Validation of a vascular access specific quality of life measure (VASQoL)

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Abstract

Background

A self-administered 11 item Vascular Access Specific Quality of Life Measure (VASQoL) was previously derived from detailed qualitative interviews with adult patients with kidney failure who have experienced vascular access using the Capabilities Approach as a theoretical base[1]. This study reports the psychometric validation of the VASQoL measure including its reliability, content validity and responsiveness to change.

Methods

Cognitive interviews were conducted with 23 adult patients with kidney failure after completion of the VASQoL measure. Focus group discussion with a vascular access professional multidisciplinary team was undertaken (n=8) and subsequently a further 101 adult kidney failure patients with vascular access (TCVC, AVF or AVG) completed the digital VASQoL measure, EQ-5D and SF-36 questionnaires in a longitudinal study with prospectively recorded vascular access events.

Results

Transcript analysis of cognitive interviews after VASQoL completion indicated that the content was comprehensive and well understood by participants. Assessment of Internal reliability for the VASQoL measure was high (Cronbach's alpha 0.858). Test-retest reliability of the overall VASQoL measure was high (intra class correlation coefficient 0.916). In those patients who experienced a vascular access event, significant differences were observed in paired analysis of the VASQoL physical domain questions and vascular access function domain questions and in the EQ-5D usual activities, pain and anxiety domains. In those with no vascular access event, variation was observed in longitudinal analysis in VASQoL questions relating to worry about VA function and capability domains, whilst no variation was observed in the EQ5D measure.

Conclusion

The VASQoL measure has good internal consistency, test-retest reliability, convergent validity and responsiveness to change for clinically relevant vascular access outcomes. This provides a validated, vascular access specific quality of life measure that can be used in future trials of vascular access, evaluation of new technologies and routine use as a patient reported outcome measure (PROM).

Introduction

Creation and maintenance of vascular access (VA) for haemodialysis contributes significantly to the burden of hospital investigations, admissions and procedures for patients with kidney failure[2]. VA is complex as there are several modalities available (TCVC, AVF and AVG) that vary considerably in short and long-term outcomes and associated complications. A national appraisal of vascular access services using a mixed methods approach highlighted impact of vascular access creation and maintenance on patients and recommended that measurement of patient experience should be developed within vascular access services [3]. Furthermore, there is widespread recognition that patient reported outcomes are important in engaging patients with chronic disease management and that capturing patients' perceptions of their health and quality of life are important for research purposes, clinical monitoring, service improvement and national benchmarking [3-7].

Although several general and disease specific quality of life (QoL) measures (SF-36, KDQOL-36, KDQOL-SF) have been used in relation to vascular access, this has mainly been on a cross sectional basis with comparison between vascular access type (AVG, AVF and TCVC) [8-12]. The Kidney Disease QOL (KDQOL) measure is disease-specific with few items specifically related to vascular access [13]. The Vascular Access Questionnaire (VAQ) was developed with a Canadian patient cohort initially as a measure of vascular access satisfaction rather than as a measure of quality of life. [14, 15] Similarly, when developing the Haemodialysis Access Related Quality of life instrument (HARQ), questions from existing health related QoL measures, previous studies and review articles were used to identify potential items that were then discussed in focus groups and initial cognitive assessment.[16] In addition, the psychometric properties of HARQ have not been assessed[16]. The VAQ and HARQ questionnaires were both developed using themes derived from clinicians within multidisciplinary teams rather than patient perspectives as the initial, foundational building block of questionnaire development. Neither has been prospectively validated for responsiveness to vascular access events or complications.

Recently the Kidney Health Initiative assembled an interdisciplinary work group to identify barriers to uptake of VA-specific PROMs[17]. They recommended the development of VA specific PROMs applicable to all VA-related interventions and populations and called for commitment to making the patient voice heard[17-20]. Indeed, the EMA and FDA have endorsed the use of

validated patient reported outcome measures in clinical trials which assess the impact of interventions from the patient perspective [21, 22]. However, given the lack of appropriately designed and validated measures, it is unsurprising that as few as 17% of trials in vascular access reported any patient reported outcomes and only 3% reported quality of life measures [23].

To address this, a pilot self-administered 11-item Vascular Access Specific Quality of Life Measure (VASQoL) was derived from detailed qualitative interviews with kidney disease patients using the Capabilities Approach as a theoretical base.[1] The Capabilities Approach provides an alternative means to understanding wellbeing, based on a person's capability or what a person is *able* to do [24]. Nussbaum's interpretation of the approach is based on the presupposition that one has the '*capability'* to do, be, or have something. *'Functionings'* are when these capabilities are realised[24]. Direct themes (physical feelings, VA function and anxiety) and Indirect themes (general enjoyment of health, relationships, autonomy and control, and everyday tasks) were derived from six scoping interviews and 18 detailed semi-structured interviews. Further content analysis and revision were then undertaken through focus groups exploring patients and vascular access professionals' perspectives, in order to derive an 11 item Vascular access specific quality of life (VASQoL) measure[1]. (Supp data)

The aim of this study is to present the psychometric validation of the VASQoL measure including its reliability, content validity and responsiveness to change.

Methods

Ethical Approval

The study protocol was approved by the London – Stanmore Research Ethics Committee Rec ref 19/LO/2005. NHSGGC Board approval was obtained (GN19RE634). Informed, written consent was obtained from all participants.

The VASQoL measure was assessed for readability using the Flesch-Kincaid reading ease test, scoring 80.8, 71.1 and 79.2 for AVF, AVG and TCVC, and were interpreted as plain English and 'fairly' easy to read. The study was undertaken in three phases (Table 1).

The pilot version of the VASQoL measure contained 11 items that were self-completed electronically during an attendance at dialysis session or other healthcare appointment (Supp

data). Responses were recorded on a 10–point, end-anchored scale. No identifiable information was included in the VASQoL measure and the data were captured on a secure server of the University of Strathclyde.

Recruitment

Inclusion criteria were patients with chronic kidney disease stage 5 and who had undergone creation of VA, who underwent regular haemodialysis, and had the ability to give informed consent. Patients were recruited from 5 satellite haemodialysis units and the inpatient kidney unit in the West of Scotland. A quota sampling technique was used to ensure that key groups were represented in our Phase 1 sample (male vs female; diabetes vs no diabetes; AVF vs AVG vs TCVC; < 65y vs > 65 years; pre-dialysis vs < 1 year vs > 1 year; retired vs working vs not working; ethnicity) (Supp data Table 1.)[25]. Recruitment continued until no new insights emerged.

Phase 1 Cognitive interviews: to determine content validity

Content validity assesses the extent to which the items in a questionnaire are representative of the theoretical construct through detailed cognitive interviews with patients [26, 27]. Patients were asked to complete the VASQoL, SF-36 and EQ-5D questionnaires independently using a specifically designed patient portal application running on an encrypted tablet [28](Supp data Appendix 1). Participants then took part in a semi-structured interview to explore if the VASQoL questions were clear, understandable and relevant. Interviews were audio recorded and transcribed verbatim (Supp data appendix 2).

Interview Analysis

Interview data were analysed using Framework Analysis [29]. All transcripts were checked for errors and during the familiarization process the transcripts were read and re–read, notes and comments added, and important or relevant statements highlighted. The interesting and meaningful passages were then labelled by question and domain. These codes were then transferred into an analytical framework, giving each domain descriptors. Following this, we allocated the labels to one of the initial 7 domains that were derived from the detailed qualitative interviews analysed through a capabilities approach[1].

In a final step these six themes and their subcategories were reduced to three domains after factor analysis: physical, VA function and capabilities. Quotes for each subcategory were recorded. The option to suggest additional items and questions was presented to ensure important aspects were not missed.

Phase 2

Content validity was further assessed through review by a focus group of eight clinical professionals closely involved with delivery of VA and conducted by an experienced professional, non-clinical qualitative researcher (SG). Informed consent from the participants was obtained prior to the focus group. Two authors (KS and SR) analysed the interview transcripts using framework analysis and had further triangulation discussion with a third researcher (SG), who had performed the original derivation interviews from which the VASQOL questions were developed, regarding the domain descriptors and allocation of quotations.

Phase 3

The content-validated VASQoL measure was assessed in a longitudinal format in comparison with established health technology assessment quality of life measures (SF-36 and EQ-5D) over a six-week period (VASQoL and EQ-5D measures on weeks 1, 2, 4, and 6; SF-36 in weeks 1 and 6). The SF 36 was only completed in the first and the last week of this period as the recall period for use of the SF36 is the preceding 4 weeks. A quota sampling technique was again employed. To detect significant differences in the temporal changes of quality of life in relation to vascular access events, we estimated a priori that at least 30% of the cohort would experience an access related event. Previous work utilising the VAQ measure identified a 25% event rate for radiological procedures alone in the preceding year [30]. The sample size required for factor analysis in Phase 3 was determined by calculating a subject to item ratio of the VASQoL questionnaire (11 items) of 9:1[31].

Responsiveness

VASQoL and EQ-5D responsiveness in a known event cohort was assessed through this longitudinal format with prospectively recorded identification of objective vascular access events. Vascular Access Events were defined as: Elective – a planned creation or revision of a vascular access including admission or attendance for insertion of a TCVC/ AVF or AVG or a

routinely requested investigation of a VA (fistulogram) ; Urgent or Unexpected events included admissions for urgent (<24 hours notice) procedures (fistulogram / thrombectomy) or salvage / revision operations or infection complications. Cannulation complications included in this study were those severe enough to require clinician (nephrology or surgeon) review or intervention (temporary VA or switch in VA). Cannulation problems or bruising that was not referred by the dialysis nurses for review was not recorded as a vascular access event in this study. We chose to define as elective and emergency/ unexpected for analysis as qualitative interview data highlighted the disruptive nature of vascular access events as a significant factor in patients' quality of life.

Data

Anonymised data were abstracted to an SPSS database and linked to baseline characteristics (age, sex, Scottish Index of Multiple Deprivation (SIMD), diabetes mellitus, underlying kidney disease, time on kidney replacement therapy, time on haemodialysis and number of previous kidney transplants). Vascular access specific data included type (AVF/AVG/TCVC); localisation and side, and number of previous VA creations and revisions.

Statistical analysis

Statistical analyses were conducted using SPSS statistics v27 (IBM, USA). The cohort was initially analysed by population demographics to ensure representative quota sampling. Descriptive characteristics for each questionnaire item are reported as median +/- interquartile range (IQR) and as frequencies by questionnaire item.

The distribution of responses for each item for the three questionnaires (VASQoL, EQ5D and SF36) were not normally distributed, therefore non-parametric analysis was undertaken. Paired data were analysed using the Wilcoxon signed rank test. Longitudinal data was compared using analysis of variance of repeated measures using the Friedman test. Data were screened for univariate outliers prior to factor analysis. The minimum amount of data for factor analysis was satisfied with a final sample size of 101. The factorability of the 11 VASQOL items were examined using correlation, Kaiser-Meyer-Olkin measure of sampling adequacy and Bartlett's test of sphericity.

Internal consistency of the VASQoL measure and its factors was investigated with Cronbach's alpha values. Test-retest reliability was assessed using the intraclass correlation coefficient (ICC) in non-event (stable) participants who repeated the measure between week 1 and week 2.

Results

Phase 1 Qualitative data

26 patients were recruited to phase 1 (Supp data Table 1). Cognitive interviews were conducted after completion of the VASQOL, EQ-5D and SF-36 questionnaires. 23 patients completed the interviews. Analysis of these transcripts indicated that patients found the items, clear, relevant and important and did not have difficulty with the response options. In those cases, where we were unsure about the correct wording, we asked the patients to suggest alternatives to replace a specific word or sentence. Participants described the term 'worried' rather than 'concerned' in the pilot questionnaire and this was replaced. No new items were identified in the cognitive interviews. Illustrative quotes by domain and question were analysed (Supp Table 2).

Physical Domain

Questions 1 to 3 relate to the physical domain of the measure, dealing with how a vascular access looks, how it feels during dialysis and whilst not on dialysis respectively. Appearance was described in terms of three different aspects: Firstly, a cosmetic aspect, which was more commonly mentioned by women; secondly whether it looked healthy or unhealthy; and thirdly a wider aspect of stigma 'draws attention to being a kidney patient" (Patient 1).

The questions relating to how an access felt during dialysis and day to day confirmed the need for this distinction and was understood and relevant for different access types

"Some days on dialysis are uncomfortable because of needling problems" (Patient 1) another said "if it's not on my dialysis days … it's not a problem (pain)" (Patient 21). Furthermore, the use of the word 'feels' was confirmed by patients as appropriate and they gave descriptions such as pain, aches, discomfort, itching and irritation from patients with all access types (Supp data Table 2). Almost all patients stated the importance of a working/ functioning access over a good appearance during interviews but also described appearance impacting across social activities and relationships.

Vascular Access Function Domain

The VA function domain assessed two sub-domains: loss of function (thrombosis) and problems or infection, assessed by question 4 and 5 respectively. Most of the patients stated the importance of a working/ functioning access and indicated that concerns about their vascular access accompany them day to day, independent of the current condition of the vascular access: “Being concerned is always on the back of my mind” (Patient 4). This concern became foregrounded during vascular access events. These worries were even more relevant in patients who already experienced one or more failed vascular accesses: “I have run out of places, so it is important for me, that it keeps working” (Patient7). Beyond these thoughts were concerns about missing treatment strategies and alternative vascular access options in case of another access problem: “I am only concerned if it gets to the point where they can’t do anything about it” (Patient 9). Stable vascular access which was viewed as non-problematic was described as less concerning by patients: “Because I have had it so long, I don´t have any concerns of it stop working” (Patient 15). On the other hand, worry was present for those who had or were experiencing problematic access: “No problems day to day but I depend on my access...I am concerned when they have a problem on dialysis” (Patient 22).

Capabilities Domain

The capabilities domain included the subdomains enjoyment, relationships, hobbies, tasks or work. Question 6 asked if their VA interfered with enjoyment. A frequent statement was that it was not the vascular access itself that limited them, but the time-consuming aspect, and side-effects of dialysis, which led to reduced positive activities. However, participants were able to separate out the aspects of their life that were impacted by their vascular access and those related to kidney failure in general.

“The days I am not on dialysis I am not going out...I am really just sitting at home…I wouldn´t say, it’s the line, it´s just my mobility and general feeling tired...If I had been a lot fitter, my fistula wouldn´t have very much limited me in doing things” (Patient 5).

The impact of VA on relationships varied significantly. The relationships subdomain was most frequently interpreted as relationships with friends and wider family and VA impact responses varied from not impacting at all “People that I value don’t see my fistula. They don’t care that I have got it” (Patient 10) to significant impact “It affects your relationship, if you are self –

conscious of your body image" (Patient 2). However, more intimate relationships also were discussed as being affected, If I lie close to my wife, she feels the pulse and can hear it; she freaks out (Patients 6) or "my husband is terrified to give me a hug because of the line" (Patient 12).

Question 10 about interference with social activities led to a wide range of answers ranging from little interference "When I am at home, I am still able to read and watch TV; it hasn't stop enjoying my days at home in between" (Patient 11) to significant interference "Its everyday silly things, how to lie, when you are sleeping, lifting the grandchildren" (Patient 7) or "It has interfered with things I enjoy, because I used to love cooking "(Patient 10)

Furthermore, this question also stimulated patients to disclose the disruptive nature of loss of VA function on wider aspects of their lives "Usually my graft never interferes with what I try to do… but in the last week it has been because it clotted" (Patient 9). Participants described activities that were important to them demonstrating that the question was understood to apply to their preferences of activity in their context suggesting that the questions captured the specific impact for that individual. Similarly, in question 11 about work, tasks or studying specific actions were discussed suggesting that the questions prompted thoughts that were relevant to the patients' situation. "I can´t hold a pen any length of time and my hands cramp and I get in pain" (Patient 10) "For some professions... it has significance...but not now I'm retired (Patient 4) and "I can still do work in the house and I can lift bags... It doesn't affect me doing tasks really" (Patient 20)

Shared Decision-making

When asked about whether they felt involved in decisions about the care of their access (Q9) participants related this to responsibility for the vascular access and involvement in decisions on treatment and care by health professionals. Often this involved practical examination and interventions. "It is important to have the option of being interested and that you are told [physically], what is going to happen" (Patient 5). This was often related to how this was discussed, cannulated and assessed by nursing staff in the dialysis unit "basically decisions with the nurses, checking it and things like that "(Patient 20) but also covered decisions about access modalities "I have the final say to whether I am getting a graft or a fistula or a line... I am always included" (Patient 17).

Phase 2 Focus Group

A multidisciplinary focus group, detailed in Table 1 subsequently undertook a semi-structured discussion led by an experienced qualitative researcher (SG) (Supp data Table 3). The focus group identified similar themes in the physical domain questions 1 to 3 only additonally mentioning concerns about 'at risk' fistulas or grafts. Professionals focused more on quality of VA function and quality of dialysis over the long term, compared to patients who were more likely to describe their vascular access as 'problematic'. The professional focus group felt that the questions regarding enjoyment and interference with hobbies or social activities were similar but allowed patients to answer for their specific situation.

Interestingly, in item 9 ('In the last week I feel I have been included in decisions about the care of my line / fistula / graft') the VA professionals focused on whether the 'decisions' related to VA were 'micro decisions' (day-to-day cannulations) or 'macro decisions' (modality choice - Line AVF AVG). In comparison, patients, acknowledging the need for decisions, more often commented on feelings of inclusion, autonomy and discussion about decisions. Professionals discussed different 'tasks' and suggested more specificity for question 11, but felt that it conveyed the necessity of general life for most patients. No new items were generated from the focus group discussions therefore no further groups were convened.

Phase 3. Quantitative Validation

101 patients were recruited to complete the VASQOL, EQ5D and SF36 questionnaires in a hospital-based setting over a 6 week period (Table 2). All item scores in the VASQoL measure, EQ5D 5L and SF36 summary components failed a Shapiro-Wilk test of normality, and thus results are presented as median and interquartile range (IQR). The ceiling effect in each questionnaire data set was significant ranging from 24-54.5% in EQ5D items and 26-50% in VASQoL items. The SF36 raw scores for 8 scales were transformed and are reported using the sub scales [32, 33] : Physical Functioning, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional and Mental Health Role (Table 3).

Factor analysis

Factorability of the 11 VASQoL items was examined. Firstly, it was observed that 11 of the 11 items correlated at least 0.3 with at least one other item, suggesting reasonable factorability. Secondly, the Kaiser-Meyer-Olkin measure of sampling adequacy was 0.804, above the

recommended value of 0.6, and Bartlett's test of sphericity was significant (χ^2 = 522.649, p < .000). Finally, the communalities were all above 0.3, confirming that each item shared some common variance with other items. Given these overall indicators, factor analysis was deemed to be suitable with all 11 items.

Principal components analysis was used because the primary purpose was to identify the factors underlying the VASQoL measure. Initial eigenvalues indicated that the first three factors explained 44.5%, 12.9 %, and 9.1% of the variance respectively. Solutions for three factors were examined using varimax rotation of the factor loading matrix. The three factor solution, which explained 66.5% of the variance, was preferred because of its previous theoretical support and the levelling off of eigenvalues on the scree plot after three factors. A varimax rotation provided the best defined factor structure. All items in this analysis had primary loadings over 0.5 and no items had a cross loading of >0.4 (Supp Table 4). The items which loaded onto the three factors could be theoretically justified and were described as Physical, VA function and Capability factors. The factor labels proposed by the theoretical basis suited the extracted factors and were retained.

Reliability

Internal reliability for the 11 item VASQoL measure was investigated by Cronbach's alpha values. Cronbach's alpha was 0.858 which indicates a high level of internal consistency. No substantial increases in alpha would have been achieved by elimination of items (questions). Internal consistency for each of the factor identified was further examined using Cronbach's alpha. The Cronbach's alpha coefficients for the 3 factors were good: 0.707 for the Physical Factor (4 items), 0.719 for the Function Factor (3 items), and 0.867 for the Capability Factor (4 items). Test-retest reliability of the overall VASQoL measure using intra class correlation coefficient one week apart (excluding participants with reported vascular access events) using a two-way mixed effects absolute agreement model was 0.916 (95% CI 0.87-0.946) indicating excellent stability.

Responsiveness analysis

VA-related events were prospectively recorded at the time of questionnaire completion. There were 36 vascular access events in 32 patients, during the 6 week study period (Supp Table 2). 26 of these events were unexpected events, whilst 10 were elective vascular access

events. Paired analysis of data collected at, or within 1 week of an event, was compared. For the SF36 questionnaire analysis was performed using events within 1 month of completion. Significant differences were observed in the VASQoL physical domain questions ('looks' and 'how it feels') and VA function domain questions and by the EQ5D measure in the 'usual activities', 'pain' and 'anxiety' domains in the vascular access event cohort. (Table 4)

When analysed by events coded as 'emergency or unexpected' additional differences were observed across the capability domains. These included interference with work, study or tasks, interference with hobbies or social activities, vascular access limiting enjoyment, as well as the VA function and physical domains. (Table 5)

VASQoL and EQ5D data from those participants who had complete data and were stable during the study period were also compared using non-parametric analysis of variance. In this non-event cohort, variation in the VASQoL measure over a 6 week period was observed only in questions relating to 'worry about VA function' and 'capability' domains. No variation was observed in the EQ5D measure in any domain (Table 6). Whilst the EQ5D measure is sufficiently sensitive to detect changes in health status and major functional deterioration during emergency or urgent events (Table 5), the VASQoL measure was more sensitive to interference in hobbies and social activities , tasks or work that patients undertake. The VASQoL measure also captured changes in the anxiety associated with vascular access function that was not identifed by anxiety domains in generic quality of life measures. (Table 6). No differences were observed in the paired SF36 summary scores in patients who experienced vascular access events. This may be due to the longer period of time (1 month) that the SF36 utilises and potentially reduces it sensitivity. However, by using objectively defined VA event measures in this prospective study we sought to limit this potential recall bias. (Table 6b supplementary data).

Discussion

The lack of validated patient reported outcome measures specific to vascular access is now well recognized, and limits not only current practice, but also future trials [23, 34, 35]. The list of pre-requisites for such measures is long and demanding: they must be based on appropriate theoretical models, have content validity, be validated in a longitudinal setting, be sensitive to clinical events relevant to objective vascular access end points and also be sensitive to the patient experience that may not be routinely reported to vascular access care providers. This disease-specific sensitivity is a known limitation of generic preference-based measures of quality of life such as EQ-5D and SF-36. Despite this lack of sensitivity they are routinely used for health economic analysis and because of the significant costs associated with vascular access creation and maintenance it is the main reason we chose these as initial comparators for the VASQoL measure to validate this for effective mapping of health economic data in the future.

We have shown that the VASQoL meets these demands, and is thus a valid instrument to measure vascular access specific quality of life in patients with kidney failure. Psychometric testing has confirmed the VASQoL measure to be robust, reliable, valid and responsive to clinically relevant changes.

Previous work in this field has sought to measure patient-reported views of access-related problems to understand the use of lines among kidney failure patients[15]. The revised Short Form – Vascular Access Questionnaire (SF-VAQ) focused on four areas: satisfaction with access modality; experience of physical symptoms, such as pain or bleeding; consideration of access and social functioning; and experience of dialysis complications [14]. Intravenous needle cannulation of fistula and grafts were considered as a 'major source of dissatisfaction,' leading Kosa to argue for the development of strategies to mitigate patient's fear and pain linked to cannulation [14, 36]. The SF- VAQ has also been used in cross-sectional cohort studies in Canada, America (n=77 patients) and the UK (n=749) of prevalent haemodialysis patients to correlate patient characteristics and VA modality differences with VAQ scores [30, 36, 37]. However, work to establish its use in frequency of measurement and responsiveness to change during prospectively recorded events has not been undertaken. The development of the HARQ instrument identified six domains during focus group discussion relating to physical function, emotional impact, physical symptoms, sleep, social role/function and healthcare

interactions[16]. Strikingly 'worry or anxiety' in relation to vascular access was mentioned twice as many times as all other domains and this was also a dominant theme in the qualitative analysis of the VASQoL derivation work and is reflected in the VASQoL measure which noted variation in questions 3 and 4, over a 6 week period even in the absence of an objective VA event[1].

This is the first study to demonstrate a vascular access specific quality of life measure that demonstrates responsiveness to change in QoL domains associated with vascular access events in a paired analysis. Furthermore, the VASQoL measure demonstrated variation in responses across the 6-week study period (not observed in 1-week test-retest reliability) in the absence of VA events in those questions which described worry about loss of VA function, interference with relationships, interference with hobbies / social activities, interference with work or tasks and involvement in decisions about care of their access. This is consistent with the wider qualitative literature which reports the significant effects of vascular access creation and maintenance, which included anxiety and worry about failure of VA, impingement on way of life, family tension and concern about cannulation and unfamiliar providers [34]. The VASQoL items are entirely consistent with the recent summary of patient reported impacts and PRO domains of importance highlighted by the recent KHI vascular access PROMS workgroup[17].

VA function has been identified as the most critically importance outcome in vascular access trials by the SONG collaboration. Six themes were identified based on comments from all stakeholder groups that reflected the reasons behind the ratings of importance of vascular access outcomes: necessity for HD (function), applicability across the vascular access types, frequency and severity of debilitation, minimizing hospitalisation, optimising technical competence (use or care of VA) and direct impacts on appearance and lifestyle[35]. These themes are reflected in the items developed within the VASQoL measure.

The VASQoL measure was derived from the patient perspective and patient rankings at focus groups (rather than professional ranking of themes) were given primacy in its development[1]. Such nuanced findings with corroboration from cognitive interviews in this validation study is reassuring that it measures aspects of quality of life important to kidney patients that are not solely identified by objective vascular access events such as loss of patency. Importantly the VASQoL is not simply an amalgamated overall score with variations detected between

patients, rather it should be seen as descriptive pattern of the influence of VA use and events on the different domains of QoL.

This study recruited patients from the West of Scotland with an age, primary kidney disease, vascular access history and mix of vascular access modalities that is representative of the UK population due to an intentional quota sampling technique, however black and minority ethnic groups although included, were less well represented and further validation work is required to understand if the VASQoL measure is sensitive in other populations. Additional translations are planned to allow validation studies in Europe to proceed. The presence of a ceiling effect in the VASQoL, EQ5D and in some domains of the SF36 is significant, although this may reflect the cohort studied as it is recognised that haemodialysis patients are a population who undergo a heavy treatment burden in establishing or maintaining vascular access. The ceiling effects observed are a potential limitation of a measure, as the presence of such an effect may limit its discriminatory value. Despite this, the VASQoL measure was associated with changes in keeping with what would be expected with a known group and was also sensitive to change over time. Further refinement of the VASQoL measure with anchored Likert scaling is underway to optimise the utility and analysability of VASQoL as is comparative work with the KD-HRQOL measure within the Anaesthesia Choice for Creation of Arteriovenous Fistulae Study (NIHR-HTA 130567).

The burden of completion of patient reported outcome measures has also been highlighted as a potential barrier to their use.[17] The 11 point VASQoL measure has also been assessed in parallel work for its usability with excellent patient feedback but highlighting the need for ongoing work to improve accessibility particularly for those with limited vision.[38]
The validation of the VASQoL measure reported in this paper now offers the opportunity to assess patient reported outcomes alongside traditional VA trial endpoints in the knowledge that it reflects outcomes that are of importance to both patients and professionals [39].

Phase 1	**Phase 2**	**Phase 3**
Questionnaire Pilot and Cognitive interviews January 2020- May 2020	Focus Group with VA Professionals June 2020	Longitudinal Study (Responsiveness) June 2020 - November 2020
34 approached • 6 declined • 2 visual impairment	10 approached	135 approached
26 recruited	8 recruited	101 recruited
23 completed VASQoL, EQ-5D and SF36 Semi-structured interview • 1 withdrew • 2 unable to interview due to Sars-Cov 2 restrictions	2 Nephrologists 1 Vascular access surgeon 1 Interventional radiologist, 2 Vascular access nurse specialist 1 Haemodialysis nurse	Questionnaires completed VASQoL + EQ-5D weeks 1,2,4 and 6 SF-36 weeks 1 and 6 Vascular Access events recorded prospectively

Table 1. Validation Study Phases

Table 2. Demographics of the Longitudinal Study Cohort

AVF- arteriovenous fistula, AVG -arteriovenous graft, TCVC -Tunnelled central venous catheter, SIMD -Scottish Index of Multiple Deprivation, VA- vascular access, HD Haemodialysis, RRT – renal replacement therapy, PD- Peritoneal Dialysis, Tx- Transplant

	Total (n = 101)	AVF (n = 57)	AVG (n = 16)	TCVC (n = 28)
Age (mean ± SD)	58.7 (±14.1)	59.1 (±14.3)	59.5 (±16.1)	57.3 (±19.5)
SIMD, n (%)				
1 (most deprived)	39 (38.6)	18(31.5)	6 (37.5)	15 (53.5)
2	20 (19.8)	14(24.5)	-	6 (21.4)
3	11 (10.9)	4 (5.7)	4 (25.0)	3 (10.7)
4	15 (14.9)	11(19.2)	1 (6.3)	3 (10.7)
5 (least deprived)	16 (15.8)	10(17.5)	5 (31.3)	1 (3.5)
Gender, n (%)				
Male	55 (54.5)	29(50.9)	12 (75)	14 (50)
Female	46 (45.5)	28(49.1)	4 (25	14 (50)
VA – Localization, n (%)				
Forearm	30 (29.7)	28(49.1)	2 (11.8)	-
Upper Arm	38 (37.6)	28(49.1)	10(62.5)	-
Thigh	5 (5.0)	1 (1.7)	4 (23.5)	-
(TCVC)	28 (27.7)	-	-	28 (100)
Side of VA, n =73 (%)				
Left	56	39(68.4)	14(87.5)	
Right	20	18(31.6)	2 (12.5)	
TCVC	28	-	-	
Diabetes Mellitus, n (%)				
Type I	6 (5.9)	2 (3.5)	2 (12.5)	2 (7.2)
Type II	21 (20.8)	11(19.3)	4 (25)	6 (21.4)
No diabetes	74 (73.3)	44 (77.2)	10 (62.5)	20 (71.4)
Primary Kidney Disease, n (%)				
Diabetes	21 (20.8)	10 (17.5)	3 (18.8)	8 (28.5)
Multisystem	39 (38.6)	22 (38.6)	7 (43.8)	10 (35.7)
Chronic Pyeloneph.	10 (9.9)	9 (15.8)	1 (6.2)	0
Glomerulonephritis	21 (20.8)	11(19.3)	5 (31.3)	5 (17.9)
Unknown	10 (9.9)	5 (8.8)	-	5 (17.9)
VA Creations, n (%)				
0	6 (5.9)	1 (1.8)	-	5 (17.9)
1	53 (52.5)	36 (63.1)	4 (25)	13 (46.4)
2	28 (27.7)	18 (31.6)	5 (31.3)	5 (17.9)
>3	14 (13.8)	2 (3.5)	7 (43.7)	5 (17.8)

VA Revisions, n (%)				
0	70 (69.3)	40 (70.1)	10 (62.5)	20 (71.4)
1	22 (21.8)	15 (26.3)	1 (6.2)	6 (21.4)
2	6 (5.9)	1 (1.8)	3 (18.8)	2 (7.1)
>3	3 (2.9)	1 (1.8)	2 (12.5)	2 (7.1)
Time on VA (days) median (IQR)	300 (56 –823)	414 (81.5-1111)	403 (35 – 898)	224 (16-529)
Time on HD (days) median (IQR)	607 (157 – 1460)	583 (174 – 1699)	949 (293 –1574)	461 (60 – 933)
Time on RRT (days) median (IQR)	737 (277 – 2140)	693 (300 – 2947)	949 (293 –1574)	657 (270 -1628)
Time on PD (months) mean (± SD)	2.9 (± 8.0)	2.1 (± 7.3)	3.4 (± 9.5)	4.4 (±8.6)
Time on HD, n (%)				
< 1 year	35 (34.7)	19 (33.3)	5 (31.3)	11 (39.3)
> 1 year	66 (65.3)	38 (66.7)	11 (68.7)	17 (60.7)
Number of Kidney Tx, n (%)				
0	78 (77.2)	43 (75.4)	13 (81.3)	22 (78.6)
1	17 (16.8)	11 (19.3)	3 (18.8)	3 (10.7)
>2	6 (5.9)	3 (5.3)	-	3 (10.7)

Table 3. Longitudinal Analysis: Descriptive Results By Measure and Week

	Week 1 (n=101)		**Week 2** (n=88)		**Week 4** (n=91)		**Week 6** (n=91)	
	Median	CE %	Median	CE %	Median	CE %	Median	CE %
VASQoL								
Q1 'looks'	9 (7-10)	43	9 (7-10)	38	9 (8-10)	34.7	9 (7-10)	38.6
Q2 'feels during dialysis'	10 (8-10)	39.6	9 8-10)	37.5	9 (8-10)	42.6	9 (8-10)	40.6
Q3 'feels day to day'	9 (8-10)	44.6	9 8-10)	40.6	9 (7.2-10)	41.6	9 (7-10)	38.6
Q4 'access stopping working'	9 (5-10)	48.5	9 (6-10)	41.6	9 (6-10)	35.6	8 (5-10)	33
Q5 'access problem or infection'	9 (6-10)	49.5	9 (7-10)	45.5	10 (8-10)	49.5	10 (6-10)	48.5
Q6 'access limits enjoyment'	9 (6-10)	47.5	8 (5-10)	34.7	8.5 5-10)	34.7	8 (5-10)	31.7
Q7 'access has got in the way of good relationships'	10 (8-10)	63.4	10 (5.8-10)	47.5	9.5 (7-10)	45.5	10 (6-10)	46.5
Q8 'satisfaction with life in general'	7 (5-10)	25.7	8 (4-9)	17.8	7 (6-9)	17.8	8 (5-9)	14.9
Q9 'included in decisions about care of access	8 (3-10)	34.7	8 (5-10)	24.8	8 (6-10)	29.7	8 (5-10)	35.2
Q10 'Interference with hobbies / social activities'	9 (7-10)	48.5	9 (5-10)	33.7	9 (5-10)	36.6	9 (4-10)	35.6
Q11 'Interference in tasks/work/study'	10 (7-10)	50.5	9 (5-10)	35.6	9 (6-10)	33.7	9 (5-10)	35.6
VASQOL:Total Overall	87.5 (75-101)	9	90 (73-101)	5.9	91 (73-103)	6.6	88 (70-102)	4.4
EQ5D								
'walking'	4 (2-4)	23.8	3 (3-4)	16.8	4 (3-5)	23.8	3 (2-4)	16.8
'washing'	5 (3-5)	50.5	5 (4-5)	45.5	5 (4-5)	49.5	4 (3-5)	43.6
'usual activities'	3 (3-4)	19.8	4 (3-5)	23.8	4 (3-5)	29.7	3 (3-4)	15.8
'pain'	4 (3-4)	22.8	4 (3-5)	22.8	4 (3-5)	26.7	4 (3-4)	13.9
'anxiety/depression'	5 (3-5)	54.5	4 (3-5)	40.6	4 (3-5)	43.6	5 (3.75)	45.5
EQ5D Health status	59 (45-75)	1	56 (43-76)	1	60 (50-76)	2.2	54 (44-75)	1.1
SF 36								
Physical Function	30 (15-65)	1	-	-	-	-	30 (15-55)	3
Physical Role	25 (0-75)	20.8	-	-	-	-	0 0-50)	10.9
Bodily Pain	41 (31-62)	13.9	-	-	-	-	41 (32-62)	5.9
General Health	32 (20-47)	1	-	-	-	-	32 (20-52)	1.1
Vitality	35 (20-50)	1	-	-	-	-	35 (20-45)	1.1
Social Functioning	50 (25-75)	7.9	-	-	-	-	50 (25-75)	13.2
Emotional Role	33 (0-100)	38.6	-	-	-	-	33 (0-100)	42.9
Mental Health	64 (50-84)	5.9	-	-	-	-	64 (52-84)	5.5

Key: VASQoL + EQ5D - raw scores. SF 36 - transformed across 8 sub-domains; median (interquartile range) + percentage ceiling.

Table 4. Paired analysis (stable state vs. all vascular access events) using VASQoL and EQ5D

	No Event (Stable)	**Vascular Access Event**	**z**	**p-value**
VASQoL (n=36)				
Q1 'looks'	9 (7.25–10)	8 (3.5-10)	-2.203	0.028*
Q2 'feels during HD'	9 (8–10)	8 (5-10)	-1.702	0.89
Q3 'feels day to day'	9 (7-10)	8 (4-10)	-2.461	0.014*
Q4 'worried will stop working'	9.5 (6.2-10)	8 (3-10)	-2.355	0.019*
Q5 'problem or infection'	9.5 (7-10)	8 (3-10)	-2.390	0.017*
Q6 'access limited enjoyment'	9 (6-10)	7.5 (2.5-10)	-1.632	0.103
Q7 'interference with relationships'	10 (7.2-10)	10 (7-10)	-.285	0.776
Q8 'life in general'	8 (5-9)	6 (4-8.8)	-1.498	0.134
Q9 'decisions about care of access'	8 (5-9.8)	9 (7.2-10)	-1.714	0.087
Q10 'interfer. with hobbies/social activities'	9 (5.2-10)	8 (4.5-10)	-1.511	0.131
Q11 'interference with work/study/tasks'	9 (6.5-10)	9 (3.2 –10)	-1.419	0.156
EQ5D (n=35)				
Q1'walking'	3 (3-5)	3 (2-5)	-0.188	0.851
Q2 'washing'	5 (3-5)	4 (3-5)	-1.284	0.199
Q3 'usual activities'	4 (3-5)	3 (2-3)	-3.225	0.001*
Q4 'pain'	4 (3-5)	3 (3-4)	-2.171	0.03*
Q5 'anxiety/depression'	5 (4-5)	4 (3-5)	-2.231	0.026*

Key: N=36 in paired analysis, median + inter-quartivle ranges, Non-parametric analysis using Wilcoxon Signed Rank test.

Table 5. VASQOL And EQ5D item Scores: stable state vs. emergency vascular access event paired non-parametric analysis

	No Event (Stable)	**Vascular Access Event**	**z**	**p-value**
VASQoL (n=26)				
Q1 'looks'	10 (7.75-10)	8 (1.75-10)	-2.05	0.04*
Q2 'feels during HD'	10 (8 – 10)	7 (4-10)	-2.00	0.045*
Q3 'feels day to day'	9.5 (7-10)	7.5 (2.75-10)	-2.623	0.009*
Q4 'worried will stop working'	9 (5-10)	5 (3-10)	-2.540	0.011*
Q5 'problem or infection'	10 (7-10)	4.5 (2-10)	-2.907	0.04*
Q6 'access limited enjoyment'	9.5 (5.75-10)	5.5 (2-10)	-2.232	0.026*
Q7 'interference with relationships'	10 (7.75-10)	9.5 (2-10)	-.947	0.344
Q8 'life in general'	7.5 (5-9.25)	9.5 (6.75-10)	-1.031	0.303
Q9 'decisions about care of access'	8 (5- 10)	6 (3.75 – 9.25)	-1.354	0.176
Q10 'interfer. with hobbies/social activities'	9.5 (5-10)	7.5 (2.75- 10)	-2.116	0.034*
Q11 'interference with work/study/tasks'	9 (5.75-10)	6 (2.75 – 10)	-2.181	0.029*
EQ5D (n=25)				
Q1 'walking'	3 (3-5)	3 (2-4.25)	-0.663	0.507
Q2 'washing'	4.5 (3-5)	4 (3-5)	-1.140	0.254
Q3 'usual activities'	4 (3-4.25)	3 (2-3)	-2.869	0.004*
Q4 'pain'	4 (3-5)	3 (3-3.25)	-2.095	0.036*
Q5 'anxiety/depression'	5 (4-5)	4 (2.75-5)	-2.543	0.011*
EQ5D Health Score	60.5 (40.5-84.25)	51.5 (40.5 – 75)	-1.279	0.201

Table 6. VASQoL and EQ-5D measured by week in the stable cohort.

	Week 1	**Week 2**	**Week 4**	**Week 6**	Chi-Sq	p value
VASQoL						
Q1'looks'	9 (7.5-10)	9 (6.5-10)	9 (7-10)	9 (6.5-10)	3.032	0.387
Q2 'feels during HD'	10 (8-10)	9 (8-10)	9 (8-10)	9 (8-10)	3.241	0.356
Q3 'feels day to day'	9 (8-10)	9 (8-10)	9 (7.5-10)	9 (7.5)	6.269	0.099
Q4 'worried will stop working'	9 (7-10)	9 (6-10)	9 (6-10)	8 (4-10)	14.715	0.002*
Q5 'Problem/infection'	9 (7-10)	10 (7-10)	10 (8-10)	10 (7-10)	0.657	0.883
Q6 'access limited enjoyment'	9 (6-10)	8 (5.5-10)	8 (4-10)	8 (5-10)	10.356	0.016*
Q7 'interfer. with relationships'	10 (8-10)	10 (6-10)	9 (6-10)	9 (6-10)	11.807	0.008*
Q8 'life in general'	8 (5-10)	8 (4-9)	7 (5.5- 9)	8 (5-9)	1.102	0.777
Q9 'decisions about care of access'	6 (2-10)	8 (5-10)	9 (7-10)	8 (5-10)	10.054	0.018*
Q10 'interfer. with hobbies or social activities'	9 (6.5-10)	9 (4-10)	8 (5-10)	8 (4-10)	10.399	0.015*
Q11 'interfer. with work, study, tasks'	9 (7-10)	9 (5-10)	9 (5-10)	8 (5-10)	9.199	0.027*
EQ-5D						
Q1 'walking'	4 (2.25-5)	3 (3-4)	3.5 (3-4.75)	3 (3-4)	3.44	0.329
Q2 'washing'	5 (4-5)	5 (4-5)	5 (4-5)	4.5 (3-5)	2.136	0.545
Q3 'Usual activities'	4 (3-4)	3 (3-5)	4 (3-5)	4 (3-4)	6.390	0.094
Q4 'Pain'	4 (3-4)	3.5 (3-5)	4 (3-5)	4 (3-4)	1.105	0.776
Q5 'Anxiety/depression'	5 (3-5)	4.5 (3-5)	4 (3-5)	5 (3.25-5)	0.797	0.850
EQ-5D Health Score	57 (45.5-75)	55 (40-75.5)	62.5 (50-75.75)	52.5 (52.5-70)	6.474	0.091

Non – Parametric ANOVA using Friedman Test (n=61 – completed all 4 weeks)

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