains, 29 subdomains, and a total of 145 items (**Electronic Supplement eTable 3**).

In the first Delphi round, 22 items reached at least 80% agreement, the previously defined threshold of consensus building. Following the first round, a discussion among the participants

was held, with the result to re-integrating another 17 items that failed to reach the limit of agreement, but almost formed consensus ($\geq 70\%$ to $<80\%$ agreement) in the second round for re-evaluation to arrive at a high consensus among experts without dismissing variables prematurely in the first round given the high number of variables.

As a result, the second and final round consisted of 39 items. Eighteen items reached consensus regarding clinical relevance (**Table 1**) with over half of them (56%) belonging to the physical domain. Twelve items exceeded the 80% threshold of consensus building regarding both clinical relevance and practicability. No consensus was achieved for indicators in the psychological domain. By including 17 items for re-evaluation, the item 'perception of IC related QoL' formed consensual agreement (81% agreement for clinical relevance). The Delphi study not only confirmed five of the six VascuQoL-6 indicators, but also attested high clinical relevance with ratings of $>90\%$ of agreement for the individual item. The only VascuQoL-6 item that did not reach consensus in the Delphi study was 'concerns about PAOD' with 68% and 50% of agreement for clinical relevance and practicability, respectively.

The panel reviewed the results in an online discussion and recommended the use of a core set of six indicators (included in the VascuQoL-6 survey) but to also consider extending it by a set of twelve additional indicators (the identified consensus items in this study) for national registry and trial data collection of patient-reported outcome QI (**Table 2**).

Discussion

The current Delphi consensus study strived to harmonise PAOD patient-reported outcome assessments across different vascular registries and countries and it included a total of 60 panel experts from 29 countries and different medical specialties as well as patient representatives. The goal of this study was to build consensus on PROs to be collected in registries and trials that include patients with intermittent claudication. Out of 145 items initially included in the two

Delphi rounds and group discussions, six core items from the VascuQoL-6 questionnaire along with twelve additional, optional items were ultimately recommended by the panel.

Clinical practice guidelines on the treatment of patients with IC aim to guide clinicians through the challenge of identifying optimal treatment pathways for their patients. In PAOD, concepts like lifestyle-limiting claudication and the degree of impairment in daily living activities are regarded as important determinants for subsequent treatment decisions.^{5, 6, 31} At the same time, there is a paucity of concurrent recommendations for appropriate PRO tools that enable measurement of such constructs in patients with IC. To our knowledge, only a now outdated PAOD guideline document covered this issue and recommended using the SF-36 or the Walking Impairment Questionnaire (WIQ) to measure HRQOL in PAOD.³² Of these, the SF-36 includes no less than 36 questions, and this relative abundance of items limits the usefulness of this particular questionnaire in busy clinical routine scenarios. While the WIQ was developed so that it can be collected by study investigators in approximately five minutes and while it has remained widely used in PAOD patients, this questionnaire primarily captures IC disease symptom severity (walking distance, walking speed and stair climbing) (32) but fails to include items that measure other important HRQoL constructs; such as pain, discomfort, social and emotional consequences of IC, all of which remain central themes in IC disease. More recent research in this area has reached heterogeneous conclusions on which PROMs to recommend^{33, 34}, and a fairly recent systematic review also pointed out that the validation process for many of the currently available PAOD-specific PROMs have been suboptimal, and such shortcomings should be taken into account when interpreting their results.³⁵ In a recent comprehensive review of the literature, Raja et al. clearly emphasised the distinct heterogeneity of PROMs currently used in both registries and trials.³⁶

Overall, it appears challenging to collect PROM data in everyday clinical practice, for both clinical and research purposes. In the prospective GermanVasc cohort study (NCT03098290),

which enrolled 5,608 patients with invasive revascularisation for symptomatic PAOD between May 2018 and December 2021, only 73% of patients enrolled during the index treatment completed the baseline PRO questionnaires, and only 21% accepted to complete the questionnaire at the 12-month follow-up. One of the most frequently documented reasons was that the 25-item-questionnaire was too complicated and cumbersome. Hence, while PRO surveys implemented in clinical routine need to satisfy certain psychometric- and scaling standards, they should also allow easy completion by the patient, and furthermore need to be easy for health professionals to administer, score, and analyze. In an attempt to improve the assessment of PROs after PAOD interventions, a pragmatic instrument, the VascuQoL-6– originally derived from the VascuQoL 25 items questionnaire– was developed and empirically tested for content validity, construct validity and test-retest reliability.^{34, 37, 38} The VascuQoL-6 was developed using modern development principles including item response theory, and furthermore multiple validation studies have confirmed its validity.^{34, 38-40} To date, the questionnaire is available in numerous languages and there are established minimally important difference and substantial clinical benefit thresholds both following either supervised exercise therapy or lower limb revascularization. Consequently, this facilitates clinical interpretation in both clinical trials and routine clinical care.^{37, 41} This current Delphi study confirmed its widespread use in 30% of clinical registries currently participating in the VASCUNET and ICVR, and five of the six items included in the VascuQoL-6 survey matched items that reached consensus during the Delphi process. The only VascuQoL-6 item that did not reach full consensus was “concerns about PAOD”. Interestingly, all proposed items included in the psychological domain of the Delphi process failed to reach consensus and were subsequently excluded. This was not only due to low ratings for practicability but also for clinical relevance, with the highest overall rating given to “anxiety caused by PAOD” (74% agreement), an item closely related to “concerns about PAOD” available in the VascuQoL-6 survey. In contrast, the items “presence of intermittent claudication

in daily living” as well as “smoking” reached highest ratings in both categories and were included among the 12 optional additional items also recommended by the expert panel.

Considering the focus on walking impairment in recent guidelines, it is interesting to note that all respective items on walking distance received rather moderate ratings for both clinical relevance and practicability. This may point to an incongruity between guideline recommendations and daily practice. The question arises how to communicate an achievable improvement of maximum walking distance to a patient with claudication after 200 meters. Are 50 meters enough? The rather modest improvements in numerous clinical trials on innovative medical devices and therapy illustrate that this aspect deserves more reflection by the community. From a clinical standpoint, patient-reported walking distance estimations also remain notoriously inaccurate⁴², and this is arguably one reason why the expert panel downgraded the clinical relevance for the proposed items aiming to capture IC walking distance.

This study has limitations. Firstly, a Delphi consensus study -although commonly accepted and broadly used in the past- can only achieve consensus among the panel experts included in the process. We aimed to be as inclusive as possible and involved experts from all medical specialties as well as patient representatives. However, it cannot be ruled out that another panel would decide differently in the future. The lack of patient representatives and panel representativeness from disciplines other than medicine most likely led to a bias that cannot be rectified retrospectively. During all steps of the process, we had to accept that the enormous amount of time necessary to participate as panel expert along with further requirements (e.g., language barriers) are obstacles that are not easy to overcome. To compensate shortcomings in the distribution of panellists and to include experts who reached out to us after the preliminary round, we accepted that the composition of the Delphi panel as well as the parameters (e.g., consensus thresholds) differed across the rounds. This, however, may have introduced another bias. The inclusion of only English and German language publications introduces another bias. By including the largest

international collaborations in the vascular registry field, we further tried to cover many global regions and societies. However, as the virtual meetings were on a voluntary basis, not all panel experts participated in these meetings. The final recommendation deserves another critical discussion. Against the background of the 18 consensus items, the panel decided to recommend the VascuQoL-6 as a set of core indicators along with 12 additional indicators. Although it likely introduced another bias, this decision was made due to the fact that the VascuQoL-6 is a psychometric construct that has been repeatedly validated and have been shown to perform well across different countries, regions, and languages. It seems reasonable to underscore that the current study was not conducted to develop PROMs but reaching a consensus on what to use in trials and registries on PAOD. Moreover, it appears challenging and time consuming to implement this consensus on PROMs into established registry structures. We will monitor whether this recommendation leads to an adaption of registries in the future. Finally, although patient representatives were involved in this process, further strengthening of patient involvement as well as empowerment are important aims of future projects within the PAOD field. The vascular community needs to find ways to include patients not only in consensus processes but also in the decision-making in everyday clinical practice.

Conclusions

In the current study, a rigorous modified Delphi method was applied to find consensus among an international panel of experts with respect to core patient-reported outcome quality indicators to be collected in registries and used in trials on the treatment of patients with intermittent claudication. At this stage, a broad integration of the VascuQoL-6 core PROM set into vascular registries and trials including patients with intermittent claudication was supported by this Delphi consensus study and would represent an important step in the development of patient-centred management pathways for PAOD patients.

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Conflicts of interest

The authors declare no conflict related to the current study.

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Figure

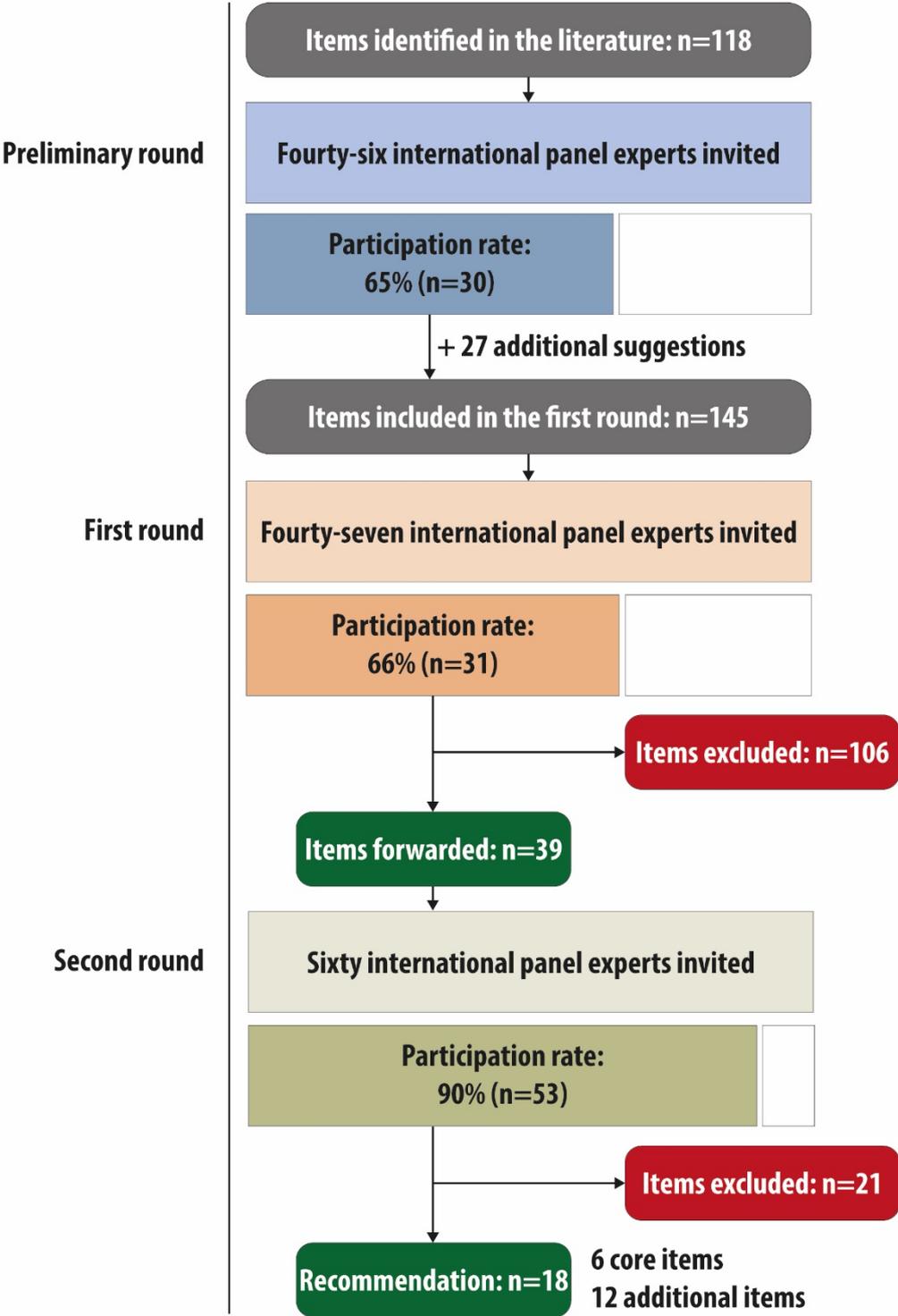


Figure 1: Flow chart of this modified Delphi process with international panel experts.

Tables

Table 1: Overview of the 18 consensus items regarding clinical relevance and practicability in this modified Delphi study.

Item name	VascuQoL-6	clinical relevance	practicability	description
intensity of IC[#]	2x Yes	93%	87%	intensity of claudication pain in activities of daily living by indicating frequency and subjective severity
degree of walking impairment due to PAOD[#]	Yes	94%	85%	degree of walking impairment due to PAOD in activities of daily living
limitation of everyday functioning (disease related) #	Yes	94%	81%	limitation of everyday functioning due to PAOD/IC (physical or emotional)
limitation of social activities due to PAOD[#]	Yes	91%	76%[‡]	limitation of social activities due to PAOD/IC (physical problems or emotional problems)
improvement of IC after treatment[#]		94%	93%	Improvement of claudication pain in daily activities after intervention or surgery
smoking[#]		100%	94%	former and actual quantification of exposure to nicotine
physical training/exercise[#]		94%	83%	participation in physical training or regular exercise (e.g., incl. long walks)
compliance to medication[#]		94%	72%[‡]	degree to which a patient correctly follows medical advice referring medication
presence of IC in daily living[†]		87%	96%	presence of claudication pain in activities of daily living
dissatisfaction with actual IC		81%	57%[‡]	presence of dissatisfaction/annoyance caused by claudication pain during daily activities
presence of post-treatment pain /symptoms or other complications		85%	85%	presence of pain/symptoms after a treatment for IC (e.g., wound pain, numbness, discomfort, superficial nerve pain, neuralgia) or other complications (e.g., disorder of wound healing)
poorly healing wounds/ulcers		87%	85%	Leg/foot wounds heal poorly (e.g., it takes more than a few weeks to heal)
presence of walking impairment due to PAOD[†]		85%	83%	presence of walking impairment caused by PAOD such as claudication, post-treatment pain, or post-treatment wound

impact of walking impairment due to PAOD		83%	69%[‡]	negative effects of walking impairment due to PAOD in daily life e.g., isolation, dependency, embarrassment, depression, lifestyle change
limitation of walking distance due to IC		89%	81%	limitation of walking distance at normal speed on level ground due to IC
limitation of work capacity due to PAOD		80%	65%[‡]	limitation of work capacity due to PAOD/IC, because of physical or emotional problems
satisfaction with current treatment (PAOD)		80%	83%	satisfaction with current treatment regarding PAOD
perception of IC related QoL		81%	65%[‡]	subjective perception of IC related quality of life (e.g., impact of IC on QoL)

Footnote: IC: Intermittent claudication; PAOD: Peripheral arterial occlusive disease; QoL: Quality of life.

denotes: high rated items (>90% agreement). [‡] denotes: failed to reach consensus for practicability

[†] denotes: these items regarding ‘presence of...’ are already covered in VascuQoL-6 (when asking for ‘intensity of IC’ or ‘degree of walking impairment’).

Table 2: Recommended data collection of patient-reported outcome quality indicators in international vascular registries and trials.

Set of 6 core indicators (from VascuQoL-6)	Optional data collection of additional 12 indicators	
limited activities due to PAOD	dissatisfaction with actual IC	limitation of work capacity due to PAOD
extent of tiredness/ weakness in legs	improvement of IC after treatment	satisfaction with current treatment (PAOD)
limited ability to walk due to PAOD	presence of post-treatment pain /symptoms or other complications	perception of IC related QoL
concerns about PAOD	poorly healing wounds/ulcers	smoking
limited participation in social activities due to PAOD	impact of walking impairment due to PAOD	physical training/exercise
degree of pain in leg or foot	limitation of walking distance due to IC	compliance to medication

Footnote: IC: Intermittent claudication; PAOD: Peripheral arterial occlusive disease; QoL: Quality of life.

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2. Darstellung der Publikation

Behandlungsoptionen und Statistik der peripher arteriellen Verschlusskrankheit

Die periphere arterielle Verschlusskrankheit (pAVK) ist eine arteriosklerotische Erkrankung, die vor allem die supraaortalen Gefäße, die Aorta mit Viszeralgefäßen und die Arterien der unteren Extremität betrifft. Nach einem lange asymptomatischen Krankheitsprogress entwickelt sich in späteren Stadien durch die zunehmende Verengung der arteriellen Blutstrombahn eine symptomatische pAVK. Diese äußert sich initial zumeist als Claudicatio intermittens (intermittent claudication - IC) (Lawall et al. 2016). Diese wird durch Belastung ausgelöst und zeigt sich durch Ermüdung, Krämpfe oder Schmerzen der unteren Extremitäten und wird zudem durch Ruhe innerhalb von Minuten gelindert (Gerhard-Herman et al. 2017). Sollte die pAVK und das zugrundeliegende kardiovaskuläre Risikoprofil unbehandelt bleiben, kann sich mit fortschreitendem Krankheitsverlauf eine weitere Stenosierung der peripheren Gefäße zu einer chronischen extremitätengefährdenden Ischämie (chronic limb-threatening ischemia - CLTI) entwickeln, gekennzeichnet durch einen ischämischen Ruheschmerz bereits ohne Belastung, nicht-heilende Wunden, Ulzerationen oder Gangrän mit der Komplikation einer Sepsis (Farber und Eberhardt 2016). In der Gefäßmedizin gilt die pAVK als eine der häufigsten Erkrankungen mit steigender Prävalenz (Behrendt et al. 2018). Entsprechend des Krankheitsstadiums reichen die Behandlungsoptionen von obligatorischen konservativen Maßnahmen, wie Änderung des Lebensstils, medikamentöse Therapie oder strukturiertes Gehtraining bis hin zu optionalen endovaskulären Interventionen oder offen-chirurgischen Maßnahmen (Düppers et al. 2017). Aktuell zeichnet sich eine stetig zunehmende Anzahl endovaskulärer Revaskularisationen mit steigenden Behandlungskosten ab (Malyar et al. 2013). Die pAVK betrifft weltweit etwa 237 Mio. Menschen (Fowkes et al. 2013) und gilt zudem als wichtiger Risikomarker für kardiovaskuläre Ereignisse und Mortalität (Bhatt et al. 2006). Nach der Auffassung der Weltgesundheitsorganisation (WHO) trägt nicht nur die Häufigkeit und Schwere von Krankheiten zur Messung der Gesundheit bei, sondern auch die Bewertung des Wohlbefindens beziehungsweise der Lebensqualität. Somit ist bei einer lebensstillimitierenden Erkrankung wie der symptomatischen pAVK neben der Verbesserung der Funktionalität und des Beinerhalts auch die Steigerung der gesundheitsbezogenen Lebensqualität von großer Bedeutung, welches auch als

primäres Behandlungsziel mehrerer Leitlinien zur Diagnose und Therapie der pAVK definiert wird (Aboyans et al. 2018 und Gerhard-Herman et al. 2017).

Wichtigkeit der Lebensqualität in der pAVK

In der Literatur wird die *allgemeine Lebensqualität* (Quality of Life – QoL) von der *gesundheitsbezogenen Lebensqualität* (Health-related Quality of life - HRQoL) differenziert. QoL wird im Gegensatz zu HRQoL auch von subjektiven Wahrnehmungen des Gesundheits- beziehungsweise Krankheitszustandes bestimmt wie zum Beispiel physikalische, psychologische oder soziale Faktoren und schließt darüber hinaus auch die individuelle Wahrnehmung der eigenen Position im Leben mit ein wie zum Beispiel die persönliche Entwicklung in einem Wertesysteme oder Kultur (Karimi und Brazier 2016). Da die Symptomschwere der pAVK eine deutliche Assoziation mit der Verringerung der HRQoL aufzeigt (Mehta et al. 2003), ist die kontinuierliche Messung der Lebensqualität als Ergebnisqualitätsindikator von besonderer Wichtigkeit. Aktuell werden in randomisierten Studien und Registern vorwiegend klinische Marker, wie zum Beispiel der Knöchel-Arm-Index (ankle brachial index - ABI) oder funktionale Klassifikationssysteme der klinischen Symptome (Fontaine oder Rutherford) als objektive Endpunkte gemessen. Diese beschreiben allerdings den Gesundheitsstatus nicht umfassend und korrelieren nur gering mit einer verbesserten Lebensqualität (Aquarius et al. 2006).

Messung des patientenberichteten Outcomes in der Gefäßmedizin

Zur Messung und Erfassung der Lebensqualität werden Instrumente verwendet, in denen Patienten die Bewertung des Therapieerfolgs durch eine systematische Befragung selbst dokumentieren (Patient-Reported Outcome Measurements – PROMs). Der patientenberichtete Therapieerfolg (Patient-Reported Outcome – PRO) beschreibt das vom Patienten berichtete Gesundheitsergebnis, ergänzt die Bewertung einer Behandlung um die subjektive Einschätzung des Patienten und hilft ein besseres Verständnis der Effektivität einer Behandlung zu erreichen. PROMs umfassen die Erhebung der HRQoL, des Gesundheitsstatus und der physikalischen Funktionalität (Brédart et al 2014) und werden in elektronischer oder papierbasierter Form dokumentiert. *Generische* PROMs, wie zum Beispiel Short-Form-36 (SF-36), WHOQOL, EuroQoL-5 Dimensions (EQ-5D) erfassen die Messung der allgemeinen Gesundheit und werden oft bei chronischen Erkrankungen angewandt. *Krankheitsspezifische* PROMs

werden zur Bewertung spezieller Erkrankungen herangezogen, wie zum Beispiel Herzversagen, Dyspnoe oder Depression (Raja et al. 2020). Ebenso wurden für die pAVK krankheitsspezifische PROMs etabliert und deren Reliabilität und Validität in mehreren Studien hervorgehoben (Nordanstig et al. 2014, Coyne et al. 2003). Hierzu zählen zum Beispiel der Vascular Quality of Life Questionnaire (VascuQoL6), Walking Impairment Questionnaire (WIQ) oder Peripheral Artery Questionnaire (PAQ).

Aktuell werden in einer deutschlandweiten prospektiven Kohortenstudie zur multizentrischen Versorgung der pAVK die generischen Fragebögen SF-36 und WIQ genutzt (Kotov et al. 2021), wobei Letzterer ausschließlich die Funktionalität und das Gehvermögen der Patienten evaluiert. Verglichen mit anderen vaskulären Registern auf internationaler Ebene, zeigt sich insgesamt eine mangelhafte Dokumentation von PROs. In der Literatur gibt es mehrere Hinweise darauf, dass die pAVK mit einer verminderten Lebensqualität einhergeht (Pell et al. 1995) und zu Depressionen sowie sozialer Isolation führen kann (Smolderen 2008). Allerdings enthalten die krankheitsspezifischen Fragebögen häufig keine Bewertung psychologischer Aspekte. Zudem mangelt es in Studien über PRO in der pAVK an der Integration psychometrischer Bewertungen (Poku et al. 2016). Weiterhin ist zu bemerken, dass für die Messung der HRQoL unterschiedliche und oft umfassende Fragebögen zur Verfügung stehen, was die Vergleichbarkeit und Validierung von Therapieergebnissen erschwert (Hedeager et al. 2011). Dies unterstreicht die Notwendigkeit einer Standardisierung von PROMs in Forschungsvorhaben zur pAVK. Obwohl eine europaweite Standardisierung von krankheitsspezifischen PROMs in der Gefäßmedizin bereits mehrfach in der medizinischen Fachliteratur empfohlen wurde - beginnend mit Chetter (et al. 1997) und gefolgt von Gulati (et al. 2009) und Haarwood (et al. 2017) - gibt es derzeit keinen Konsens darüber, welche Variablen in den verschiedenen Messumfragen verwendet werden sollten. Darüber hinaus empfiehlt Mays (et al. 2011) „die Implementierung und Interpretation dieser Instrumente in klinischen Settings zu standardisieren“. Eine wichtige Voraussetzung für eine standardisierte Integration und Auswertung von PROMs im klinischen Alltag ist, dass die in den strukturierten Fragebögen enthaltenen Variablen objektiv, messbar und vergleichbar sind (Nordanstig et al. 2022). Diese Variablen sollen die Qualität des Outcomes auf der Grundlage von Patientenberichten messen.

Vergleich und aktuelle Verwendung von PROMs in Studien zur pAVK

In einer ausführlich durchgeführten systematischen Literaturübersicht von Harwood (et al. 2017) zur Lebensqualität von pAVK Patienten, betonen die Autoren die breite Verwendung verschiedener PROM Instrumente in Studien, sowie deren mangelhafte Erwähnung in Studienberichten, obwohl diese initial in der Datenerhebung miteingeschlossen wurden. Laut diesem systematischen Review ist das meist genutzte Instrument in Studien der SF-36 (74%, n=23), gefolgt von dem WIQ (25%, n=8), wobei letzteres vorwiegend die eingeschränkte Funktionalität erfasst (Raja et al. 2020) ohne Betrachtung wichtiger HRQoL Komponenten. Der PROM SF-36 beinhaltet als generisches Instrument einerseits ein breites Spektrum an Qualitätsindikatoren (QI), hat jedoch den Nachteil sensible krankheitsspezifische Aspekte der pAVK, welche jedoch von klinischer Bedeutung sind, nicht zu erfassen. Zudem stellt die Anzahl der Fragen einen hohen Zeitaufwand für Patienten dar, was für die Implementierung von PROMs in den klinischen Alltag eine Herausforderung darstellt. Aufgrund der ausgesprochenen lebensstillimitierenden Auswirkungen der pAVK sind potentielle Lösungsansätze bezüglich deren kontinuierlichen Gebrauch essentiell. Wichtige Anforderungen an PROMs stellen neben der Validität und Reliabilität, die gute Verständlichkeit der Fragen für Patienten dar, sowie die Länge eines Fragebogens und der damit verbundene Zeitaufwand diesen auszufüllen, welche in Korrelation mit der Abbruchquote steht (Rolstad et al. 2011). Aus diesem Grund wurde der VascuQoL-6 Fragebogen entwickelt, der ursprünglich aus dem von Morgan (et al. 2001) publizierten VascuQoL-Fragebogen mit 25 Items (VascuQoL-25) abgeleitet wurde. Neben wichtigen Funktionalitätseinschränkungen erfasst dieser als krankheitsspezifischer Fragebogen auch Aspekte der HRQoL wie zum Beispiel der eingeschränkten Teilnahme an sozialen Aktivitäten aufgrund der pAVK (Morgan et al. 2001).

Qualitätsindikatoren in der Gesundheitsversorgung und Registern

Gemäß der Verfassung der WHO wird die *Qualität der Gesundheitsversorgung* definiert als „das Ausmaß, in dem Gesundheitsleistungen für Einzelne und Bevölkerungsgruppen die Wahrscheinlichkeit des erwünschten Outcomes erhöhen“. Um die Qualität beurteilen zu können, sollten die „erwünschten Outcomes“ in Form von QI im Voraus präzise definiert werden (Kötter 2011 et al.). Aufgrund des oben erwähnten primären Behandlungsziels der pAVK, sollten "erwünschte Outcomes" somit patientenzentriert beschrieben werden, die zur Messung und dem Vergleich der Qualität in der

Gesundheitsversorgung verwendet werden können. Erstmals wurden QI von Donabedian 1966 beschrieben und in drei Typen unterteilt. Sie können die Struktur, den Prozess oder das Ergebnis der Gesundheitsversorgung erfassen. **Abbildung 1** zeigt Beispiele für Indikatoren der Qualität entsprechend den einzelnen Typen. Als wichtiger Bestandteil der Versorgungsforschung sammeln medizinische Register zur Qualitätsverbesserung patientenspezifische Daten und zuvor definierte QI. Zudem informieren QI das Gesundheitspersonal darüber, inwieweit die Interventionen den Bedürfnissen des Patienten gerecht werden und können daher zur Dokumentation der Versorgungsqualität, zum Benchmarking und zur Qualitätsverbesserung eingesetzt werden (Mainz 2003). Im Mittelpunkt der Studie standen Ergebnisqualitätsindikatoren, welche als Endergebnis in den Patientenberichten entnommen werden können (siehe Markierung in **Abbildung 1**: Funktionsstatus, Messung des Gesundheitszustands, Arbeitsstatus, Lebensqualität, Patientenzufriedenheit). In dieser Studie wurde der Outcome definiert als Therapieergebnisse von Patienten mit symptomatischer pAVK im Stadium der IC nach einer konservativen oder invasiven Behandlung.

Ergebnisqualitätsindikatoren in der pAVK-Behandlung

Die Forschungsgruppe GermanVasc am Universitätsklinik Hamburg-Eppendorf hat kürzlich drei modifizierte Delphi-Studien und ein systematisches Review veröffentlicht, die sich mit der Erfassung von Parametern für vaskuläre Register befassen (Rieß et al. 2018, Behrendt et al. 2019, Hischke et al. 2019). Die Empfehlungen der drei Studien basieren auf dem Konsens von Gefäßspezialisten und Mitgliedern der internationalen und europäischen kollaborativen Plattformen von Gefäßregistern (VASCUNET, ICVR und MDEpiNet). Die genannten QI beschreiben hier objektive Endpunkte (z.B. schwere Blutung, Schlaganfall, Amputation, Tod), was von entscheidender Bedeutung für die Messung des Therapieerfolgs ist. Allerdings geben diese QI keine Auskunft darüber aus ob sich durch eine bestimmte therapeutische Maßnahme die spezifische Situation des Einzelnen verbessert hat, beziehungsweise ob eine Verbesserung der Lebensqualität des Patienten erreicht werden konnte.

Patientenberichtete Ergebnisqualitätsindikatoren in der pAVK-Behandlung

Da PROs insbesondere bei einer lebensstillimitierenden Erkrankung, wie der IC eine signifikante Rolle spielen, ergänzt die hier vorliegende Studie die oben genannten Empfehlungen zur Datensammlung von Ergebnisqualitätsindikatoren hinsichtlich der

Sicht des Patienten. In dieser Studie werden sowohl PRO QI erfasst, die einen direkten Hinweis auf das funktionale Ergebnis nach der Therapie geben (zum Beispiel Verbesserung der Gehstrecke nach einer Revaskularisation) als auch auf PRO QI, die insbesondere Ausschluss über die Lebensqualität oder subjektive Wahrnehmung des Patienten geben (zum Beispiel Intensität der IC oder Gradeinteilung der Gehbehinderung). Andere wichtige Faktoren, die sich aus Patientenberichten ableiten lassen, können das Behandlungsergebnis ebenfalls beeinflussen und wurden als "Risikoanpassung" klassifiziert; wie zum Beispiel Lebensstilfaktoren, wie Nikotinkonsum, Ernährungsgewohnheiten und sozialer Status (Mainz 2003, Rubin et al. 2001). Bislang gibt es weder eine internationale Vereinheitlichung noch einen Konsens über die Datenerhebung von PRO QI in pAVK-Registern. Ziel dieser Studie war es, einen Kernsatz von PRO QI nach einer pAVK-Behandlung auf Grundlage eines modifizierten Delphi-Expertenkonsenses zu generieren (Waggoner et al. 2016). Darüber hinaus soll die Veröffentlichung der vorliegenden Empfehlungen einen Beitrag zur internationalen Standardisierung von PROMs leisten und zur Verbesserung der Qualitätssicherung in pAVK-Registern beitragen.

Literaturrecherche zu PRO QI

Der Ablauf der Studie erfolgte gemäß einem festgelegten Zeitplan (**Tabelle 1**), angefangen mit der Literaturrecherche von Juli bis Dezember 2020, über die Erstellung eines Indikator-Index im Januar 2021, der Expertenrekrutierung von Februar bis April 2021, bis hin zur Evaluation der PRO QI mittels der modifizierten Delphi-Methode von Mai bis November 2021. Die strukturierte narrative Literaturrecherche zur Ermittlung von PRO QI schloss Meta-Analysen, systematische Reviews und Leitlinien für die Behandlung der pAVK ein und basierte auf einem definierten Suchprotokoll (**Tabelle 2**). Dabei wurde das Outcome als patientenberichtete Behandlungsergebnisse nach einer konservativen oder invasiven pAVK-Behandlung von Patienten im Stadium der IC definiert. Alle in der Literatur gefundenen Indikatoren (*Items*) wurden einheitlich in einem Indikatoren-Verzeichnis dokumentiert. Die Struktur der Dokumentation orientierte sich dabei an den in **Tabelle 3** aufgeführten Gliederung und entspricht den Empfehlungen von Bellmunt et al. 2014 und Mainz 2003. Die hierbei identifizierten 118 Items wurden im Verzeichnis in 8 Domänen und 29 Sub-Domänen untergliedert (siehe **Abbildung 2**: Physical, Level of independence, Psychological, Social, Environment, General Health, Personal Beliefs, Risk adjustment).

Die modifizierte Delphi-Methode

Die Delphi-Methode ist eine strukturierte interaktive Kommunikationstechnik, die dazu dient, einen Konsens zu einem bestimmten Thema oder einer bestimmten Frage unter einer Gruppe von Experten zu generieren. Dabei stützt sich die Konsensfindung auf die Fachkenntnisse der Teilnehmer, strukturierte Berichte über die Abstimmungsergebnisse sowie Diskussionen unter den Experten unter Leitung des Gruppenmoderators (Waggoner et al. 2013). Die Anzahl der Evaluationsrunden sowie der Grenzwert zur Konsensbildung werden zuvor definiert. Zwischen den Abstimmungsrunden werden die Ergebnisse anonym präsentiert. Die Abbildungen 2-8 zeigen Beispiele aus dieser Studie zu den strukturierten Ergebnisberichten mit grafischen Diagrammen. Die Diskussionen zwischen den einzelnen Runden, in denen die anonymisierten Evaluationsergebnisse innerhalb des Gremiums geteilt werden, ermöglichen Feedback und dienen zur weiteren Meinungsfindung. Der Einsatz der Delphi-Methode zur Konsensbildung ist global anerkannt und findet sich in neueren Veröffentlichungen verschiedener Fachgebiete, darunter auch der Gefäßmedizin (Behrendt et al. 2019, Hinchliffe et al. 2016, Rieß et al. 2016).

Vor Beginn der eigentlichen Delphi-Studie wurde eine Vorbefragung der eingeladenen Experten durchgeführt. Ziel dieser Befragung war die Vollständigkeit der Variablen zu verbessern und Items miteinzuschließen, welche nicht mit der angewandten Suchstrategie auffindbar waren. Darüber hinaus wurden die Experten vor Beginn der eigentlichen Konsensfindung durch Berichte mit grafischen Abbildungen über den Ablauf der Delphi-Studie informiert (siehe Beispiel in **Abbildung 3**). Letztlich wurde den Teilnehmern die Liste der Indikatoren inklusive detaillierter Definitionen vorgelegt. Die am Bewertungsprozess beteiligten Experten wurden aufgefordert, die ermittelten Indikatoren in einem freien Textfeld zu beurteilen und zusätzliche Indikatoren vorzuschlagen. Das Indikatoren-Verzeichnis wurde schließlich um 27 zusätzliche Items ergänzt, woraus insgesamt 145 Items resultierten.

Expertengremium

In der Vorrunde sowie der ersten Abstimmungsrunde stellte sich der Evaluierungsprozess durch die hohe Anzahl der Items als sehr zeitintensiv dar und stützte vor allem auf Gefäßspezialisten, die Mitglied in den größten internationalen Konsortien für Gefäßregister sind (VASCUNET, ICVR und MDEpiNet). Das breit gefächerte Gremium bestand aus insgesamt 60 Gefäßspezialisten aus 29

verschiedenen Ländern, die jahrelange Erfahrung mit Versorgungsforschung und Qualitätsentwicklung, klinischen Studien und der klinischen Versorgung von Patienten mit pAVK haben. In der zweiten Delphi-Runde wurde das Expertengremium um 13 Teilnehmer erweitert, wobei auch zwei erfahrene Pflegekräfte eingebunden werden konnten, die sich durch ihre langjährige enge Zusammenarbeit mit pAVK-Patienten auszeichneten. Die Teilnahme erfolgte online und anonym über einen Open-source Fragebogen-Software (www.limesurvey.org). Die weitere Kommunikation, wie Einladungen zur Teilnahme, Erinnerungen und Berichterstattung der Bewertungsergebnisse erfolgte ebenfalls in elektronischer Form via E-Mail.

Konsensfindung von PRO QI mittels Delphi-Methode

Die hier vorliegende Studie nutzte zur Konsensbildung ein zweistufiges modifiziertes Delphi-Verfahren. Die Evaluation der einzelnen Items erfolgte dabei auf einer 5-Punkte-Likert Skala (strongly disagree/disagree/neutral/agree/strongly agree) sowie in zwei Matrices hinsichtlich der klinischen Relevanz und Praktikabilität. Die Bewertung erfolgte subjektiv erfahrungsbasiert ohne a priori festgelegte Gütekriterien. Den Teilnehmern wurde zudem die Möglichkeit gegeben, individuelle Argumente für ihre Bewertungen, Anmerkungen oder Fragen in einem freien Kommentarfeld anzugeben. Der Schwellenwert zur Konsensbildung wurde mit 80% Übereinstimmung festgesetzt. Somit wurde ein Item in die zweite Abstimmungsrunde inkludiert, wenn mindestens 80% der Teilnehmer das Item in der ersten Runde entweder deren klinischen Relevanz oder Praktikabilität mit "stimme voll und ganz zu" oder "stimme zu" bewerteten. Die Onlinediskussionen nach der Vorbefragung und ersten Runde, welche sich aus dem Forschungsteam und Experten aus internationalen vaskulären Gefäßregistern zusammensetzte, hatten den übereinstimmenden Beschluss folgender Modifikationen des Delphi-Verfahrens zur Folge: (1) die Erweiterung des Expertengremiums zur Steigerung der Expertise des Gremiums, welches sich zuvor auf Registermitglieder beschränkte, (2) die Änderung der Likert-Skala auf ein forced-choice Format um Antwortverzerrungen zu vermeiden, sodass eine neutrale Antwortmöglichkeit nicht gegeben ist (4-point Likert scale: strongly disagree/disagree/agree/strongly agree), sowie (3) die Re-Evaluation von 17 Items in der finalen Runde, welche in der ersten Runde den Konsens knapp verfehlten ($\geq 70\%$ bis $<80\%$) um Items aus der ersten Runde angesichts der großen Anzahl nicht vorschnell zu verwerfen. Das Forschungsteam stimmte diesen Vorschlägen zu und verwies darauf, dass die Möglichkeit der

Modifikation der Delphi-Methode allgemein und in verschiedenen Fachbereichen praktiziert wird (Jebara et al. 2020, Jordans et al. 2019, Behrendt et al. 2019).

Ergebnisse und Empfehlung zur Datensammlung von PRO QI in pAVK-Registern

Die Teilnahmerate der Vorrunde betrug 65% (n=30), im Vergleich zu 66% (n=31) in der ersten und 90% (n=53) in der zweiten Delphi-Runde. Die genauen Ergebnisse der einzelnen Evaluationsrunden wurden den Teilnehmern in Zwischenberichten mitgeteilt (**Abbildungen 2-8**). **Abbildung 6** zeigt die Anzahl der Items, welche in der Vorrunde definiert wurden (insgesamt 145 Items), sowie in der ersten (22 Items) und zweiten Runde (18 Items) jeweils einen Konsens erreichten. Insgesamt erzielten achtzehn Items in der zweiten Runde die 80% Grenze zur Konsensbildung, wobei 56% der Items der Domäne „physical“ zuzuordnen waren, gefolgt von den Domänen „risk adjustment“ (17%) und „level of independence“ (11%) (**Abbildung 5**). Im Gegensatz dazu erzielten Variablen der Domänen „psychological“ und „personal beliefs“ keinen Konsens. Items die einen Konsens erreichten wurden einzeln grafisch dargestellt mit den genauen prozentualen Angaben jeder Bewertung der Likert-Skala zur klinischen Relevanz und Praktikabilität (**Abbildung 4**). Von den 18 Items, übertrafen zwölf die 80%-Schwelle der Konsensbildung sowohl hinsichtlich der klinischen Relevanz als auch der Praktikabilität (**Abbildung 7**). Von den 17 Items, die in der zweiten Runde erneut evaluiert wurden, erreichte der QI „perception of IC related QoL“ mit 81% für klinischen Relevanz einen Konsens (**Abbildung 7**). Andererseits schieden fünf Items in der zweiten Runde aus, welche zuvor in der ersten Runde einen Konsens erreicht haben (**Abbildung 9**). Hierunter fallen unter anderem alle Items, welche eine absolute beziehungsweise metrische Gehstreckenangabe beinhalteten, zum Beispiel „absolute claudication distance (ACD)“ oder „initial claudication distance (ICD)“. Die höchste Übereinstimmung erreichte der QI „smoking“, wobei 100% der Experten diesen als klinisch relevant einstufen. Ebenso wurden zwei weitere Items (physical training und medical compliance) der Domäne „risk adjustment“ hochrangig bewertet mit jeweils 94% (**Abbildung 7**).

Abschließend führte das Expertengremium eine Onlinediskussion zur Besprechung der Konsens-Items und Findung einer einheitlichen Empfehlung zur Datenerhebung von PRO QI in der pAVK-assoziierten Forschung und Versorgung. Ergebnis hiervon waren folgende drei Punkte:

- (1) Zwei der gelisteten Items in **Abbildung 7** zeigen einen ähnlichen Wortlaut und wurden deshalb zu einem Item kombiniert, weil sie von anderen Items miterfasst werden. So wird das Auftreten einer IC („presence of IC“) von dem Item „intensity of IC“ miterfasst, ebenso bei den Items, welche das Auftreten oder die Gradeinteilung einer Gehbehinderung erfassen („presence / degree of walking impairment“).
- (2) Der VascuQoL-6 stellte sich als der am Häufigsten verwendete PROM in internationalen Gefäßregistern dar. Ein genauerer Vergleich des VascuQoL-6 mit den Ergebnissen dieser Studie zeigte auf, dass fünf von sechs Items des VascuQoL-6 eine hohe Übereinstimmung von >90% mit dieser Studie haben (**Abbildung 8**). Nur das psychologische Item („concerns about PAD“) erreichte in der Delphi Studie mit 68% Zustimmung zur klinischen Relevanz nicht die Grenze zur Konsensbildung. Der krankheitsspezifische PROM VascuQoL-6 wurde methodisch hochwertig entwickelt und ist das am Häufigsten eingesetzte Tool zur Datenerhebung von PRO in pAVK-Registern auf internationaler Ebene. Seine Validität und Reliabilität wurde dabei ebenfalls mehrfach belegt (Nordanstig et al. 2017 und Larsen et al. 2017)
- (3) Es wurden Empfehlungen des Expertengremiums zur einheitlichen Datenerhebung von patientenberichteten QI in internationalen pAVK-Registern und Studien formuliert, welcher alle teilnehmenden Experten zustimmten. Auf Grundlage der Konsensbildung mittels der Delphi-Methode wurde nach zwei Evaluationsrunden und drei Diskussionsrunden die finale Empfehlung zur Datensammlung eines Kernsatzes von sechs Indikatoren ausgesprochen, welche von dem VascuQoL-6 erfasst werden. Außerdem wurde eine mögliche Erweiterung durch zwölf zusätzliche Indikatoren empfohlen, die in dieser Studie ebenfalls einen Konsens erreichten (**Abbildung 10**).

Erörterung der Ergebnisse im Vergleich zum aktuellen Wissenschaftsstand

Es zeigen sich anhand der vorliegenden Studienergebnisse neue Ergebnisse zur Empfehlung der Datensammlung von PRO QI, welche sich mit dem aktuellen Stand und der Handhabung im klinischen Alltag unterscheiden und somit weiterführende wissenschaftliche Fragen aufwerfen. In der vorliegenden Delphi-Studie erreichten QI einen Konsens, welche aktuell in vaskulären Registern noch nicht erfasst werden. Der Langzeiteffekt von Nikotinkonsum auf die Pathogenese kardiovaskulärer Ereignisse und der damit bestehende signifikante Zusammenhang eines schlechteren Outcomes der pAVK ist bekannt (Wang et al 2021). Zudem steht der Zeitraum der Rauchentwöhnung in Relation zu einem geringeren pAVK Risiko (Ding et al. 2019). In einer aktuellen

multizentrischen prospektiven Kohortenstudie der Forschungsgruppe GermanVasc mit insgesamt 5.608 pAVK-Patienten gaben insgesamt 75% der Teilnehmer an, aktuell oder in der Vorgeschichte zu rauchen (Kotov et al. 2021). In Anbetracht dieses hohen prozentualen Anteils, wird der Nikotinkonsum als PRO QI nicht in vaskulären Registern erfasst. Ebenso beinhaltet die Datenerhebung von PRO QI in Registern kein strukturiertes Gehtraining, obwohl diese Maßnahme entsprechend der Empfehlung mehrerer Leitlinien mit einem Empfehlungsgrad A und der Evidenzklasse 1 (Aboyans et al. 2017 und Gerhard-Herman et al. 2017) empfohlen wird und maßgeblich zu einer Outcome-Verbesserung führt (Hageman et al. 2018).

Desweiteren bestehen Kontraste bei der Angabe der schmerzfreien Gehstrecke versus der aktuell praktizierten Datensammlung von PRO QI. In dieser Studie erreichten QI, welche eine metrische Angabe der Gehstrecke beinhalten keinen Konsens (**Abbildung 9**: Übereinstimmung von $\leq 70\%$). Allerdings erfassen die meist verwendeten PROMs in klinischen Studien (SF-36 und WIQ) diesen Aspekt zur Messung des Outcomes (Haarwood et al. 2017). Es stellt sich hierbei die Frage der Genauigkeit einer geschätzten Gehstrecke und ob eine erzielte Verbesserung dieser zu demselben verbesserten Outcome verschiedener Patienten führt oder sich dieser individuell subjektiv unterscheidet. In der klinischen Praxis und in verfügbaren Leitlinien wird hierbei das Konstrukt der lebensstillimitierenden Claudicatio nicht näher definiert, da die individuelle Gehstrecke von zahlreichen komplexen Erwägungen abhängt. Es zeigt sich zudem eine Diskrepanz zwischen dem aktuellen wissenschaftlichen Stand hinsichtlich psychologischer Auswirkungen einer pAVK, wie Depression und soziale Isolation (Ponte et al. 1996 und Smolderen et al. 2008) und den Konsens dieser Studie. Alle Items der psychologischen Domäne wurden von den Experten auf Grundlage ihrer täglichen Praxis als weder klinisch relevant noch praktikabel gewertet. Dies könnte auf ein geringeres Risiko einer beeinträchtigten mentalen Gesundheit in einem frühen Stadium der pAVK hinweisen, da dieser Konsens in Anbetracht einer IC erreicht wurde. Es bedarf weiterer Forschung zu dem Zusammenhang zwischen mentaler Gesundheit und psychologischer Auswirkung einer pAVK im Stadium der IC.

Schlussfolgerungen

Die vorliegenden erstmalig publizierten Empfehlungen zur Datensammlung von patientenberichteten Outcome QI in pAVK-Registern und klinischen Studien basieren auf dem Konsens eines breiten internationalen Expertengremiums, welches mittels einer

modifizierten Delphi-Methode generiert wurde. Eine kontinuierliche und standardisierte Qualitätsentwicklung hinsichtlich des PRO könnte zur internationalen Vereinheitlichung und besseren Vergleichbarkeit der generierten Daten führen. Dies kann darüber hinaus die Patientenzentrierung in der pAVK-Behandlung unterstützen. Es bedarf jedoch weiterer Studien im Gebiet der pAVK-Behandlung, welche die Involvierung und Befähigung von Patienten stärken.

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Abbildungsverzeichnis

<p>Structure</p> <ul style="list-style-type: none"> Proportion of specialists to other doctors Access to specific technologies (e.g. MRI scan) Access of specific units (e.g. stroke units) Clinical guidelines revised every 2nd year Physiotherapists assigned to specific units <p>Process</p> <ul style="list-style-type: none"> Proportion of patients with diabetes given regular foot care Proportion of patients with myocardial infarction who received thrombolyses Proportion of patients assessed by a doctor within 24 hours of referral Proportion of patients treated according to clinical guidelines <p>Outcome</p> <p>Intermediate</p> <ul style="list-style-type: none"> HbA1c results for diabetics Lipid profile results for patients with hyperlipidemia Blood pressure results for hypertensive patients <p>End result (should be specified for diseases)</p> <ul style="list-style-type: none"> Mortality Morbidity <div style="border: 1px solid black; padding: 5px;"> <ul style="list-style-type: none"> Functional status Health status measurement Work status Quality of life Patient satisfaction </div>

Abb. 1: Beispiele von Qualitätsindikatoren hinsichtlich Struktur, Prozess und Outcome¹

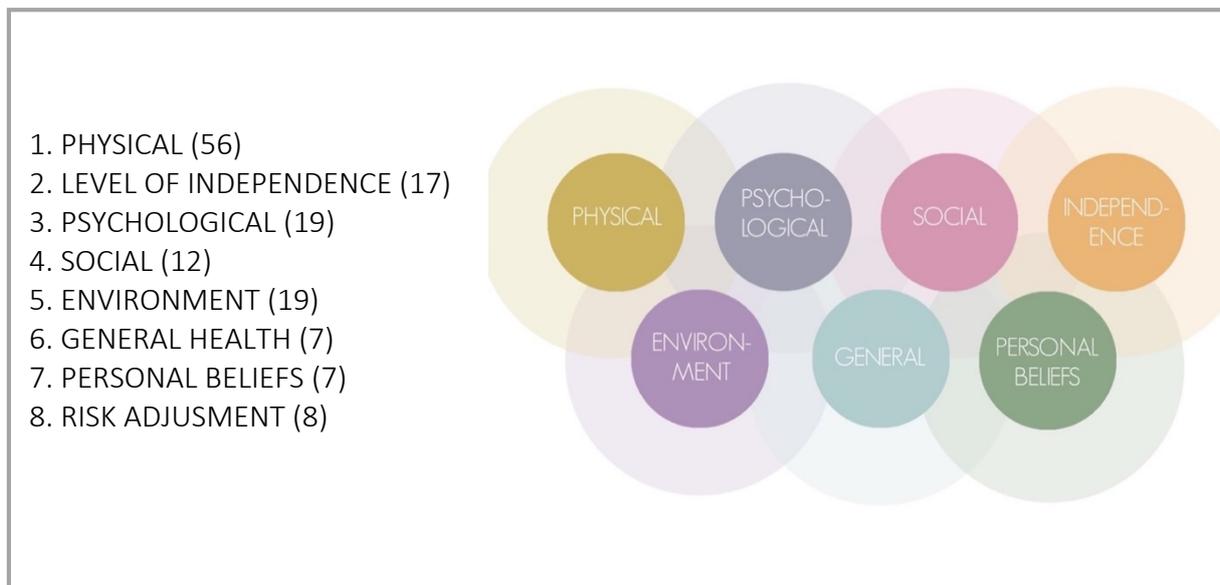


Abb. 2: 8 Domänen, 29 Sub-Domänen und 145 Items des QI Verzeichnisses

¹ Mainz J (2003) Defining and classifying clinical indicators for quality improvement. Int J Qual Health Care. 15:523-30.

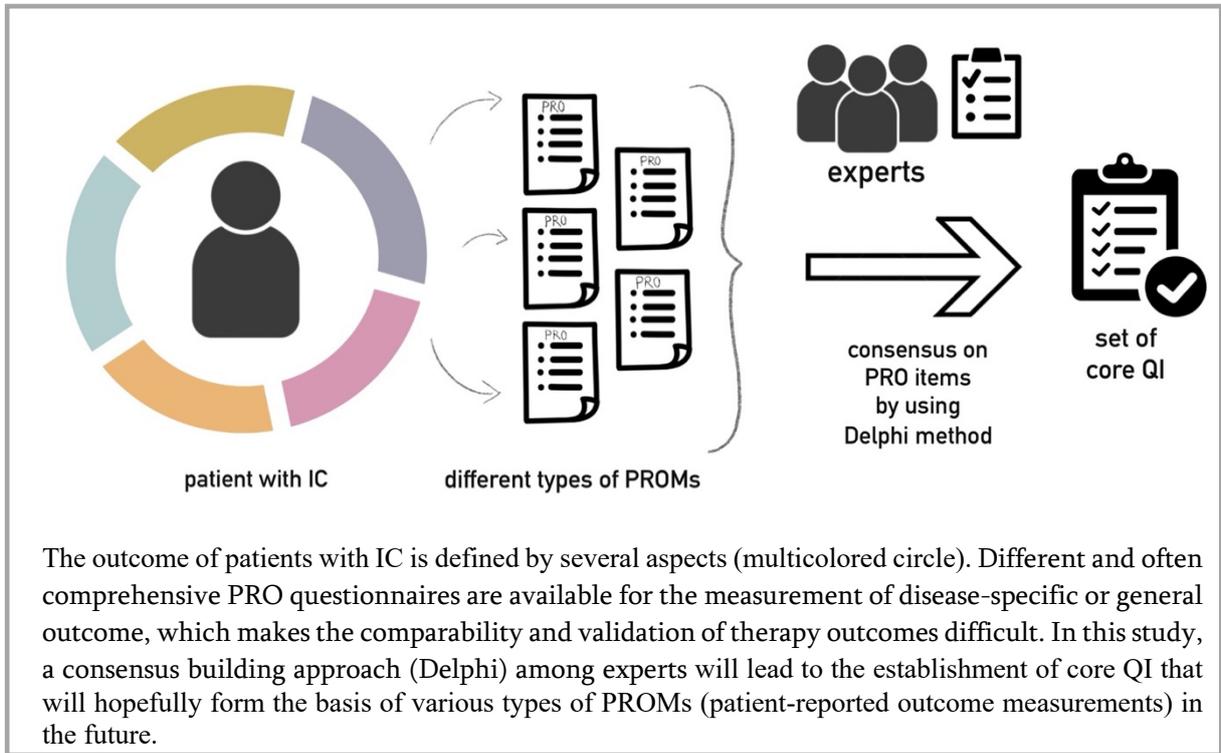


Abb. 3: Beispiel aus einem Bericht zur Erläuterung des Ablaufs einer Delphi-Studie

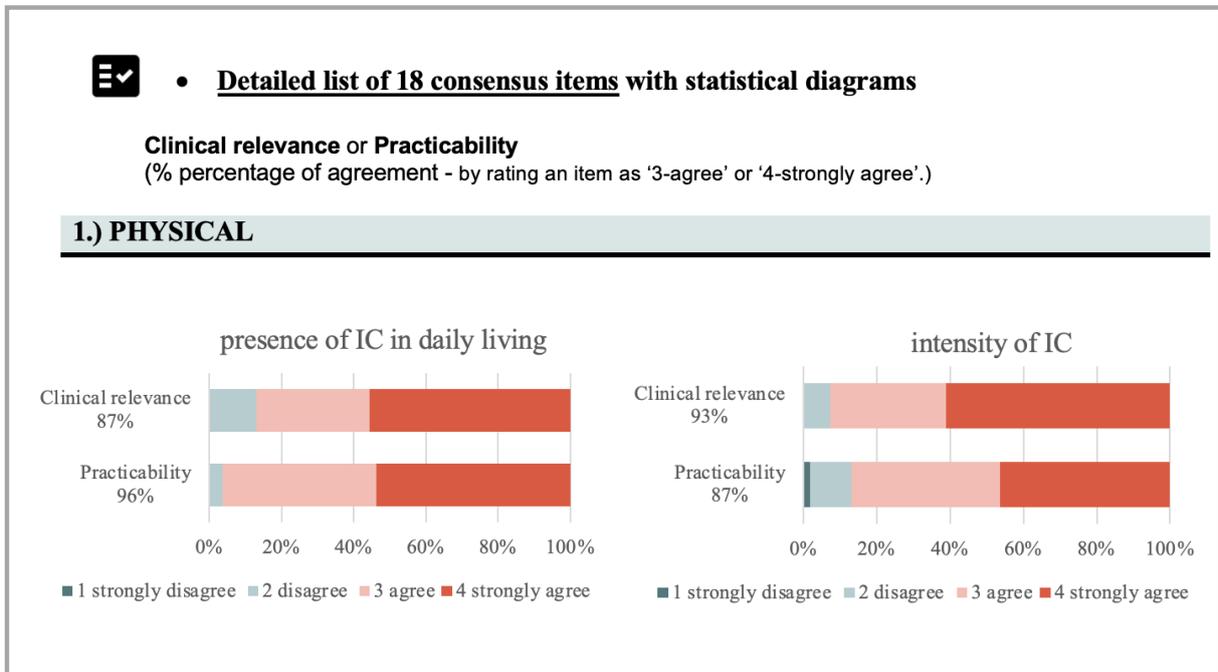


Abb. 4: Auszug aus dem strukturierten Report mit graphischen Diagrammen der Ergebnisse nach der zweiten Delphi Runde

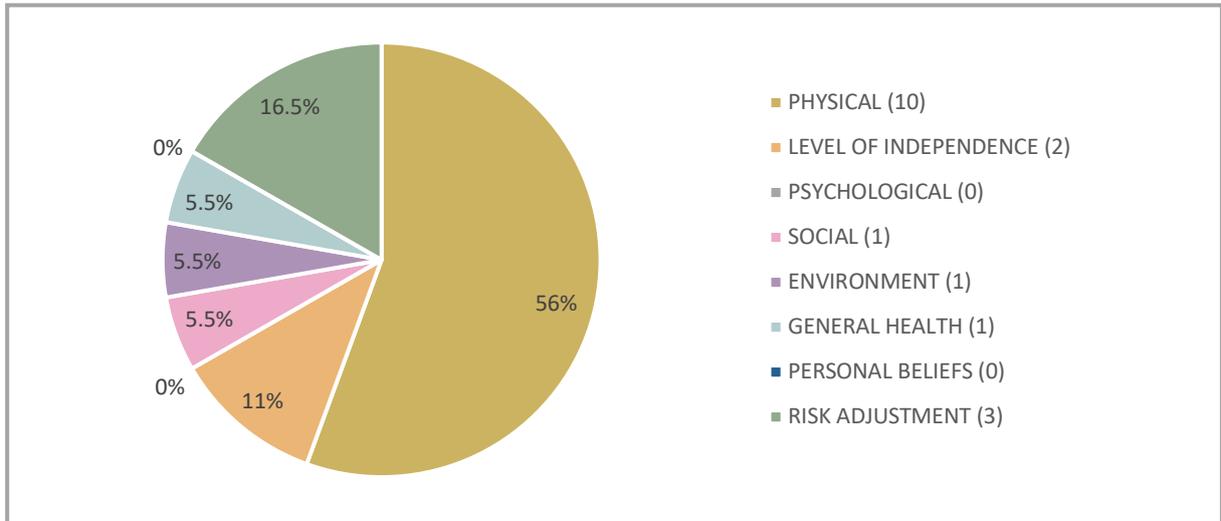


Abb. 5: Übersicht aller Domänen mit prozentualen und numerischem Anteil der PRO QI, welche einen Konsens erreicht haben

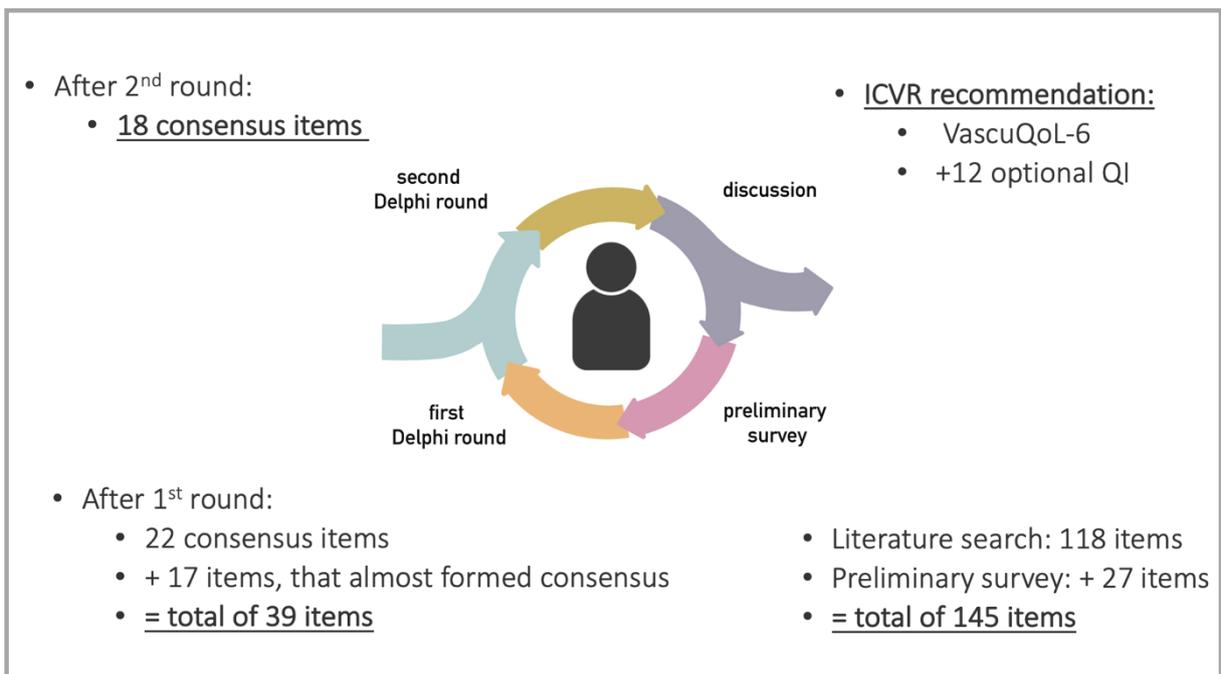


Abb. 6: Anzahl der Items, welche in den einzelnen Delphi-Runden einen Konsens erreicht haben, sowie Ergebnis der finalen Diskussion

Item name	clinical relevance	practicability	description
presence of IC in daily living	87%	96%	presence of claudication pain in activities of daily living
intensity of IC	93%	87%	intensity of claudication pain in activities of daily living by indicating frequency and subjective severity
dissatisfaction with actual IC	81%	57%	presence of dissatisfaction/annoyance caused by claudication pain during daily activities
improvement of IC after treatment	94%	93%	Improvement of claudication pain in daily activities after intervention or surgery
presence of post-treatment pain /symptoms or other complications	85%	85%	presence of pain/symptoms after a treatment for IC (e.g., wound pain, numbness, discomfort, superficial nerve pain, neuralgia) or other complications (e.g., disorder of wound healing)
poorly healing wounds/ulcers	87%	85%	Leg/foot wounds heal poorly (e.g., it takes more than a few weeks to heal)
presence of walking impairment due to PAOD	85%	83%	presence of walking impairment caused by PAOD such as claudication, post-treatment pain, or post-treatment wound
degree of walking impairment due to PAOD	94%	85%	degree of walking impairment due to PAOD in activities of daily living
impact of walking impairment due to PAOD	83%	69%	negative effects of walking impairment due to PAOD in daily life e.g., isolation, dependency, embarrassment, depression, lifestyle change
limitation of walking distance due to IC	89%	81%	limitation of walking distance at normal speed on level ground due to IC
limitation of everyday functioning (disease related)	94%	81%	limitation of everyday functioning due to PAOD/IC (physical or emotional)
limitation of work capacity due to PAOD	80%	65%	limitation of work capacity due to PAOD/IC, because of physical or emotional problems
limitation of social activities due to PAOD	91%	76%	limitation of social activities due to PAOD/IC (physical problems or emotional problems)
satisfaction with current treatment (PAOD)	80%	83%	satisfaction with current treatment regarding PAOD
perception of IC related QoL	81%	65%	subjective perception of IC related quality of life (e.g., impact of IC on QoL)
smoking	100%	94%	former and actual quantification of exposure to nicotine
physical training/exercise	94%	83%	participation in physical training or regular exercise (e.g., incl. long walks)
compliance to medication	94%	72%	degree to which a patient correctly follows medical advice referring medication

* Intermittent Claudication (IC): fatigue, discomfort, cramping, or pain of vascular origin in the muscles of the lower extremities that is consistently induced by exercise and consistently relieved by rest within 10 min [AHA/ACC Guideline, 2016]

Abb. 7: Übersicht der 18 Konsens Items hinsichtlich klinischer Relevanz und Praktikabilität. Items mit hoher Übereinstimmung sind gelb hervorgehoben (>90%).

VascuQoL-6	Item in Delphi survey	clinical relevance	practicability	Consensus in 2 nd round
1. limited activities due to PAOD	limitation of everyday functioning ¹ due to PAOD	94%	81%	
3. limited ability to walk due to PAOD	degree of walking impairment due to PAOD	94%	85%	
4. concerns about PAOD	anxiety ² caused by PAOD	68%	50%	
5. limited participation in social activities due to PAOD	limitation of social activities due to PAOD	91%	76%	
2. extent of tiredness/ weakness in legs	intensity of IC ³	93%	87%	
6. degree of pain in leg or foot				

¹ everyday functioning: household chores, errands, grocery shopping, odd jobs around the home, participating in sports, self-care/-sufficiency
² anxiety caused by PAOD: Feelings like nervousness, worry, **concern**, despair about pain/ future/ worsening
³ Intermittent Claudication (IC): **fatigue**, discomfort, cramping, or **pain** of vascular origin in the muscles of the lower extremities that is consistently induced by exercise and consistently relieved by rest within 10 min [AHA/ACC Guideline, 2016]

Abb. 8: Vergleich des VascuQoL-6 mit den Ergebnissen der zweiten Delphi-Runde

Item name	clinical relevance	practicability	description
walking distance on average	70%	63%	average walking distance at normal speed on level ground without stopping
absolute claudication distance (ACD) or maximum walking distance (MWD)	69%	67%	absolute possible or maximum walking distance on level ground without stopping despite of IC pain
initial claudication distance (ICD) or maximum pain-free walking distance (MPWD)	67%	65%	initial walking distance on level ground before the onset of IC pain
perception of QoL in general	67%	54%	subjective perception of perceived overall quality of life in general
healthy diet	76%	56%	subjective perception of whether a healthy diet is being followed

Abb. 9: Fünf Items erreichten in der ersten Runde einen Konsens, schieden jedoch in der zweiten Runde aus.

Set of 6 core indicators (from VascuQoL-6)	Optional data collection of additional 12 indicators	
limited activities due to PAOD	dissatisfaction with actual IC	limitation of work capacity due to PAOD
extent of tiredness/ weakness in legs	improvement of IC after treatment	satisfaction with current treatment (PAOD)
limited ability to walk due to PAOD	presence of post-treatment pain /symptoms or other complications	perception of IC related QoL
concerns about PAOD	poorly healing wounds/ulcers	smoking
limited participation in social activities due to PAOD	impact of walking impairment due to PAOD	physical training/exercise
degree of pain in leg or foot	limitation of walking distance due to IC	compliance to medication

Abb. 10: Empfehlung zur Erhebung von PRO QI in pAVK Registern basierend auf der Evaluation und Diskussionen in dieser Delphi Studie

Tabellenverzeichnis

Tab. 1: Zeitlicher Rahmen des Studienablaufs

Literaturrecherche	Juli bis Dezember 2020
Erstellung eines Indikator Index	Januar 2021
Rekrutierung eines Expertengremiums	Februar bis April 2021
Vorbefragung	10. – 31. Mai 2021
Ergebnisbericht der Vorrunde	Juni 2021
Erste Delphi Runde	28. Juli – 25. August 2021
Ergebnisbericht der ersten Delphi Runde	September 2021
Zweite Delphi Runde	18. Oktober – 8. November 2021
Ergebnisbericht der zweiten Delphi Runde	November 2021
Finale Diskussion	16. November 2021

Tab.2: Suchprotokoll der Literaturrecherche

“Patient Reported Outcome Measures [MeSH Terms] AND Intermittent Claudication [MeSH Terms]”
“Patient Reported Outcome Measures [MeSH Terms] AND Peripheral Artery Disease [MeSH Terms]”
“Patient reported" AND Intermittent Claudication [MeSH Terms]”
“Quality of life" AND Intermittent Claudication [MeSH Terms]”
“PROM" AND Intermittent Claudication [MeSH Terms]”
“Patient reported" AND Peripheral Artery Disease [MeSH Terms]”
“Quality of life" AND Peripheral Artery Disease [MeSH Terms]”
“PROM" AND Peripheral Artery Disease [MeSH Terms]”

Tab. 2: Indikator Index – Struktur und Dokumentation von Outcome Qualitätsindikatoren

Domain	Terms of reference	Physical	Physical	Physical
Sub domain		Pain	Pain	Vitality
Item	Subject heading	Presence of pain	Pain intensity	Fatigue level
Definition in detail	explicit statement of what is to be assessed	presence of pain due to PAD (pain type: ischaemic pain, postoperative pain, wound/ulcer pain, phantom pain)	intensity of pain due to PAD symptoms*	level of fatigue in daily activities**. Fatigue is defined as rapid energy loss, tiredness, effort in daily living.
Measurement	units/dimension of measurement		frequency (e.g., none/ some of the time/ 3 times a day/ constant)	frequency (e.g., never/ half of the day/ 3 times a week)
			severity (e.g., no/ moderate/ extreme)	degree (e.g., never/ a little/ moderate/ extreme)
	other	Presence of above-mentioned pain type (answer: yes/no)		
Indicator	Description of quality indicator	Proportion of patients with no PAD related pain	Proportion of patients with reduced pain intensity or freedom of pain	Proportion of patients with low fatigue level
Indicator target	Definition of the target	Freedom of pain	Reduction of pain intensity. Best case: freedom of pain.	Decrease of fatigue level. Best case: freedom of fatigue.
Type of indicator	outcome, structural or process indicators	outcome	outcome	outcome
	Indicator of desirable or undesirable events	desirable	desirable	undesirable
	generic or disease-specific indicator	disease-specific	disease-specific	generic
Explicit data specification	Description of the source of information to compute the indicator	e.g., administrative databases	e.g., surveys	e.g., Clinical documentation

*PAD symptoms:

defined as claudication, which means pain/aches/cramps in calves/buttocks/thighs or weakness in legs

**daily activities such as grocery shopping, household, commute to work

3. Zusammenfassung

Ziel: Ziel dieser Studie war es, einen Kernsatz von Qualitätsindikatoren (QIs) aus patientenberichteten Outcomes (PRO) für die Behandlung von Patienten mit Claudicatio intermittens (IC) zu erstellen, welche eine breite internationale Implementierung in verschiedenen Gefäßregistern sowie in Studien ermöglichen.

Methodik: Es wurde ein modifiziertes, zweistufiges Delphi-Verfahren angewandt, um ein Konsens zu patientenberichteten Outcome QIs unter einem Expertengremium zu generieren, welches sich aus internationalen Gefäßspezialisten, Patientenvertretern und Registermitgliedern des VASCUNET, des International Consortium of Vascular Registries und des Medical Device Epidemiology Network zusammensetzte. Potenzielle QIs wurden durch eine umfangreiche Literaturrecherche identifiziert oder zusätzlich vom Gremium vorgeschlagen und anschließend von den Experten in einer Vorprüfung validiert und in zwei Delphi-Runden evaluiert. Ein Konsens wurde erreicht, wenn $\geq 80\%$ der Teilnehmer der Meinung waren, dass ein QI klinisch relevant oder praktikabel ist.

Ergebnisse: Die Teilnahme an der ersten und zweiten Delphi-Runde betrug 66% (31 von 47 eingeladenen Teilnehmern) bzw. 90% (54 von 60). Anfänglich wurden 145 QI aus Patientenberichte in einem Index dokumentiert. Nach den beiden Delphi-Runden erreichten 18 Qualitätsindikatoren einen Konsens hinsichtlich klinischer Relevanz oder Praktikabilität. Der VascuQoL-Fragebogen (VascuQoL-6) beinhaltet sechs Items und ist derzeit das am häufigsten verwendete Instrument zur Messung des Patientenoutcomes (PROM) in Gefäßregistern. Fünf dieser sechs Items stimmen den in der Delphi-Studie ermittelten Indikatoren mit hoher Bewertung ($>90\%$) überein. Das Gremium empfiehlt die Verwendung des VascuQoL-6 als bevorzugten PROM für die Datenerhebung in internationalen Registern sowie eine optionale Erweiterung um 12 zusätzliche patientenbezogene QI, die ebenfalls in dieser Studie Konsens erreichten.

Fazit: Die auf dem Delphi-Konsensverfahren basierende Empfehlung stärkt die internationale Harmonisierung der Registerdatenerfassung in Bezug auf die PRO Qualität. Eine kontinuierliche und standardisierte Qualitätssicherung ermöglicht, dass die Registerdaten für künftige Qualitäts-Benchmarking-Studien verwendet werden können und sich letztlich positiv auf die Versorgung von Patienten mit IC auswirken.

Summary

Objective: This study aimed to develop a core set of patient-reported outcome quality indicators (QIs) for the treatment of patients with intermittent claudication (IC), that allow a broad international implementation across different vascular registries and within trials.

Methods: We utilized a rigorous modified two-stage Delphi technique to promote consensus building on patient-reported outcome QIs among an expert panel consisting of international vascular specialists, patient representatives and registry members of the VASCUNET, the International Consortium of Vascular Registries, and the Medical Device Epidemiology Network. Potential QIs identified through an extensive literature search or additionally proposed by the panel were validated by the experts in a preliminary survey and included for evaluation. Consensus was reached if $\geq 80\%$ of participants agreed that an item was both clinically relevant and practical.

Results: Participation rates in the first and second Delphi rounds were 66% (31 participants out of 47 invited) and 90% (54 out of 60), respectively. Initially, 145 patient-reported outcome QI were documented. Following the two Delphi rounds, 18 quality indicators remained, all of which reached consensus regarding clinical relevance and practicability. The VascuQoL questionnaire (VascuQoL-6), currently the most common patient-reported outcome measurement (PROM) used within vascular registries, includes a total of six items. Five of these six items also matched with high rated indicators identified in the Delphi study. Consequently, the panel recommends the use of the VascuQoL-6 survey as a preferred core PROM QI set for international registry data collection, as well as an optional extension of 12 additional patient-reported QI that were also identified in the study.

Conclusion: The current recommendation based on the Delphi consensus building approach, strengthens the international harmonisation of registry data collection in relation to patient-reported outcome quality. Continuous and standardized quality assurance will ensure that registry data may be used for future quality benchmarking studies and ultimately positively impact the overall quality of care provided to IC patients.

4. Glossar

ABI	Ankle-Brachial Index
ACD	Absolute Claudication Distance
CLTI	Chronic limb-threatening ischemia
HRQoL	Health Related Quality of Life
IC	Intermittent Claudication
ICD	Initial Claudication Distance
ICVR	International Consortium of Vascular Registries
MDEpiNET	Medical Device Epidemiology Network
pAVK	peripher Arterielle Verschlusskrankheit
PRO	Patient-Reported Outcome
PROs	Patient-Reported Outcomes
PROM	Patient-Reported Outcome Measurement
PROMs	Patient-Reported Outcome Measurements
QI	Quality Indicator, Qualitätsindikator
QIs	Quality Indicators, Qualitätsindikatoren
QoL	Quality of Life
SF-36	36-item Short Form Survey
VASCUNET	committee of the European Society for Vascular Surgery (ESVS)
VascuQoL-6	Vascular Quality of Life – 6 item questionnaire
WIQ	Walking Impairment Questionnaire
WHO	World Health Organization
WHOQOL	Quality of Life questionnaire of the WHO

5. Anhang

List of Patient-Reported Quality Indicators in Peripheral Arterial Occlusive Disease (145 items)

Overview of domains:

1. PHYSICAL
2. LEVEL OF INDEPENDENCE
3. PSYCHOLOGICAL
4. SOCIAL
5. ENVIRONMENT
6. GENERAL HEALTH
7. PERSONAL BELIEFS
8. RISK ADJUSTMENT

1.) PHYSICAL

1.1.) Pain (IC*: Intermittent Claudication/general)

Item name	description
presence of IC* in daily living	presence of claudication pain in activities of daily living**
presence of IC* during regular exercise	presence of claudication pain during regular exercises (e.g., jogging, swimming, biking)
intensity of IC	intensity of claudication pain in activities of daily living by indicating frequency and subjective severity
IC localisation	explicit localisation of claudication pain (side/s and body part/s)
occurrence of IC	situational occurrence of claudication pain e.g., walking pain, while climbing stairs, going down stairs
perception of IC	subjective description of IC perception e.g., cramps, numbness, discomfort, exhaustion
dissatisfaction with actual IC	presence of dissatisfaction/annoyance caused by claudication pain during daily activities
analgetic dependency due to IC	need for analgesics due to claudication pain on daily basis
improvement of IC after treatment	Improvement of claudication pain in daily activities after intervention or surgery
presence of post-treatment pain/symptoms or other complications	presence of pain/symptoms after a treatment for IC (e.g., wound pain, numbness, discomfort, superficial nerve pain, neuralgia) or other complications (e.g., disorder of wound healing)
bodily pain or pain in general (other health issues)	presence, degree and neg. impact of bodily pain in general (pain due to other health problems than PAOD)

* Intermittent Claudication (IC): fatigue, discomfort, cramping, or pain of vascular origin in the muscles of the lower extremities that is consistently induced by exercise and consistently relieved by rest within 10 min [AHA/ACC Guideline, 2016]

** activities of daily living: grocery shopping, household, commute to work

1.2.) PAOD Symptoms (Peripheral Arterial Occlusive Disease)

Item name	description
presence of coldness	sensation/feeling of coldness or objective coldness (temperature of skin when touching foot with hands) in lower leg/foot
presence of discoloration	change in the colour of leg/foot (e.g., pale, bluish, reddish)
presence of numbness	long-lasting or unexplained numbness in leg/foot
poorly healing wounds/ulcers	Leg/foot wounds heal poorly (e.g., it takes more than a few weeks to heal)
hair loss/slower hair growth	hair loss/slower hair growth on feet or leg
erectile dysfunction	presence of erectile dysfunction in men (erectile dysfunction: inability to get or keep an erection firm enough to have sexual intercourse)
fungal nails and foot skin infection	presence of fungal nails and foot skin infection

paraesthesia in leg/foot	subjective perception of paraesthesia in leg/foot (abnormal sensation, typically tingling or pricking)
muscle atrophy at the thigh/calf level	subjective visual evaluation of presence/absence of muscle atrophy (one leg looks thinner than the other) or objective muscle atrophy by measuring the circumference on thigh/calf level by patients at home

1.3.) Vitality (general)

Item name	description
energy level	level of energy in activities of daily living* Energy is defined as comparative/age-appropriate stable level of capacity for activities
fatigue level	level of fatigue in daily activities. Fatigue is defined as rapid energy loss, tiredness or effort in daily living, which doesn't resolve completely with rest.
satisfaction with energy level	satisfaction with energy level in daily activities in general

* activities of daily living: grocery shopping, household, commute to work

1.4.) Sleep and Rest (PAOD/general)

Item name	description
long time period until falling asleep due to PAOD	subjective perception that falling asleep takes longer due to PAOD (physical problems or emotional problems*)
limitation of sleeping through the night due to PAOD	sleep disorder, limitation in sleeping through the night or sleeplessness/awakening due to PAOD (physical problems or emotional problems*)
waking up early due to PAOD	subjective perception of waking up earlier than usual due to PAOD (physical problems or emotional problems*)
sleeping drug dependency in general	need for sleep medication in general
satisfaction with sleep & rest regarding PAOD	satisfaction with sleep and rest regarding PAOD
limitation of sleep and rest in general	limitation of falling asleep, sleep disorders, and satisfaction with sleep & rest in general (regarding other health issues)

*physical problems due to PAOD e.g., claudication, post-treatment wounds, lost limb or emotional problems due to PAOD e.g., worries, depressed feelings

1.5.) Mobility

1.5.1) Walking Impairment (PAOD)

Item name	description
presence of walking impairment due to PAOD	presence of walking impairment caused by PAOD such as claudication, post-treatment pain, or post-treatment wound
degree of walking impairment due to PAOD	degree of walking impairment due to PAOD in activities of daily living *
impact of walking impairment due to PAOD	negative effects of walking impairment due to PAOD in daily life e.g., isolation, dependency, embarrassment, depression, lifestyle change

* activities of daily living: grocery shopping, household, commute to work

1.5.2.) Walking Distance (IC)

Item name	description
limitation of walking distance due to IC	limitation of walking distance at normal speed on level ground due to IC*
walking distance on average	average walking distance at normal speed on level ground without stopping
absolute claudication distance (ACD) or maximum walking distance (MWD)	absolute possible or maximum walking distance on level ground without stopping despite of IC pain
initial claudication distance (ICD) or maximum pain-free walking distance (MPWD)	initial walking distance on level ground before the onset of IC pain

satisfaction with walking distance regarding IC	satisfaction with walking distance in relation to IC in activities of daily living **
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*Intermittent Claudication (IC): fatigue, discomfort, cramping, or pain of vascular origin in the muscles of the lower extremities that is consistently induced by exercise and consistently relieved by rest within 10 min [AHA/ACC Guideline, 2016]

** activities of daily living: grocery shopping, household, commute to work

1.5.3.) Walking Speed (IC and general)

Item name	description
limitation of walking speed due to IC	limited walking speed on level ground without stopping due to IC e.g., hurrying or jogging, as if to catch a bus
average walking speed regarding IC	walking speed on level ground without stopping to rest due to IC (e.g., period of time for specific distance OR period of time with specific pace OR compared to others of the same age)
limitation of walking speed in general	limitation of walking speed on level ground due to general health problems e.g., orthopaedic, cardiopulmonary health issues or other
satisfaction with walking speed regarding IC	satisfaction with walking speed allowed by IC symptoms in daily living

1.5.4.) General Mobility

Item name	description
limitation of general mobility	evaluation of independency in walking. Reduced mobility in general (need of crutches, rollator) or total immobility (wheelchair accessibility or bedridden)
limitation of walking distance due to general health	limitation of walking distance on level ground due to general health problems e.g., orthopaedic, cardiopulmonary health issues or other
impact of limited mobility in general	negative impact of limited mobility on daily life e.g., isolation, need of social support, psychological, employment
satisfaction with general mobility	satisfaction with general mobility in daily living
daily physical activity level in general	self-reported, subjective physical daily activity level in general (e.g., on VAS*, compared to other people, quantity of vigorous/moderate activities)
lower-extremity strength and balance	subjective lower-extremity strength and balance in general (e.g., on VAS*, compared to other people)
limitation of standing due to pain	limitation of standing due to pain in general (e.g., leg pain, back pain)
increased number of falls	subjectively increased falls in general (e.g., balance disorder, heavy legs, numbness in foot)

*VAS: Visual Analogue Scale

1.5.5.) Stair Climbing (IC and general)

Item name	description
limitation when climbing stairs in general	limitations when climbing stairs because of general health problems (orthopaedic, cardiopulmonary health issues or other)
limitations when descending stairs in general	limitations when descending stairs because of general health problems (orthopaedic, cardiopulmonary health issues or other)
limitations when climbing stairs due to IC	limitations when climbing stairs due to claudication pain

1.5.6.) Agility (general)

Item name	description
limitations of agility in general	limitations of general agility (like bending, kneeling) in daily activities*
impact of limited agility	negative impact of limited agility on daily life (e.g., isolation, need of social support, lifestyle change, psychological)

*examples of daily activities regarding agility are e.g., getting in and out of bed, bending down to pick up clothing from the floor, kneeling, getting in/out of the car

1.5.7.) High Impact Activities (IC)

Item name	description
limitations of walking up a hill due to IC	limitations of walking up a hill due to claudication pain (e.g., inability to walk in the mountains)
limitations of vigorous physical activities* due to IC	limitations of vigorous physical activities* due to claudication pain

*examples of vigorous physical activities include long period of jogging/running, carrying heavy loads, sports such as soccer, basketball or swimming.

2.) LEVEL OF INDEPENDENCE

2.1.) Everyday Functioning

Item name	description
limitation of everyday functioning* (disease related)	limitation of everyday functioning* due to PAOD/IC (physical or emotional)
limitation of everyday functioning in general	limitation of everyday functioning* in general (physical or emotional)
presence of negative impact due to limited everyday functioning (disease related)	presence of negative impact due to limitation of everyday functioning due to PAOD/IC (e.g., need of assistance/social support, dependency, reducing activities, extra effort, emotional: feelings of stress, depression, sadness)
physical exertion in everyday functioning (disease related)	presence of physical exertion or extra effort in everyday functioning due to PAOD/IC
satisfaction with everyday functioning	satisfaction with ability to perform daily living activities (e.g., regarding amount of time, efficiency, accuracy, extra effort)
limitation of body care	limitation of body care like washing entire body, bathing
limitation of household chores	limitation of household chores (e.g., cleaning, cooking, grocery shopping, odd jobs around the home)
limitation of sport activities	limitation of sport activities (like running, playing golf, soccer)
dependence on medication and treatments for everyday functioning	need for medication/ treatments in everyday functioning in general
satisfaction with exercise capacity	satisfaction with exercise capacity in daily living in general
disease burden regarding PAOD/IC	perception of PAOD/IC as a burden in everyday functioning (physical or emotional)

*everyday functioning: household chores (cleaning/cooking), errands (going to the post office/bank), grocery shopping, odd jobs around the home, participating sports (running, playing golf), self-care/self-sufficiency (washing, dressing)

2.2. Employment

Item name	description
limitation of work capacity due to PAOD	limitation of work capacity due to PAOD/IC, because of physical or emotional problems*
impact of limited work capacity due to PAOD	negative impact of limited work capacity due to PAOD/IC on employment (e.g., limited ability to earn money, unemployment, lack of money, loss of income, financial dependency, lifestyle change, depression)
satisfaction with work capacity	satisfaction with work capacity, regarding efficiency and accuracy

*physical problems (e.g., pain, post-treatment wounds, lost limb) or emotional problems (e.g., worries, stress, depressed feelings)

2.3.) Living Status

Item name	description
current living status in general	independent or assisted living status e.g., independent at home, living in an assisted-living facility, or living in a nursing home

change in living status due to PAOD	living status has changed due to PAOD (e.g., because of disease worsening, change of living status after intervention/s)
satisfaction with living status	Satisfaction with actual living status

3.) PSYCHOLOGICAL

3.1.) General Mental Health

Item name	description
positive*, negative** or neutral feelings in general	general psychological well-being described with positive feelings* or general psychological distress described with negative feelings**
positive*, negative** or neutral feelings regarding PAOD/IC	positive adaptation to PAOD (hopeful about outcome, managing disease, succeeded in life changes, understanding the causes), negative feelings** or neutral feelings
positive adaptation regarding PAOD	positive adaptation to PAOD (hopeful about outcome, managing disease, succeeded in life changes, understanding the causes)
anxiety caused by PAOD	anxiety caused by PAOD 1. Feelings like nervousness, worry, concern, despair about pain/future/worsening 2. Loss of control over feelings of anxiety
depression caused by PAOD	depression caused by PAOD 1. Feelings like hopelessness, unhappiness, frustration 2. Loss of life value, perception of life as a burden
limited enjoyment of life due to PAOD	limited enjoyment of life caused by PAOD (e.g., physical: exercise, walking impairment/ social: relationships, meeting with family, friends/ environment: leisure activities, hobbies, vacation.)
suicidal thoughts	suicidal thoughts related to depression (in general)

*positive feelings: feelings of peace, calm, happiness, content, enjoying life, pos. feelings about future

**negative feelings: nervousness, listlessness, loneliness, anxiety, tension, anger, confusion, depression, worries, embarrassment, frustration, life as a burden

3.2.) Body Image

Item name	description
negative, neutral or positive feelings due to body image caused by PAOD	negative feelings due to body image caused by PAOD (feeling inhibited, uncomfortable, embarrassed because of post-treatment wounds, scars, discoloration), or positive feelings (satisfied with body image, feeling comfortable) or neutral
satisfaction with body image regarding PAOD	satisfaction with body appearance regarding PAOD.
change in body image due to PAOD	PAOD has changed the body image

3.3.) Self-Esteem /-Confidence

Item name	description
reduced self-esteem* / self-confidence** due to PAOD	reduction of self-esteem /-confidence due to PAOD e.g., feelings of otherness, vulnerability, helplessness, shame
loss of self-esteem / self-confidence due to PAOD	complete loss of self-esteem/-confidence due to PAOD e.g., loss of contentment with oneself, identity, abilities, independence
satisfaction with self-esteem in general	satisfaction with contentment of oneself, self-worth in general
satisfaction with self-confidence in general	satisfaction with personal abilities or with ability to make own decisions in general

*self-esteem = emotional appraisal of one's own worth (e.g., how much do you value yourself?)

**self-confidence = to trust in oneself, and, in particular, in one's ability (e.g., how much confidence do you have in yourself?)

3.4.) Learning/New Information

Item name	description
ability to think, memorize, learn, concentrate	subjective perception of ability to think, memorize, learn, concentrate
acquiring new information and skills	Opportunity and ability to acquire new information and skills (e.g., reading the newspaper)
ability to acquire new lifestyle habits	ability to acquire new lifestyle habits (drinking more water, walking daily etc)

3.5.) Stress

Item name	description
perceived stress	degree to which situations within a person's life are appraised as stressful (e.g., on visual analogue scale)
attempts to limit stress level	active attempts to minimize the stress

4.) SOCIAL

4.1.) Social Relationships

Item name	description
limitation of social activities due to PAOD	limitation of social activities* due to PAOD/IC (physical problems or emotional problems)
impact of limited social activities due to PAOD	negative impact of limited social activities due to PAOD on personal relationships (e.g., relationship losses, changes in relationships) or on feelings (loneliness, isolation, alienation)
satisfaction with social activities and personal relationships	satisfaction with social activities and personal relationships

*social activities examples: like meetings with friends/family, going out to eat, movie nights, going hiking

4.2.) Social In-/Exclusion

Item name	description
social exclusion due to PAOD	presence of social exclusion or discrimination due to PAOD (e.g., blaming by others)
social inclusion regarding PAOD	presence of social inclusion or acceptance regarding PAOD
satisfaction with social inclusion in general	satisfaction with social inclusion or social acceptance in general

4.3.) Social Support

Item name	description
need for social support due to PAOD	need for social support/care by family and/or friends due to PAOD (mental or physical need of support)
impact for need of social support	negative impact on relationships because of need for social support (experience of relation losses, changes in relationships) or on feelings (feeling of guilt about need for support, feeling like a burden)
satisfaction with social support regarding PAOD	satisfaction with perceived social support in relation to PAOD (existing emotional and social support through family and/or friends)
ability to care for others	ability to provide care and social support to others

4.4.) Sex Life

Item name	description
limitations in sex life due to PAOD	limitations in sex life due to PAOD (physical or emotional) e.g., erectile dysfunction* in men, embarrassment about body image, depression
satisfaction with sex life in general	satisfaction with sex life in general

*erectile dysfunction= inability to get or keep an erection firm enough to have sexual intercourse

5. ENVIRONMENT

5.1.) Home

Item name	description
domestic safety regarding PAOD	safety in domestic environment regarding PAOD (suitable to a persons' need)
impact of insecure home environment	negative impact of insecure home environment (e.g., need for support, limited independence, emotional)
satisfaction with safety in home environment	satisfaction with safety in home environment/ satisfaction with home environment (suitable to needs)
satisfaction with physical environment	satisfaction with physical environment (e.g., noise pollution, traffic, climate, healthy/unhealthy environment)

5.2.) Financial

Item name	description
limited financial resources in general	limited financial resources in general
impact of limited financial resources	negative impact of limited financial resources (e.g., financial dependency, lifestyle change, worries, depression, feeling of guilt)
satisfaction with financial resources	satisfaction with financial resources in general.

5.3.) Health Care/ Treatment

Item name	description
satisfaction with the quality of health care services in general	satisfaction with the quality of health care services
satisfaction with the availability to health care services in general	satisfaction with the availability of timely, affordable care
satisfaction with current treatment (PAOD)	satisfaction with current treatment regarding PAOD
satisfaction with health education regarding PAOD	satisfaction with health education regarding PAOD before and after treatment

5.4.) Leisure

Item name	description
ability to participate in leisure activities in general	physical and emotional ability to participate in leisure activities*
opportunity for leisure activities	opportunity to participate in leisure activities* in general
limitations of ability to engage in leisure activities due to PAOD	limitations of ability to engage in leisure activities due to PAOD including physical or emotional problems**
impact of limited leisure activities	negative impact of limited leisure activities such as loss of enjoyment in life, loss of personal relationships, lifestyle change, depression
satisfaction with leisure activities	satisfaction with the ability and opportunity to participate in leisure activities

*leisure activities: interests, hobbies, vacation, sports, arts which leads to enjoyment of life

**physical problems (e.g., pain, post-treatment wounds, walking impairment) or emotional problems (e.g., worries, stress, depressed feelings)

5.5.) Transport

Item name	description
limitations of transport	problems, difficulties with transport such as driving a car, using public transportation, organizing a ride
satisfaction with transport	satisfaction with transport in general and satisfaction of availability of transport opportunities
fear/worries regarding transportation	Fear/worries regarding transportation like fear of not being able to catch the bus or fear of getting a cardio-/cerebrovascular event while driving

6. GENERAL

6.1.) General Health

Item name	description
general health	self-perceived overall general health status
satisfaction with general health	satisfaction with the health status in general
general health change	change in perceived general health compared to one year ago
subjective perception of frailty	subjective perception of frailty (being weak and delicate)

6.2.) Overall Quality of Life (QoL)

Item name	description
perception of QoL in general	subjective perception of perceived overall quality of life in general
satisfaction with QoL	satisfaction with quality of life in general
perception of IC related QoL	subjective perception of IC related quality of life (e.g., impact of IC on QoL)

7. PERSONAL BELIEFS

7.1.) Future

Item name	description
concerns/fear about future due to PAOD	concerns, anxiety or fear about future due to PAOD (e.g., future pain, future physical limitations, absence of complete cure, disease progression, fear of future amputation, deterioration of general health due to PAOD, losing one's life due to PAOD)
worries/fear about death	worries and fear about death or suffering before dying
confidence in future regarding PAOD	feeling confident about future regarding PAOD (confident about recovery, improvement of disease in future, symptom relief, disease is under control)

7.2.) Guilt

Item name	description
assignment of guilt due to PAOD	feelings of guilt about illness/ blaming oneself due to PAOD
blaming/accusation by others due to PAOD	feelings of finger pointing/ blaming by others due to PAOD

7.3.) Spirituality

Item name	description
positive emotional impact through spirituality	positive emotional impact through spirituality like having a meaning in life, understanding difficulties, strength to face difficulties
negative emotional impact through spirituality	negative emotional impact through spirituality like suffering from fate or being predestined for an illness

8. RISK ADJUSTMENT

8.1.) Lifestyle

Item name	description
smoking	former and actual quantification of exposure to nicotine
alcohol use	quantification of alcohol use or alcohol addiction
physical training/exercise	participation in physical training or regular exercise (e.g., incl. long walks)
healthy diet	subjective perception of whether a healthy diet is being followed
excessive intake of alcohol/ coffee/ nicotine	immoderate or excessive consumption of alcohol/ coffee/ nicotine
other drug addictions	for instance, narcotics, opioid, cocaine
compliance to medication	degree to which a patient correctly follows medical advice referring medication

8.2.) Socio-Economic Status

Item name	description
socio-economic status (SES) and subjective socio-economic status (SSS)	SES: objective socio-economic status (employment, education, income, marital status) SSS: subjective socio-economic status

6. Erklärung des Eigenanteils an der Publikation

Ich, Helene Arndt, versichere folgende Arbeitsteilung hinsichtlich der Erstellung der Publikationspromotion: „A Delphi Consensus on Patient-reported Outcomes for Registries and Trials including Patients with Intermittent Claudication: Recommendations and Reporting Standard “

Die Studie wurde unter der wissenschaftlichen Leitung von Herrn Priv.-Doz. Dr. med. Behrendt in der Klinik für Gefäßmedizin am Universitären Herz- und Gefäßzentrum durchgeführt. Die Konzeption des Studienverlaufs erfolgte durch mich unter Supervision von PD Dr. Behrendt.

Eigenständig erbrachte Leistungen waren die Erstellung einer schriftlichen 26-seitigen Projektskizze in englischer Sprache, systematische Literaturrecherche, strukturelle Dokumentation der 145 QIs in einem zuvor präzise festgelegten Indikator Index, Erstellung der internetbasierten Fragebögen in den 3 Runden, statistische Auswertung der Ergebnisse sowie Erstellung der strukturellen Ergebnisberichte mit graphischen Diagrammen. Einzelne Details der Berichte wurden mit PD Dr. Behrendt diskutiert und ebenfalls von mir selbstständig ergänzt.

Die Zusammenstellung des Expertenpanels erfolgte durch mich und wurde von PD Dr. med. Behrendt supervisiert. Kommunikation und Hilfestellung bei Fragen der Teilnehmer wurde von mir durchgeführt. Die Studienergebnisse wurden in von mir selbstständig erarbeiteten Vorträgen dem Expertengremium präsentiert und dienten bei den jährlichen ICVR Konferenzen als Grundlage für Diskussionen. Die Leitung und Moderation der Ergebnisdiskussionen führte ich selbstständig durch.

Ich versichere das Manuskripts selbstständig verfasst zu haben. Es erfolgte eine eigenständige abschließende Überarbeitung des Manuskriptes bei der ich Vorschläge und Kommentare der Ko-Autoren einarbeitete.

7. Danksagung

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8. Eidesstattliche Versicherung

Ich versichere ausdrücklich, dass ich die Arbeit selbständig und ohne fremde Hilfe verfasst, andere als die von mir angegebenen Quellen und Hilfsmittel nicht benutzt und die aus den benutzten Werken wörtlich oder inhaltlich entnommenen Stellen einzeln nach Ausgabe (Auflage und Jahr des Erscheinens), Band und Seite des benutzten Werkes kenntlich gemacht habe.

Ferner versichere ich, dass ich die Dissertation bisher nicht einem Fachvertreter an einer anderen Hochschule zur Überprüfung vorgelegt oder mich anderweitig um Zulassung zur Promotion beworben habe.

Ich erkläre mich einverstanden, dass meine Dissertation vom Dekanat der Medizinischen Fakultät mit einer gängigen Software zur Erkennung von Plagiaten überprüft werden kann.

Unterschrift:

Helene Arndt