# SAP FLOW: Flow dysfunction of hemodialysis vascular access: a randomized controlled trial on the effectiveness of surveillance of arteriovenous fistulas and grafts: Statistical Analysis Plan

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| **Roles and Responsibilities** | Bianca Zomer, nephrologist and PhD candidate, author of SAP<br>Lloyd Brandts, statistician<br>Maarten Snoeijs, vascular surgeon and project leader FLOW study<br>Maastricht University Medical Centre |
| **Signatures** | Bianca Zomer<br>---<br>Lloyd Brandts<br>---<br>Maarten Snoeijs<br>--- |

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# 1. Introduction

## 1.1. Background and rationale

Vascular access surveillance by flow volume measurements with dilution techniques during dialysis sessions is the standard of care in the Netherlands. However, there is a large practice variation in surveillance frequency and the threshold to trigger referral for vascular access intervention. Combined with the limited evidence base supporting the use of access surveillance, this variation in protocols indicates the need for further studies to determine the most effective method for follow-up of the vascular access for hemodialysis.

## 1.2. Objectives

The FLOW project evaluates the follow-up of the vascular access for hemodialysis. In current clinical care, vascular access flow volume is periodically assessed to detect and treat asymptomatic stenosis. The FLOW project will determine whether it is safe to abandon this practice of active surveillance. Vascular access stenosis will then be treated only when clinical problems of flow dysfunction occur during hemodialysis.

## 2. Study Methods

### 2.1. Trial design

It is a double-blind, multicenter randomized controlled trial with a superiority framework and a 1:1 individual participant treatment allocation ratio over two study arms. In the intervention group, only symptomatic vascular access stenosis detected by clinical monitoring are treated, whereas in the comparison group asymptomatic stenosis detected by surveillance are treated as well (current standard of care in the Netherlands). Prevalent hemodialysis patients with a functional arteriovenous vascular access are eligible to participate in the trial. Patients will be followed up for a minimum of 2 years and a maximum of 3 years (follow up will end for all participants when the last included patient has reached a 2 year follow-up period) and will be censored when their mode of renal replacement therapy is changed to kidney transplantation, peritoneal dialysis, or conservative treatment.

### 2.2. Randomization

Patients will be randomized using a 1:1 individual participant treatment allocation ratio. The data management center will generate the treatment allocation sequence by a random number producing algorithm on a computer. Randomization will be stratified by treatment center and for vascular access type (graft vs fistula). The study coordinator will enroll participants and will be informed of treatment assignment through an online service provided by the data management center.

### 2.3. Sample size

Sample sizes were estimated for the number of interventions required for each patient-year of dialysis treatment (i.e. the primary outcome), which will be analysed using a general linear model with Poisson distribution and time as off-set variable. In the FLOW project, we aim to detect a difference in the intervention rate of 0.25 per year between study groups in a superiority analysis. This difference is associated with an economically relevant effect of saving approximately 1 million euros per year at a 75% de-implementation rate. The minimal clinically relevant difference in the intervention rate remains to be defined for this core outcome measure, but will likely be greater than 0.25 per year. In the Netherlands, the access-related intervention rate in hemodialysis patients with arteriovenous fistulas and grafts was 1.56 and 3.30 per year, respectively, in a retrospective observation cohort study in 10 dialysis units. As the distribution between fistulas and grafts is approximately 8:1, these figures amount to an average of 1.77 interventions per patient-year in the Netherlands. Since the study includes young hemodialysis patients waiting for kidney transplantation and old hemodialysis patients with limited life expectancy, 20% of participants are expected to leave the study per year before completing the follow-up period. A total follow-up time of 828 patient-years (414 patient-years in each treatment arm) achieves 80% power to detect a 0.25 decrease in the number of interventions per patient-year between the study groups using a two-sided, large-samples z-test of the Poisson event-rate difference at a significance level of 0.05. With a standard follow-up of 2 years and a drop-out rate of 20% per year, this would require a sample size of 518 patients. Implementing a variable follow-up time of a minimum of 2 years and a maximum of 3 years is expected to result in 162 additional patient-years. This corresponds to 101 patients with 2-years of follow-up and a drop-out rate of 20% per year, and therefore leads to a new sample size estimation of 417 patients. An interim analysis for safety requires a sample size of 144 patients (72 in each treatment arm) contributing 1 year of follow-up with an expected event rate of 0.5 events per patient-year to show non-inferiority with regards to access-related serious adverse events at a margin of 0.5 events per patient-year with a power of 90%.

## 2.4. Framework

Superiority framework. The intervention group will be compared to the control group. Analyses will be stratified for treatment center and for vascular access type (graft vs fistula). Every effort is made to establish eligibility of participants prior to randomization; no withdrawals due to ineligibility are allowed and the analyses include all participants enrolled. The primary analysis will be on the intention to treat population (i.e. no participants are withdrawn from analysis for lack of adherence to treatment allocation); exploratory on-treatment analyses will be performed. A comparison of included and excluded patients is done to provide insight into the external validity of the clinical trial. Every effort is made to avoid missing data, including assistance from dialysis nurses in obtaining patient-reported outcome measures during dialysis sessions. Primary outcome data are not expected to be missing, as interventions on vascular access will be reported in the patients' medical files. We expect no loss to follow-up in the study participants since they are observed three times per week in the dialysis unit. Patient-reported outcomes will be analysed using generalized estimating equations that allow for missing data. Other missing data will be handled by using 5 imputation cycles with regression methods. Outliers will not be removed from the analysis unless the data can clearly be shown to be erroneous.

## 2.5. Interim analyses and stopping guidance

### 2.5.1. Statistical interim analyses and stopping guidance

The study had a Data Safety Monitoring Board. The members of the DSMB are not involved with the trial in any other way and have no competing interests. The members of the DSMB and the study coordinator will meet annually. The task and responsibility of the DSMB is to do an interim safety analysis when the trial participants have contributed 72 access-related serious adverse events (which is expected at 144 patient-years of follow-up time).

### 2.5.2. Planned adjustments

This interim analysis is for safety only (i.e. vascular access thrombosis rate, access-related serious adverse event rate and mortality) and not for early stopping for efficacy.

### 2.5.3. Guidelines for stopping the trial early

The number of vascular access thrombosis and access-related serious adverse events per person-year will be analysed using general linear models with Poisson distribution, and mortality will be analysed using Cox regression. When 72 access-related serious adverse events have taken place, an interim safety analysis has sufficient power to show non-inferiority with regards to access-related serious adverse events at a margin of 0.5 events per patient-year with a power of 90%. When non-inferiority has not been reached, further analysis for superiority of either study group will be done. Statistically significant differences between study groups will be used as a guideline to issue recommendations by the DSMB. Reasons to disregard a statistically significant difference between study groups by the DSMB will be recorded. More weight will be given to access-related serious adverse events than to vascular access thrombosis. When the analysis shows neither non-inferiority nor superiority, additional interim safety analyses with more follow-up time may be done at the discretion of the DSMB.

## 2.6. Timing of final analysis

All results will be analyzed at the end of the study. Patients will be followed up for a minimum of 2 years and a maximum of 3 years (follow up will end for all participants when the last included patient has reached a 2 year follow-up period).

### 2.7. Timing of outcome assessments

Physical examination of the vascular access will be done at each dialysis session. Volume measurements by ultrasound dilution will be done every month. Duplex ultrasound examination of the vascular access will take place in case of flow dysfunction, and interventions for flow dysfunction are part of standard clinical care for hemodialysis patients. Subjects enrolled in the trial will be asked to fill out questionnaires (SF-VAQ, EQ-5D-5L, MCQ and PCQ) at baseline and every 3 months until 24 months of follow up.

# 3. Statistical Principles

## 3.1. General principles

Descriptive analyses will be reported using summary tables and figures. Continuous variables will be summarized with counts, means, standard deviations, medians, confidence intervals, minimums, and maximums were appropriate. Categorical variables will be reported by counts and percentages. Formal inferential statistical analyses techniques will be discussed in subsequent sections of this SAP. P-values <0.05 are considered statistically significant, unless otherwise stated in the SAP. 95% confidence intervals around estimates will be reported, unless otherwise stated in the SAP. Analyses and tabulations will be performed using R. All reported output will undergo a senior level statistical review to ensure valid methods were used, and that all data manipulations and calculations are correct and consistent with the SAP. Upon completion of the analysis, the analyses code will be collected and filed. Missing or invalid data will be treated as missing data (Section 5.3), unless otherwise stated.

## 3.2. Adherence and protocol deviations

### 3.2.1. Definition of adherence

When there is a clinical problem suggesting a vascular access stenosis or access flow is below 500mL/min (the latter only in the control group) there is an indication for intervention according the study protocol.
Non-adherence to the protocol may occur when patients are referred for correction of presumed vascular access stenosis based on parameters outside the study design (e.g. dynamic venous pressure).

### 3.2.2. Description of presenting adherence

In theory all interventions are done because of clinical problems or an access flow < 500mL/min in the control group. Only interventions done for other reasons or cases where an intervention was not performed when necessary will be mentioned in the discussion.

### 3.2.3. Definition of protocol deviations

Not all possible protocol deviations are described in advance of the study. We focus on the protocol violations with regard to the primary endpoint and actively monitor those during the study period. For example, an intervention should be done when there are signs of vascular access stenosis present. On the other hand, no interventions are needed when there is no clinical problem or when based on other parameters outside the study design.

### 3.2.4. Description of which protocol deviations will be summarized

All protocol deviations a listed during the follow up. The protocol deviations that possibly influenced the final outcome will be mentioned in the discussion.

# 4. Trial Population

## 4.1. Screening data

All hemodialysis patients will be screened. Hemodialysis patients at the study sites who are not included in the clinical trial are registered in a screening log to determine the generalizability of the study population.

## 4.2. Eligibility

The study population are patients with end-stage renal disease who are treated with hemodialysis using arteriovenous vascular access.

### 4.2.1. Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

1. Adult patients aged 18 years or older
2. End-stage renal disease with unlikely recovery of kidney function according to the attending nephrologist
3. Arteriovenous fistula of arteriovenous graft as hemodialysis vascular access that fulfils both of the following criteria at the time of trial enrolment:
   a. Maturation: access flow volume of at least 500mL/min; and
   b. Functional: the vascular access was cannulated with 2 needles and achieved the prescribed access circuit flow in at least 6 dialysis sessions over the past 30 days. Patients who have single needle hemodialysis for reasons other than vascular access dysfunction (e.g. for nocturnal hemodialysis) but who can be cannulated with 2 needles for flow measurements and fulfil the other requirements for a functional vascular access can be enrolled as well.
4. Planning to remain in one of the participating dialysis centers for at least 1 year

### 4.2.2. Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

1. Arteriovenous fistulas with multiple venous outflow paths upstream of the cannulation sites, that are not suitable for flow volume measurements using ultrasound dilution (e.g. Gracz fistulas and Ellipsys of WavelingQ endovascular fistulas)
2. Home hemodialysis
3. Thrombosis of the current vascular access in the past year
4. Planned access-related intervention
5. Living donor kidney transplantation, switch to peritoneal dialysis, or switch to home hemodiaysis planned within 6 months
6. Life expectancy of less than 6 months, in the opinion of the attending nephrologist
7. Unable to provide informed consent.

## 4.3. Recruitment

Recruitment information will be presented using a flow diagram according the CONSORT statement for interventional studies. The recruitment and informed consent procedures are described in the main protocol section 11.2. The flow diagram will contain information on numbers of patients included in the study and screen failures. Reasons for nonparticipation are provided for each stage.

## 4.4. Withdrawal/follow up

### 4.4.1. Level of withdrawal

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. The investigator can decide to withdraw a subject from the study for urgent medical reasons.

### 4.4.2. Timing of withdrawal

Patients who decided to leave the study or who have been withdrawn from the study for medical reasons will not be replaced. Data collected for the study will be used until the patient has withdrawn from the study. Patients who discontinue hemodialysis treatment after kidney transplantation, peritoneal dialysis, recovery of renal function, or refusal of further hemodialysis will be censored from the trial. Patients who decided to leave the study or who have been withdrawn from the study for medical reasons will receive standard medical care.

### 4.4.3. Reasons and details of presented data

We expect to have no lost-to-follow up, because all study participants are dialysis patients actively on dialysis. The amount of patients and their different reasons for withdrawal will be presented in a flow chart.

## 4.5. Interim Analysis population

All patients who were enrolled and randomized in the trial at the time of the interim analysis.

## 4.6. Final analysis population

All patients who were enrolled and randomized in the trial.

## 4.7. Baseline patient characteristics

Baseline characteristics will include age (years, continuous) , gender (men/women), dialysis details (vascular access (fistula/graft), sessions per week, duration of treatment in hours, baseline access flow in mL/min), medical and vascular access history, smoking history, use of anticoagulants.

## 4.8. Details of how baseline characteristics will be descriptively summarized

Baseline characteristics will be presented in a table by treatment arm after the initial randomization. Means and standard deviations (SDs) will be used to report continuous variables, and median and interquartile ranges (IQR) to report categorical values. (See tables and figures – Section 1)

# 5. Analysis

## 5.1. Outcome definitions

### 5.1.1. Primary outcome

The primary outcome will be defined as the number of interventions required for each patient-year of hemodialysis treatment (number of interventions per patient-year). This core outcome measure was defined in an international consensus workshop including patients, clinicians, researchers, policy makers and industry representatives, and includes all percutaneous access interventions (including central venous catheter placement, removal and guidewire exchange, angioplasty, stent placement, percutaneous thrombectomy) and surgical access procedures (including subsequent access placements if the current access failed, and surgical revisions to promote maturation or maintain long-term patency, including open thrombectomy). Interventions that are done under general anesthesia or that require hospital admission of more than one day are scored as major interventions, whereas interventions under local or locoregional anesthesia as day-case of office procedures are scored as minor interventions. These interventions correspond to grade 3A and 3B surgical complications in the Clavien-Dindo classification (30). Access-related complications that are resolved using conservative or pharmacological treatment are not considered as interventions.

### 5.1.2. Secondary outcomes

1. Access-related complications per patient-year

Separate analyses will be performed on access-related complications graded as Clavien-Dindo grade 2 or higher and on access-related complications graded as Clavien-Dindo grade 4 or 5. The outcome will be defined as the number of access-related complications per patient-year.

- Access-related complications of Clavien-Dindo grade 2 of higher will be registered (30). Grade 2 complications require pharmacological treatment including catheter thrombolysis, antibiotics and blood transfusions. Complications that require no pharmaceutical of interventional treatment (grade 1) are not considered relevant for this clinical trial.
- Access-related complication of Clavien-Dindo grade 4 or 5 (i.e. admission to intensive care unit or death) are considered serious adverse events. As an exception, postoperative intensive care unit admission for vasopressor therapy to prevent early vascular access thrombosis is not considered a serious adverse event or complication.

2. Vascular access thrombosis rate

Vascular access thromboses will be be defined as the absence of thrill and bruit, with confirmation of no flow by duplex ultrasound if deemed necessary by the treating physician at the study site. The outcome will be defined as the number of vascular access thrombosis events per person-year.

3. All-cause mortality

All-cause mortality will be defined as death by any cause during follow-up.

4. Access-related health care costs from randomization until the end of follow-up

Healthcare costs will be derived from hospital registration systems at the individual participant level. Costs to patients and families will be measured at the individual participants level using a study-specific adaptation of the Medical Consumption Questionnaire and Productivity Cost Questionnaire

developed by the institute for Medical Technology Assessment. Patients will be asked to report the data from their cost questionnaire every 3 months during the follow-up period.

5. Patient-reported outcome measures

For the patient-reported outcome measures the Short-form Vascular Access Questionnaire (SF-VAQ) and the Dutch version of the 5-level EuroQol 5-dimensional questionnaire (EQ-5D-5L) will be used.

- SF-VAQ measured at baseline and every 3 months during the follow-up period. The Short-Form Vascular Access Questionnaire (SF-VAQ) was developed to measure hemodialysis patients' satisfaction with their vascular access (31). The questionnaire contains 13 items (7-point Likert scale) in 4 domains (overall satisfaction, physical symptoms, social functioning and complications), and has a single summary score.
- EQ-5D-5L measured at baseline and every 3 months during the follow-up period. The EQ-5D-5L was developed to measure health-state utility values. The questionnaire contains self-classifiers at 5 levels in 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) (32). Utility values will be calculated from these health states using preferences elicited from the Dutch general population (36). Quality-adjusted life years will be calculated with these utility values using the area under the curve method.

6. Quality of the surveillance program

- Repeatability and reproducibility of vascular access flow volume measurements (mL/min) using ultrasound dilution in routine clinical practice.
- Diagnostic accuracy of vascular access flow volume measurements to predict clinical signs of flow dysfunction and access thrombosis within 1 month in the intervention group. Diagnostic accuracy will be reported as sensitivity, specificity, negative predictive value, and positive predictive value.
- The percentage of vascular access balloon angioplasties that have resulted in technical success (residual stenosis <30%) and clinical success (increase in flow volume to >500mL/min, restoration of vascular access function and resolution of any clinical signs of flow dysfunction).
- Vascular access primary, primary assisted, and secondary patency after balloon angioplasty (time to event).
- Adherence (in %) to the vascular access follow-up protocol and to the study protocol for referral to correct vascular access stenosis.

7. Other outcome measures will be registered for explanatory analyses and are defined according to the ESVS guidelines on vascular access (1):

- Primary patency of vascular access (intervention-free vascular access survival): the interval (in days) between randomization and the first intervention for vascular access dysfunction of thrombosis or its abandonment.
- Assisted primary patency of vascular access (thrombosis-free vascular access survival): the interval (in days) between randomization and the first occlusion or its abandonment.
- Secondary patency of vascular access: the interval (in days) between randomization and the day on which the vascular access is deemed to be permanently unusable (i.e. access abandonment).
- The number of hemodialysis sessions with cannulation difficulties (i.e. needing >1 attempt to place and secure two dialysis needles) and cannulation failure (i.e. the inability to place and secure two dialysis needles) per patient-year of hemodialysis treatment.
- Days in hospital per patient-year for any reason and for vascular access-related reasons.

## 5.2. Analysis methods

### 5.2.1. Primary outcome

The number of interventions required for each patient-year of haemodialysis treatment will be analysed using a general linear mixed effect model with Poisson distribution and identity link, and with time as off-set variable. The outcome will be expressed as a ratio (exponential of β1) of events (number of interventions) per 1 unit increase of exposure time between both groups. A random intercept for each individual participant will be estimated to account for dependence of observations. Expected counts will be plotted against observed counts to check whether the distribution of counts follow a Poisson distribution. Furthermore, the Pearson dispersion statistic will be assessed to check whether there is equidispersion of the variance compared to the mean. In case of overdispersion of the data, a quasi-Poisson model or negative binomial model will be performed. Sensitivity analyses will be done for the primary outcome with major interventions having twice the weight of minor interventions, and with exclusion of patients with access-related interventions with technical failure (residual stenosis >30%) and clinical failure (flow volume <500mL/min in the first week after intervention and/or failure to restore vascular access function and clinical signs of flow dysfunction).

Vascular access patency will be assessed using a Cox proportional hazards regression with a clustered standard error (SE) using a time-to-event framework to account for repeated events in which the same person experiences multiple events over time, some occurring while on the intervention arm, and others occurring while on the control arm. The outcome will be expressed as a Hazard Ratio (HR) including 95% confidence intervals and p-values. Before running the analyses, we will test the proportional hazards assumption by visual inspection of the log-log survival plots, and the Schoenfeld residuals test to statistically evaluate the assumption.

### 5.2.2. Secondary outcomes

Serious adverse events, access-related complications and vascular access thrombosis:

The number of access-related complications and access-related thromboses for each patient-year of haemodialysis treatment will be analysed using a general linear mixed effect model with Poisson distribution and identity link, and with time as off-set variable. The outcome will be expressed as a ratio (exponential of β1) of events (number of interventions) per 1 unit increase of exposure time between both groups. A random intercept for each individual participant will be estimated to account for dependence of observations. Expected counts will be plotted against observed counts to check whether the distribution of counts follow a Poisson distribution. Furthermore, the Pearson dispersion statistic will be assessed to check whether there is equidispersion of the variance compared to the mean. In case of overdispersion of the data, a quasi-Poisson model or negative binomial model will be performed. Sensitivity analyses will be done for the primary outcome with major interventions having twice the weight of minor interventions, and with exclusion of patients with access-related interventions with technical failure (residual stenosis >30%) and clinical failure (flow volume <500mL/min in the first week after intervention and/or failure to restore vascular access function and clinical signs of flow dysfunction).

## 5.3. Missing data

Primary outcome data are not expected to be missing, as interventions on vascular access will be reported in the patients' medical files. We expect no loss to follow-up in the study participants since they are observed three times per week in the dialysis unit. Patient-reported outcomes will be

analysed using generalized estimating equations that allow for missing data. Other missing data will be handled by using 5 imputation cycles with regression methods. Outliers will not be removed from the analysis unless the data can clearly be shown to be erroneous.

## 5.4. Additional analyses

Sensitivity analysis have already been described in section 5.2

### 5.4.1. Interim analysis

Interim analysis has already been described in section 2.5 and uses the same statistical techniques as described in section 5.2.2.

## 5.5. Harms

Safety endpoints are vascular access related (serious) adverse events (including vascular access thrombosis and abandonment). Statistical analysis of these endpoints have been described in section 5.2.2.

## 5.6. Statistical software

Statistical analysis will be done with the latest available version of R.

## 5.7. References

None

## 6. Tables and Figures

**Table 1A: Baseline characteristics - demographics**

| | All patients (N=…) | | Monitoring (N=…) | | Surveillance (N=…) | | P |
|---|---|---|---|---|---|---|---|
| Sex (male) | % | (N) | % | (N) | % | (N) | … |
| Age (years) | Mean ± SD | (N) | Mean ± SD | (N) | Mean ± SD | (N) | … |
| Body mass index (kg/m$^2$) | Mean ± SD | (N) | Mean ± SD | (N) | Mean ± SD | (N) | … |
| Race | | (N) | | (N) | | (N) | … |
| White | % | (N) | % | (N) | % | (N) | |
| Black | % | (N) | % | (N) | % | (N) | |
| Asian | % | (N) | % | (N) | % | (N) | |
| Other | % | (N) | % | (N) | % | (N) | |
| Cause of end-stage renal disease | | (N) | | (N) | | (N) | … |
| Diabetes | % | (N) | % | (N) | % | (N) | |
| Vascular/hypertension | % | (N) | % | (N) | % | (N) | |
| Glomerulonephritis | % | (N) | % | (N) | % | (N) | |
| Polycystic kidney disease | % | (N) | % | (N) | % | (N) | |
| Interstitial nephritis | % | (N) | % | (N) | % | (N) | |
| Congenital/hereditary | % | (N) | % | (N) | % | (N) | |
| Systemic disease | % | (N) | % | (N) | % | (N) | |
| Other | % | (N) | % | (N) | % | (N) | |
| Unknown | % | (N) | % | (N) | % | (N) | |
| Smoking history | | (N) | | (N) | | (N) | … |
| Current | % | (N) | % | (N) | % | (N) | |
| Stopped | % | (N) | % | (N) | % | (N) | |
| Never | % | (N) | % | (N) | % | (N) | |
| Use of antithrombotics | | (N) | | (N) | | (N) | … |
| No | % | (N) | % | (N) | % | (N) | |
| Antiplatelet therapy | % | (N) | % | (N) | % | (N) | |
| Anticoagulant therapy | % | (N) | % | (N) | % | (N) | |
| Fish oil supplements | % | (N) | % | (N) | % | (N) | … |
| Serum albumin (g/L) | Mean ± SD | (N) | Mean ± SD | (N) | Mean ± SD | (N) | … |
| Mobility | | (N) | | (N) | | (N) | … |
| Independent (with cane or walker if needed) | % | (N) | % | (N) | % | (N) | |
| With help of other person | % | (N) | % | (N) | % | (N) | |
| Wheelchair | % | (N) | % | (N) | % | (N) | |

Groups are based on initial randomization

Statistical analysis: Chi squared tests for categorical variables and Student t-test for continuous variables

**Table 1B: Baseline characteristics – comorbidities**

| | All patients (N=…) | | Monitoring (N=…) | | Surveillance (N=…) | | P |
|---|---|---|---|---|---|---|---|
| Hypertension | % | (N) | % | (N) | % | (N) | … |
| Diabetes mellitus | % | (N) | % | (N) | % | (N) | … |
| Ischemic cardiac disease | | (N) | | (N) | | (N) | … |
| No | % | (N) | % | (N) | % | (N) | |
| Yes, with myocardial infarction | % | (N) | % | (N) | % | (N) | |
| Yes, without myocardial infarction | % | (N) | % | (N) | % | (N) | |
| Heart failure | | (N) | | (N) | | (N) | … |
| No | % | (N) | % | (N) | | (N) | |
| NYHA 1 | % | (N) | % | (N) | % | (N) | |
| NYHA 2 | % | (N) | % | (N) | % | (N) | |
| NYHA 3 | % | (N) | % | (N) | % | (N) | |
| NYHA 4 | % | (N) | % | (N) | % | (N) | |
| Arrhythmia | % | (N) | % | (N) | % | (N) | … |
| Pacemaker | % | (N) | % | (N) | % | (N) | … |
| Cerebrovascular disease | % | (N) | % | (N) | % | (N) | … |
| Peripheral arterial disease | | (N) | | (N) | | (N) | … |
| No | % | (N) | % | (N) | % | (N) | |
| Rutherford stage 1-3 | % | (N) | % | (N) | % | (N) | |
| Rutherford stage 4-6 | % | (N) | % | (N) | % | (N) | |
| Chronic pulmonary disease | % | (N) | % | (N) | % | (N) | … |
| Active malignancy | | (N) | | (N) | | (N) | … |
| No | % | (N) | % | (N) | % | (N) | |
| Solid malignancy | % | (N) | % | (N) | % | (N) | |
| Hematologic malignancy | % | (N) | % | (N) | % | (N) | |
| Psychiatric disease | % | (N) | % | (N) | % | (N) | … |

Groups are based on initial randomization
Statistical analysis: Chi squared tests for categorical variables

**Table 1C: Baseline characteristics – dialysis history**

| | All patients (N=…) | | Monitoring (N=…) | | Surveillance (N=…) | | P |
|---|---|---|---|---|---|---|---|
| Time on renal replacement therapy (months) | Median ± IQR | (N) | Median ± IQR | (N) | Median ± IQR | (N) | … |
| Time on hemodialysis (months) | Median ± IQR | (N) | Median ± IQR | (N) | Median ± IQR | (N) | … |
| Dialysis treatments per week | Mean ± SD | (N) | Mean ± SD | (N) | Mean ± SD | (N) | … |
| Vascular access type | | (N) | | (N) | | (N) | … |
| Arteriovenous fistula | % | (N) | % | (N) | % | (N) | … |
| Radiocephalic fistula | % | (N) | % | (N) | % | (N) | |
| Brachiocephalic fistula | % | (N) | % | (N) | % | (N) | |
| Brachiobasilic fistula | % | (N) | % | (N) | % | (N) | |
| Other fistula configuration | % | (N) | % | (N) | % | (N) | |
| Baseline diameter outflow vein (mm) | Median ± IQR | (N) | Median ± IQR | (N) | Median ± IQR | (N) | … |
| Arteriovenous graft | % | (N) | % | (N) | % | (N) | … |
| Forearm loop graft | % | (N) | % | (N) | % | (N) | |
| Upper arm straight graft | % | (N) | % | (N) | % | (N) | |
| Upper arm loop graft | % | (N) | % | (N) | % | (N) | |
| Other graft configuration | % | (N) | % | (N) | % | (N) | |
| Age vascular access (months) | Median ± IQR | (N) | Median ± IQR | (N) | Median ± IQR | (N) | … |
| Vascular access side (left) | % | (N) | % | (N) | % | (N) | … |
| Previous vascular access | % | (N) | % | (N) | % | (N) | … |
| Previous vascular access interventions | % | (N) | % | (N) | % | (N) | … |
| Baseline access flow (mL/min) | Median ± IQR | (N) | Median ± IQR | (N) | Median ± IQR | (N) | … |

Groups are based on initial randomization
Statistical analysis: Chi squared tests for categorical variables, Student t-test for continuous variables with normal distribution, and Mann-Whitney U-test for continuous variables deviating from normal distribution

**Figure 1D: Access flow distribution in screened population**

Exclude home hemodialysis patients and patients with central venous catheters

**Table 1E: Comparison of enrolled patients with normal and high-flow vascular access**

| | Normal flow (<1500 mL/min) (N=…) | | High flow (>1500 mL/min) (N=…) | | P |
|---|---|---|---|---|---|
| Age (years) | Mean (SD) | N | Mean (SD) | N | … |
| Sex (male) | % | N | % | N | … |
| Hypertension | % | N | % | N | … |
| Diabetes mellitus | % | N | % | N | … |
| Ischemic cardiac disease | | N | | N | … |
| No | % | N | % | N | |
| Yes, with myocardial infarction | % | N | % | N | |
| Yes, without myocardial infarction | % | N | % | N | |
| Heart failure | | N | | N | … |
| No | % | N | % | N | |
| NYHA 1 | % | N | % | N | |
| NYHA 2 | % | N | % | N | |
| NYHA 3 | % | N | % | N | |
| NYHA 4 | % | N | % | N | |
| Cerebrovascular disease | % | N | % | N | … |
| Peripheral arterial disease | | N | | N | … |
| No | % | N | % | N | |
| Rutherford stage 1-3 | % | N | % | N | |
| Rutherford stage 4-6 | % | N | % | N | |
| Vascular access | | N | | N | … |
| Fistula | % | N | % | N | … |
| Radiocephalic | % | N | % | N | |
| Brachiocephalic | % | N | % | N | |
| Brachiobasilic | % | N | % | N | |
| Graft | % | N | % | N | |

**Table 2A: Trial screening and enrollment log**

| | Prevalent hemodialysis patients | |
|---|---|---|
| Total | N | % |
| Exclusion criteria | N | % |
| Home hemodialysis | N | % |
| Central venous catheter | N | % |
| Informed consent not possible | N | % |
| Planned kidney transplantation < 6 months | N | % |
| Life expectancy < 6 months | N | % |
| Transfer to another dialysis unit <6 months | N | % |
| Enrolled in another vascular access trial | N | % |
| Vascular access thrombosis in the past year | N | % |
| Vascular access flow <500 mL/min | N | % |
| Planned vascular access-related intervention | N | % |
| Vascular access not functional[a] | N | % |
| Multiple outflow veins in cannulation zone | N | % |
| Total study candidates | N | % |
| No informed consent | N | % |
| Unwilling to participate in trials | N | % |
| Feeling insecure with blind flow measurements | N | % |
| Total participants | N | % |

**Table 2B: Comparison of enrolled patients with unselected hemodialysis population - Baseline characteristics**

| | Unselected population (N=…) | | Enrolled patients (N=…) | | P |
|---|---|---|---|---|---|
| Sex (male) | % | N | % | N | … |
| Age (years) | Mean ± SD | N | Mean ± SD | N | … |
| Body mass index (kg/m$^2$) | Mean ± SD | N | Mean ± SD | N | … |
| Cause of end-stage renal disease | | N | | N | … |
| Diabetes | % | N | % | N | |
| Vascular/hypertension | % | N | % | N | |
| Glomerulonephritis | % | N | % | N | |
| Polycystic kidney disease | % | N | % | N | |
| Interstitial nephritis | % | N | % | N | |
| Congenital/hereditary | % | N | % | N | |
| Systemic disease | % | N | % | N | |
| Other | % | N | % | N | |
| Unknown | % | N | % | N | |
| Comorbidities | | | | | |
| Diabetes mellitus | % | N | % | N | … |
| Ischemic cardiac disease | % | N | % | N | … |
| Heart failure | % | N | % | N | … |
| Cerebrovascular disease | % | N | % | N | … |
| Peripheral arterial disease | % | N | % | N | … |
| Chronic pulmonary disease | % | N | % | N | … |
| Active malignancy | % | N | % | N | … |
| Psychiatric disease | % | N | % | N | … |
| Time on hemodialysis (months) | Median ± IQR | N | Median ± IQR | N | … |
| Vascular access type | | N | | N | … |
| Arteriovenous fistula | % | N | % | N | |
| Arteriovenous graft | % | N | % | N | |

Patients with home hemodialysis and central venous catheters are excluded.
Statistical analysis: Chi squared tests for categorical variables, Student t-test for continuous variables with normal distribution, and Mann-Whitney U-test for continuous variables deviating from normal distribution

**Table 2C: Comparison of enrolled patients with unselected hemodialysis population - Vascular-access related interventions and serious adverse events**

| | Unselected population (… patient-years) | Enrolled population (…patient-years) | Event rate ratio (95% CI) | P |
|---|---|---|---|---|
| **Interventions for flow dysfunction** | **N** | **N** | **… (…-…)** | **…** |
| Percutaneous interventions | N | N | … (…-…) | … |
| Balloon angioplasty without stent | N | N | … (…-…) | … |
| Balloon angioplasty with stent | N | N | … (…-…) | … |
| Percutaneous thrombectomy | N | N | … (…-…) | … |
| Surgical interventions | N | N | … (…-…) | … |
| Open thrombectomy | N | N | … (…-…) | … |
| Patch angioplasty | N | N | … (…-…) | … |
| Revision of anastomosis | N | N | … (…-…) | … |
| New arteriovenous fistula | N | N | … (…-…) | … |
| New arteriovenous graft | N | N | … (…-…) | … |
| Ligation of arteriovenous fistula | N | N | … (…-…) | … |
| Ligation of arteriovenous graft | N | N | … (…-…) | … |
| Central venous catheter interventions | N | N | … (…-…) | … |
| Catheter insertion | N | N | … (…-…) | … |
| Guidewire exchange | N | N | … (…-…) | … |
| Catheter removal | N | N | … (…-…) | … |
| Other vascular access interventions | N | N | … (…-…) | … |
| Repair (pseudo)aneurysm | N | N | … (…-…) | … |
| Ligation of accessory vein | N | N | … (…-…) | … |
| Embolisation of accessory vein | N | N | … (…-…) | … |
| Superficialisation | N | N | … (…-…) | … |
| Distal revision and interval ligation | N | N | … (…-…) | … |
| Proximalisation of arterial inflow | N | N | … (…-…) | … |
| Revision using distal inflow | N | N | … (…-…) | … |
| Banding | N | N | … (…-…) | … |
| Serious adverse events | | | | |
| Thrombosis | N | N | … (…-…) | … |
| Access abandonement | N | N | … (…-…) | … |

Statistical analysis: Poisson test with time as offset variable.

**Figure 2D: Comparison of enrolled patients with unselected hemodialysis population - Survival**
Kaplan-Meier survival curve of unselected hemodialysis population and enrolled patients
Statistical analysis: Log rank test

**Figure 2E: Patient allocation to study groups**

X-axis: time (1-1095 days)

Y-axis: patients (N=375)

The grid is filled with colors: red when allocated to the monitoring group, blue when allocated to the surveillance group, and grey after the end of the study (different shades of grey may be considered for different reasons to end study participation)

Patients will be ordered according the time of shifting between groups to facilitate interpretation (with patients who remained in the monitoring group the entire study duration at the top of the grid, and patients who remained in the surveillance group the entire study duration at the bottom of the grid)

**Table 2F: Vascular access dysfunction detected by monitoring and surveillance - Available measurements**

| | Monitoring | | Surveillance | |
|---|---|---|---|---|
| | N | Follow-up | N | Follow-up |
| Monitoring reports[a] | … | … person-years | … | … person-years |
| Flow measurements | … | … person-years | … | … person-years |

**Table 2G: Vascular access dysfunction detected by monitoring and surveillance - Monitoring reports**

| | Monitoring (… reports) | Surveillance (… reports) | P |
|---|---|---|---|
| Clinical indicators of flow dysfunction | % | % | … |
| Physical examination | % | % | … |
| Weak or discontinuous thrill | % | % | … |
| High pitched or discontinuous bruit | % | % | … |
| Hyperpulsatile vascular access | % | % | … |
| Weak vascular access | % | % | … |
| No thrill or bruit | % | % | … |
| Recurrent problems during dialysis | % | % | … |
| Inability to achieve target blood flow | % | % | … |
| New cannulation problems | % | % | … |
| Prolonged bleeding | % | % | … |
| Unexplained fall in dialysis efficiency | % | % | … |
| Other findings at inspection | | | |
| Aneurysm | % | % | … |
| Hand ischemia | % | % | … |
| Infection | % | % | … |
| Edema | % | % | … |
| Skin lesions | % | % | … |
| Hematoma | % | % | … |

Statistical analysis: Chi squared tests.

**Table 2H: Vascular access dysfunction detected by monitoring and surveillance - Surveillance flow measurements**

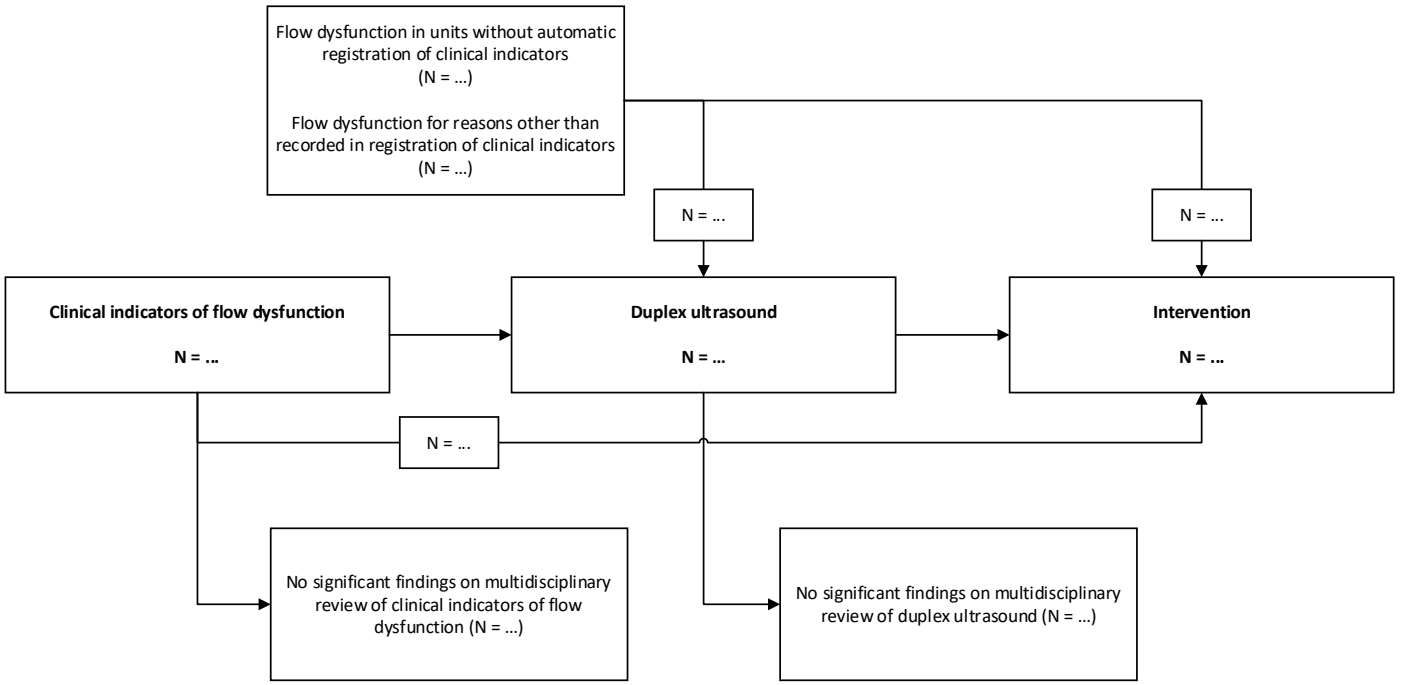
| | Monitoring (… measurements) | Surveillance (… measurements) | P |
|---|---|---|---|
| Access flow <500 mL/min[b] | % | % | … |
| With clinical indicators of flow dysfunction | % | % | … |
| Without clinical indicators of flow dysfunction | % | % | … |
| Access flow 500-1000 mL/min with >20% reduction from baseline[c] | % | % | … |
| With clinical indicators of flow dysfunction[d] | % | % | … |
| Without clinical indicators of flow dysfunction[d] | % | % | … |

Data are presented as proportions. The sum of the proportions may not add up to 100% because patients may have more than one clinical indicator of flow dysfunction.

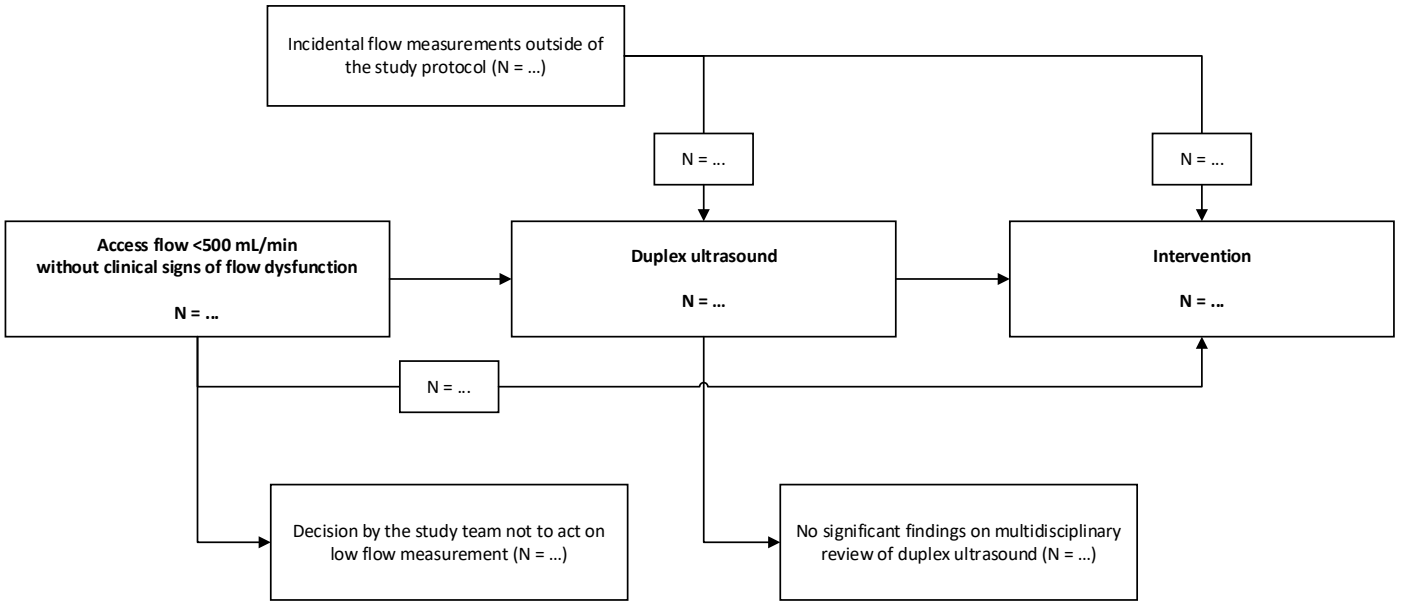
[a] Monitoring reports were not transferred to the research database in two study sites (OLVG and MUMC+ from 11-2024 onwards) because of technical issues with the electronic patient files.
[b] Access flow is considered <500 mL/min only when the initial low flow measurement was confirmed in a subsequent dialysis session.
[c] Baseline is the first flow measurement after randomization.
[d] Clinical indicators of flow dysfunction refer to the decision rules for interventions defined in the study protocol (used to send notifications to the study sites).
When counting flow measurements, only measurements for surveillance and confirmatory measurements after low flow are counted. Flow measurements to evaluate interventions or as random repeats are excluded from analysis.
Statistical analysis: Chi squared tests.

**Flow chart 2I: Consequence of flow dysfunction detected by monitoring and surveillance**

Monitoring reports




Surveillance flow measurements (only for patients allocated to the surveillance group)




Listing of reasons for:

- Flow dysfunction for reasons other than recorded in registration of flow dysfunction
- Decision by the study team not to act on low flow measurement (PROTOCOL VIOLATION)

Clinical indicators of flow dysfunction refer to the decision rules for interventions defined in the study protocol (used to send notifications to the study sites).

No significant findings on duplex ultrasounds is defined as the absence of hemodynamically significant stenosis AND no clinically significant stenosis as determined by multidisciplinary review.

**Table 2J: Time between surveillance flow measurements**

| | Monitoring | | Surveillance | | P |
|---|---|---|---|---|---|
| Time between regular flow measurements | Median (IQR) | N | Median (IQR) | N | … |
| >6 weeks | % | | % | | … |
| Thrombosis during delay | - | | % | | |
| Time until confirmatory flow measurement for low flow | Median (IQR) | N | Median (IQR) | N | … |
| >1 week | % | | % | | … |
| Thrombosis during delay | - | | % | | |

Statistical analysis: Mann-Whitney U-test comparing median time between monitoring and surveillance groups; Chi squared test for categorical variables.

**Table 2K: Time between indication and intervention**

| | Monitoring (N=…) | | | | Surveillance (N=…) | | | | P |
|---|---|---|---|---|---|---|---|---|---|
| | Median (IQR) | N | >1 week | Thrombosis in waiting time | Median (IQR) | N | >1 week | Thrombosis in waiting time | |
| All cases | | | % | % | | | % | % | … |
| Indications | | | | | | | | | |
| Clinical indicators of flow dysfunction | | | % | % | | | % | % | … |
| Access flow <500 mL/min without clinical indicators of flow dysfunction | - | - | - | - | | | % | % | |
| Interventions | | | | | | | | | |
| Percutaneous interventions | | | % | % | | | % | % | … |
| Open surgical interventions | | | % | % | | | % | % | … |

Interventions for thrombosis outside the waiting time for interventions for clinical indicators of flow dysfunction or access flow <500 mL/min (in the surveillance group) are excluded.
Statistical analysis: Mann-Whitney U-test comparing median time between monitoring and surveillance groups.

**Table 2L: Time between intervention and subsequent randomization**

| | Monitoring | | Surveillance | | P |
|---|---|---|---|---|---|
| Time between intervention and assessment of clinical success | Median (IQR) | N | Median (IQR) | N | … |
| >4 weeks | % | | % | | … |
| Thrombosis during delay | % | | % | | … |
| Time between confirmation of clinical success and subsequent randomization[a] | Median (IQR) | N | Median (IQR) | N | … |
| >2 weeks | % | | % | | … |
| Thrombosis during delay | % | | % | | … |

Interventions resulting in or from vascular access abandonment are excluded.
[a] Only for interventions with clinical success.
Statistical analysis: Mann-Whitney U-test comparing median time between monitoring and surveillance groups; Chi squared test for categorical variables.

**Table 2M: Duplex ultrasound for vascular access flow dysfunction - Available measurements**

| | Monitoring (… person-years) | Surveillance (… person-years) | Event rate ratio (95% CI) | P |
|---|---|---|---|---|
| Duplex ultrasound for clinical indicators of flow dysfunction[a] | N | N | … (…-…) | … |
| Duplex ultrasound for access flow <500 mL/min without clinical indicators of flow dysfunction[a] | N | N | … (…-…) | … |
| Duplex ultrasound not for flow dysfunction | N | N | … (…-…) | … |

Statistical analysis: general linear mixed effect model with Poisson distribution and identity link, and with time as off-set variable (see Table 3A for details).

**Table 2N: Findings of duplex ultrasound for flow dysfunction**

| | All patients (N=…) | | Monitoring (N=…) | | Surveillance (N=…) | | P |
|---|---|---|---|---|---|---|---|
| Access flow (mL/min) | … + SD | N | … + SD | N | … + SD | N | … |
| Diameter outflow vein (mm)[b] | … + SD | N | … + SD | N | … + SD | N | … |
| Stenosis | | N | | N | | N | … |
| None | % | N | % | N | % | N | |
| Single | % | N | % | N | % | N | |
| Multiple | % | N | % | N | % | N | |
| Stenosis characteristics[c] | | | | | | | |
| Location | | N | | N | | N | … |
| Fistulas | % | N | % | N | % | N | … |
| Arterial inflow | % | N | % | N | % | N | |
| Juxta-anastomotic vein | % | N | % | N | % | N | |
| Outflow vein | % | N | % | N | % | N | |
| Graft | % | N | % | N | % | N | … |
| Arterial inflow | % | N | % | N | % | N | |
| Juxta-anastomotic arterial | % | N | % | N | % | N | |
| In graft | % | N | % | N | % | N | |
| Juxta-anastomotic venous | % | N | % | N | % | N | |
| Outflow vein | % | N | % | N | % | N | |
| Vessel diameter | | | | | | | |
| Stenosis (mm) | … + SD | N | … + SD | N | … + SD | N | … |
| Reference vessel (mm) | … + SD | N | … + SD | N | … + SD | N | … |
| Diameter reduction (%) | … + SD | N | … + SD | N | … + SD | N | … |
| Peak systolic velocity | | | | | | | |
| Stenosis (cm/s) | … + SD | N | … + SD | N | … + SD | N | … |
| Reference vessel (cm/s) | … + SD | N | … + SD | N | … + SD | N | … |
| PSV ratio | … + SD | N | … + SD | N | … + SD | N | … |
| Hemodynamic significance (yes) | % | N | % | N | % | N | … |

[a] Clinical indicators of flow dysfunction refer to the decision rules for interventions defined in the study protocol (and used to send notifications to the study sites).
[b] Mean of diameter proximal / mid / distal outflow vein.
[c] For multiple stenosis, the most severe stenosis (i.e. highest PSV-ratio) is chosen.

Statistical analysis: Chi squared tests for categorical variables and Student t-test for continuous variables

**Table 2O: End of study**

| | All patients (N=…) | | Monitoring (N=…) | | Surveillance (N=…) | |
|---|---|---|---|---|---|---|
| End of follow-up period | N | % | N | % | N | % |
| Stopped hemodialysis | N | % | N | % | N | % |
| Kidney transplantation | N | % | N | % | N | % |
| Peritoneal dialysis | N | % | N | % | N | % |
| Conservative care | N | % | N | % | N | % |
| Recovery of renal function | N | % | N | % | N | % |
| Death | N | % | N | % | N | % |
| Transfer to other dialysis unit[a] | N | % | N | % | N | % |
| Withdrawal of informed consent | N | % | N | % | N | % |
| Decision by treating physician | N | % | N | % | N | % |

Groups are based on allocation at end of study.

[a] This includes patients who transferred to home hemodialysis or single needle nighttime hemodialysis.

**Table 3A: Vascular access intervention types**

| | Monitoring (… patient-years) | Surveillance (…patient-years) | Event rate ratio (95% CI) | P |
|---|---|---|---|---|
| Diagnostic angiography | N | N | … (…-…) | … |
| **Interventions for flow dysfunction** | **N** | **N** | **… (…-…)** | **…** |
| Percutaneous interventions | N | N | … (…-…) | … |
| Balloon angioplasty without stent | N | N | … (…-…) | … |
| Balloon angioplasty with stent | N | N | … (…-…) | … |
| Percutaneous thrombectomy | N | N | … (…-…) | … |
| Surgical interventions | N | N | … (…-…) | … |
| Open thrombectomy | N | N | … (…-…) | … |
| Patch angioplasty | N | N | … (…-…) | … |
| Revision of anastomosis | N | N | … (…-…) | … |
| New arteriovenous fistula | N | N | … (…-…) | … |
| New arteriovenous graft | N | N | … (…-…) | … |
| Ligation of arteriovenous fistula | N | N | … (…-…) | … |
| Ligation of arteriovenous graft | N | N | … (…-…) | … |
| Central venous catheter interventions | N | N | … (…-…) | … |
| Catheter insertion | N | N | … (…-…) | … |
| Guidewire exchange | N | N | … (…-…) | … |
| Catheter removal | N | N | … (…-…) | … |
| Other vascular access interventions | N | N | … (…-…) | … |
| Repair (pseudo)aneurysm | N | N | … (…-…) | … |
| Ligation of accessory vein | N | N | … (…-…) | … |
| Embolisation of accessory vein | N | N | … (…-…) | … |
| Superficialisation | N | N | … (…-…) | … |
| Distal revision and interval ligation | N | N | … (…-…) | … |
| Proximalisation of arterial inflow | N | N | … (…-…) | … |
| Revision using distal inflow | N | N | … (…-…) | … |
| Banding | N | N | … (…-…) | … |

Statistical analysis (intention to treat population): general linear mixed effect model with Poisson distribution and identity link, and with time as off-set variable. The outcome will be expressed as a ratio (exponential of β1) of events (number of interventions) per 1 unit increase of exposure time between both groups. A random intercept for each individual participant will be estimated to account for dependence of observations. Expected counts will be plotted against observed counts to check whether the distribution of counts follow a Poisson distribution. Furthermore, the Pearson dispersion statistic will be assessed to check whether there is equidispersion of the variance compared to the mean. In case of overdispersion of the data, a quasi-Poisson model or negative binomial model will be performed.
Stratification: study site and vascular access type (fistula / graft).
Subgroup analysis: vascular access type (fistula / graft).
Sensitivity analysis:

- Major interventions counting twice (see Table 3a-2)
- Exclusion of patients with interventions with technical failure (see Table7A)
- Exclusion of patients with interventions with clinical failure (see Table 7A)

**Table 3B: Characteristics of vascular access interventions**

| | Monitoring (N=…) | Surveillance (N=…) | P |
|---|---|---|---|
| Indication | | | |
| Clinical indicators of flow dysfunction[a] | % | % | … |
| Physical examination | | | |
| Weak or discontinuous thrill | % | % | … |
| High pitched or discontinuous bruit | % | % | … |
| Hyperpulsatile vascular access | % | % | … |
| Weak vascular access | % | % | … |
| No thrill or bruit | % | % | … |
| Recurrent problems during dialysis | | | |
| Inability to achieve target blood flow | % | % | … |
| New cannulation problems | % | % | … |
| Prolonged bleeding | % | % | … |
| Unexplained fall in dialysis efficiency | % | % | … |
| Access flow <500 mL/min without clinical indicators of flow dysfunction[a] | % | % | … |
| Vascular access thrombosis | % | % | … |
| New vascular access | % | % | … |
| Non-maturation | % | % | … |
| Central venous catheter dysfunction | % | % | … |
| Unused vascular access | % | % | … |
| Other than flow dysfunction | % | % | … |
| High flow | % | % | … |
| Central vein obstruction | % | % | … |
| Hand ischemia | % | % | … |
| Vascular access (pseudo)aneurysm | % | % | … |
| Vascular access infection | % | % | … |
| New vascular access | % | % | … |
| Non-maturation | % | % | … |
| Central venous catheter dysfunction | % | % | … |
| Unused vascular access | % | % | … |
| Anesthesia | | | … |
| Local anesthesia | % | % | |
| Local anesthesia with sedation | % | % | |
| Locoregional anesthesia | % | % | |
| Regional anesthesia | % | % | |
| Hospital admission | | | … |
| Outpatient | % | % | |
| Day case | % | % | |
| Multiple days | % | % | |

[a] Clinical indicators of flow dysfunction refer to the decision rules for interventions defined in the study protocol (used to send notifications to the study sites).
Statistical analysis: Chi squared test for categorical variables.
Major interventions are defined as interventions with general anesthesia and/or multiple day hospital admission.

**Table 3C: Characteristics of percutaneous interventions**

| | All patients (N=…) | | Monitoring (N=…) | | Surveillance (N=…) | | P |
|---|---|---|---|---|---|---|---|
| Stenosis | | N | | N | | N | … |
| None | % | N | % | N | % | N | |
| Single | % | N | % | N | % | N | |
| Multiple | % | N | % | N | % | N | |
| Stenosis characteristics[a] | | | | | | | |
| Location | | N | | N | | N | … |
| Fistulas | % | N | % | N | % | N | … |
| Arterial inflow | % | N | % | N | % | N | |
| Juxta-anastomotic vein | % | N | % | N | % | N | |
| Outflow vein[b] | % | N | % | N | % | N | |
| Central vein | % | N | % | N | % | N | |
| Graft | % | N | % | N | % | N | … |
| Arterial inflow | % | N | % | N | % | N | |
| Juxta-anastomotic arterial | % | N | % | N | % | N | |
| In graft | % | N | % | N | % | N | |
| Juxta-anastomotic venous | % | N | % | N | % | N | |
| Outflow vein | % | N | % | N | % | N | |
| Central vein | % | N | % | N | % | N | |
| Vessel preparation | | | | | | | |
| Balloon type | | | | | | | … |
| Standard balloon | % | | % | | % | | |
| High pressure balloon | % | | % | | % | | |
| Cutting balloon | % | | % | | % | | |
| Balloon diameter (mm) | … + SD | N | … + SD | N | … + SD | N | … |
| Balloon inflation time (min) | … + SD | N | … + SD | N | … + SD | N | … |
| Balloon inflation pressure (atm) | … + SD | N | … + SD | N | … + SD | N | … |
| Additional treatment | | | | | | | |
| Paclitaxel-coated balloon | % | | % | | % | | … |
| Paclitaxel-coated balloon diameter (mm) | … + SD | N | … + SD | N | … + SD | N | … |
| Stent | % | N | % | N | % | N | … |
| Covera | % | N | % | N | % | N | |
| Viabahn | % | N | % | N | % | N | |
| Wrapsody | % | N | % | N | % | N | |
| Supera | % | N | % | N | % | N | |
| Stent diameter (mm) | … + SD | N | … + SD | N | … + SD | N | … |
| Stent length (mm) | … + SD | N | … + SD | N | … + SD | N | … |
| Treatment effect | | | | | | | |
| Subjective assessment | | | | | | | |
| Luminal loss before treatment (%) | … + SD | N | … + SD | N | … + SD | N | … |
| Luminal loss after treatment (%) | … + SD | N | … + SD | N | … + SD | N | … |
| Core lab assessment | | | | | | | |
| Luminal loss before treatment (%) | … + SD | N | … + SD | N | … + SD | N | … |
| Luminal loss after treatment (%) | … + SD | N | … + SD | N | … + SD | N | … |

[a] For multiple stenoses, the most severe stenosis (i.e. highest PSV-ratio with duplex ultrasound) is chosen.

[b] Outflow vein may be subdivided into cannulation zone / outflow vein / cephalic arch / swing segment when angiography images are available.
Statistical analysis: Chi squared tests for categorical variables and Student t-test for continuous variables

**Table 3D: Complications of percutaneous interventions**

| | All patients (N=…) | | Monitoring (N=…) | | Surveillance (N=…) | | P |
|---|---|---|---|---|---|---|---|
| No complications | % | N | % | N | % | N | … |
| Extravasation after angioplasty | % | N | % | N | % | N | … |
| Balloon dilation | % | N | % | N | % | N | |
| Covered stent | % | N | % | N | % | N | |
| Other treatment | % | N | % | N | % | N | |
| Bleeding from access site | % | N | % | N | % | N | … |
| Compression dressing | % | N | % | N | % | N | |
| Thrombin injection | % | N | % | N | % | N | |
| Surgical closure | % | N | % | N | % | N | |
| Other treatment | % | N | % | N | % | N | |
| Other complication | % | N | % | N | % | N | … |

Statistical analysis: Chi squared tests.

**Figure 3E: Patency of vascular access**
Kaplan-Meier curves for primary patency (any access-related intervention), assisted primary patency, and secondary patency after randomization. Censoring after loss of primary patency.

Primary patency: interval between randomization and first access-related intervention or thrombosis or access abandonment
Assisted primary patency: interval between randomization and first thrombosis or access abandonment
Secondary patency: interval between randomization and access abandonment

Statistical analysis: Cox proportional hazards regression with a clustered standard error (SE) using a time-to-event framework to account for repeated events in which the same person experiences multiple events over time, some occurring while on the intervention arm, and others occurring while on the control arm. The outcome will be expressed as a hazard ratio (HR) including 95% confidence intervals and p-values. Before running the analyses, we will test the proportional hazards assumption by visual inspection of the log-log survival plots, and the Schoenfeld residuals test to statistically evaluate the assumption.

**Table 4A: Serious adverse events**

| | Monitoring (… patient-years) | Surveillance (…patient-years) | Event rate ratio (95% CI) | P |
|---|---|---|---|---|
| All serious adverse events | N | N | … (…-…) | … |
| Related to vascular access | N | N | … (…-…) | … |
| Unrelated to vascular access | N | N | … (…-…) | … |
| Vascular access thrombosis | N | N | … (…-…) | … |
| Vascular access abandonment | N | N | … (…-…) | … |
| Unplanned hospital admittance | N | N | … (…-…) | … |
| Related to vascular access | N | N | … (…-…) | … |
| Unrelated to vascular access | N | N | … (…-…) | … |
| Death | N | N | … (…-…) | … |
| Related to vascular access | N | N | … (…-…) | … |
| Unrelated to vascular access | N | N | … (…-…) | … |

Serious adverse events may be included in more than one category.
Statistical analysis (intention to treat population): general linear mixed effect model with Poisson distribution and identity link, and with time as off-set variable (see Table 3A for details).
Stratification for study site and vascular access type (fistula / graft).
Subgroup analysis: vascular access type (fistula / graft).
Sensitivity analysis:

- Exclusion of patients with interventions with technical failure (see Table 7A)
- Exclusion of patients with interventions with clinical failure (see Table 7A)

**Table 4B: Access-related adverse events**

| | Monitoring (… patient-years) | Surveillance (…patient-years) | Event rate ratio (95% CI) | P |
|---|---|---|---|---|
| Access-related adverse events | N | N | … (…-…) | … |
| Pain requiring medication (days) | N | N | … (…-…) | … |
| Infection requiring antibiotics (days) | N | N | … (…-…) | … |
| Bleeding requiring blood transfusion | N | N | … (…-…) | … |
| Central venous catheter thrombolysis | N | N | … (…-…) | … |

Statistical analysis (intention to treat population): general linear mixed effect model with Poisson distribution and identity link, and with time as off-set variable (see Table 3A for details).

**Table 4C: Hospital admittance**

| | Monitoring (…patient-years) | Surveillance (…patient-years) | Event rate ratio (95% CI) | P |
|---|---|---|---|---|
| Hospital admittance (days) | N | N | … (…-…) | … |
| Related to vascular access | N | N | … (…-…) | … |
| Unrelated to vascular access | N | N | … (…-…) | … |

Statistical analysis (intention to treat population): general linear mixed effect model with Poisson distribution and identity link, and with time as off-set variable (see Table 3A for details).

**Table 4D: Line listing of serious adverse events**

**Table 4E: Line listing of protocol deviations**

**Table 5A: SF-VAQ scores at baseline**

| | All patients (N=…) | Monitoring (N=…) | Surveillance (N=…) | P |
|---|---|---|---|---|
| Total score | … | … | … | … |
| Physical domain | … | … | … | … |
| Pain | … | … | … | … |
| Bleeding | … | … | … | … |
| Swelling | … | … | … | … |
| Bruising | … | … | … | … |
| Social functioning domain | … | … | … | … |
| Daily activities | … | … | … | … |
| Appearance | … | … | … | … |
| Sleep | … | … | … | … |
| Bathing and showering | … | … | … | … |
| Dialysis complications domain | … | … | … | … |
| Problem on dialysis | … | … | … | … |
| Access care | … | … | … | … |
| Hospitalization | … | … | … | … |
| Worry about access longevity | … | … | … | … |

Groups are based on initial randomization
Include only questionnaires with complete data. Questions are Likert scores from 1 to 7. Domain scores are the sum of the 4 questions. The total score is the sum of the 3 domains.
Statistical analysis: Students t-test.

**Table 5B: SF-VAQ scores according to the number of interventions during follow-up**

| | No interventions during follow-up (N=…) | 1 intervention during follow-up (N=…) | >1 intervention during follow-up (N=…) | P |
|---|---|---|---|---|
| Total score | … | … | … | … |
| Physical domain | … | … | … | … |
| Pain | … | … | … | … |
| Bleeding | … | … | … | … |
| Swelling | … | … | … | … |
| Bruising | … | … | … | … |
| Social functioning domain | … | … | … | … |
| Daily activities | … | … | … | … |
| Appearance | … | … | … | … |
| Sleep | … | … | … | … |
| Bathing and showering | … | … | … | … |
| Dialysis complications domain | … | … | … | … |
| Problem on dialysis | … | … | … | … |
| Access care | … | … | … | … |
| Hospitalization | … | … | … | … |
| Worry about access longevity | … | … | … | … |

Include only questionnaires with complete data. Questions are Likert scores from 1 to 7. Domain scores are the sum of the 4 questions. The total score is the sum of the 3 domains.
Sensitivity analysis: exclude patients with interventions on the current vascular access before enrollment
Statistical analysis: mixed linear model

**Table 5C: Change in SF-VAQ scores with access-related interventions**

| | Before intervention (>30 days) | Around intervention (30 days before – 90 days after) | P | Clinically relevant change |
|---|---|---|---|---|
| Total score | Mean (SD) | Mean (SD) | … | % |
| Physical domain | Mean (SD) | Mean (SD) | … | % |
| Pain | Mean (SD) | Mean (SD) | … | |
| Bleeding | Mean (SD) | Mean (SD) | … | |
| Swelling | Mean (SD) | Mean (SD) | … | |
| Bruising | Mean (SD) | Mean (SD) | … | |
| Social functioning domain | Mean (SD) | Mean (SD) | … | % |
| Daily activities | Mean (SD) | Mean (SD) | … | |
| Appearance | Mean (SD) | Mean (SD) | … | |
| Sleep | Mean (SD) | Mean (SD) | … | |
| Bathing and showering | Mean (SD) | Mean (SD) | … | |
| Dialysis complications domain | Mean (SD) | Mean (SD) | … | % |
| Problem on dialysis | Mean (SD) | Mean (SD) | … | |
| Access care | Mean (SD) | Mean (SD) | … | |
| Hospitalization | Mean (SD) | Mean (SD) | … | |
| Worry about access longevity | Mean (SD) | Mean (SD) | … | |

Compare SF-VAQ scores before (latest but >30 days before) and around (closest to the intervention but <30 days before and <90 days after) the access-related intervention. Calculate the proportion of patients with a clinically relevant change in SF-VAQ scores.
The clinically relevant change in SF-VAQ scores is defined as 0.5 times the standard deviation of the difference in SF-VAQ scores between two adjacent measurements in patients without vascular access-related interventions or vascular access-related (serious) adverse events.
Statistical analysis: paired Student t-test

**Table 5D: Change in SF-VAQ scores with thrombosis**

| | Before thrombosis (>30 days) | After thrombosis (<90 days) | P | Clinically relevant change |
|---|---|---|---|---|
| Total score | Mean (SD) | Mean (SD) | … | % |
| Physical domain | Mean (SD) | Mean (SD) | … | % |
| Pain | Mean (SD) | Mean (SD) | … | |
| Bleeding | Mean (SD) | Mean (SD) | … | |
| Swelling | Mean (SD) | Mean (SD) | … | |
| Bruising | Mean (SD) | Mean (SD) | … | |
| Social functioning domain | Mean (SD) | Mean (SD) | … | % |
| Daily activities | Mean (SD) | Mean (SD) | … | |
| Appearance | Mean (SD) | Mean (SD) | … | |
| Sleep | Mean (SD) | Mean (SD) | … | |
| Bathing and showering | Mean (SD) | Mean (SD) | … | |
| Dialysis complications domain | Mean (SD) | Mean (SD) | … | % |
| Problem on dialysis | Mean (SD) | Mean (SD) | … | |
| Access care | Mean (SD) | Mean (SD) | … | |
| Hospitalization | Mean (SD) | Mean (SD) | … | |
| Worry about access longevity | Mean (SD) | Mean (SD) | … | |

Compare SF-VAQ scores before (latest but >30 days before) and after (earliest but <90 days after) the thrombosis. Calculate the proportion of patients with a clinically relevant change in SF-VAQ scores. The clinically relevant change in SF-VAQ scores is defined as 0.5 times the standard deviation of the difference in SF-VAQ scores between two adjacent measurements in patients without vascular access-related interventions or vascular access-related (serious) adverse events.
Statistical analysis: paired Student t-test

**Table 5E: Predictors of SF-VAQ scores at baseline**

| | Total score | | Physical domain | | Social domain | | Complications domain | |
|---|---|---|---|---|---|---|---|---|
| | β (95% CI) | P | β (95% CI) | P | β (95% CI) | P | β (95% CI) | P |
| Sex (male) | | | | | | | | |
| Age (/year) | | | | | | | | |
| Body mass index (/kg/m$^2$) | | | | | | | | |
| Diabetes mellitus (yes) | | | | | | | | |
| Dialysis treatments per week | | | | | | | | |
| Vascular access type | | | | | | | | |
| Arteriovenous fistula | | | | | | | | |
| Radiocephalic fistula | | | | | | | | |
| Brachiocephalic fistula | | | | | | | | |
| Brachiobasilic fistula | | | | | | | | |
| Arteriovenous graft | | | | | | | | |
| Age vascular access (/month) | | | | | | | | |
| Previous vascular access | | | | | | | | |
| Previous vascular access interventions | | | | | | | | |
| Baseline access flow (/100 mL/min) | | | | | | | | |

Groups are based on initial randomization. Include only questionnaires with complete data.
Statistical analysis: all variables will be entered into multivariable linear regression models
Check for assumptions of statistical model: linearity, multicollinearity, and independence of errors

**Table 6A: Repeatability / Test-retest reliability of ultrasound dilution flow measurements**

| | Point estimate | 95% CI |
|---|---|---|
| Standard error of measurements (SEM) | | |
| Coefficient of variation (CV) | | |

Same observer under the same conditions using the same measurement instrument (test-retest)
Include all ultrasound dilution flow measurements with 3 replicates (N=…)
Check for assumptions of statistical model: normal distribution of measurements and homogeneity of variance within subjects

**Table / Figure 6B: Reproducibility / Inter-session reliability of ultrasound dilution flow measurements**

Without correction for blood pressure

| | N | Bias | Limits of agreement |
|---|---|---|---|
| Flow measurements within 2 weeks | | | |
| All measurements | | mL/min | mL/min |
| Only random controls | | mL/min | mL/min |
| Flow measurements within 1 week | | | |
| All measurements | | mL/min | mL/min |
| Only random controls | | mL/min | mL/min |

With correction for blood pressure

| | N | Bias | Limits of agreement |
|---|---|---|---|
| Flow measurements within 2 weeks | | | |
| All measurements | | mL/min | mL/min |
| Only random controls | | mL/min | mL/min |
| Flow measurements within 1 week | | | |
| All measurements | | mL/min | mL/min |
| Only random controls | | mL/min | mL/min |

Figure: Bland-Altman plots

- Y-axis: difference second – first measurement
- X-axis: mean second – first measurement
- Lines at bias and limits of agreement (95% CI)
- For each of the 4 subgroups in the table, with and without correction for blood pressure

Different observers under different conditions using the same measurement instrument (between session variation)
Include all ultrasound dilution flow measurements (with 3 replicates) repeated within 2 weeks
Check for assumptions of statistical model: normal distribution of measurements and homogeneity of variance within subjects

**Table / Figure 6C: Agreement of ultrasound dilution and duplex flow measurements**

Without correction for blood pressure

| | N | Bias | Limits of agreement | ICC(2,1) |
|---|---|---|---|---|
| Flow measurements within 2 weeks | | mL/min | mL/min | |
| Flow measurements within 1 week | | mL/min | mL/min | |

With correction for blood pressure

| | N | Bias | Limits of agreement | ICC(2,1) |
|---|---|---|---|---|
| Flow measurements within 2 weeks | | mL/min | mL/min | |
| Flow measurements within 1 week | | mL/min | mL/min | |

Figure: Bland-Altman plots

- Y-axis: difference ultrasound dilution – duplex measurement
- X-axis: mean ultrasound dilution – duplex measurement
- Lines at bias and limits of agreement (95% CI)
- For each of the 2 subgroups in the table, with and without correction for blood pressure

Different observers under different conditions using different measurement instruments (agreement)

Include all ultrasound dilution flow measurements (with 3 replicates) and duplex flow measurements for flow dysfunction done within 2 weeks

Check for assumptions of statistical model: normal distribution of measurements and homogeneity of variance within subjects

**Table 6D: Diagnostic accuracy of vascular access surveillance to predict clinical indicators of flow dysfunction, thrombosis, and access loss**

**Cross-tables**

| | Intervention for clinical indicators of flow dysfunction <30 days | | No intervention for clinical indicators of flow dysfunction <30 days | | Total | |
|---|---|---|---|---|---|---|
| Access flow >500 mL/min | N | % | N | % | N | % |
| Access flow <500 mL/min | N | % | N | % | N | % |
| Total | N | % | N | % | N | 100% |
| | Thrombosis <30 days | | No thrombosis <30 days | | Total | |
| Access flow >500 mL/min | N | % | N | % | N | % |
| Access flow <500 mL/min | N | % | N | % | N | % |
| Total | N | % | N | % | N | 100% |
| | Loss of vascular access <30 days | | No loss of vascular access <30 days | | Total | |
| Access flow >500 mL/min | N | % | N | % | N | % |
| Access flow <500 mL/min | N | % | N | % | N | % |
| Total | N | % | N | % | N | 100% |

| | Intervention for clinical indicators of flow dysfunction <30 days | | No intervention for clinical indicators of flow dysfunction <30 days | | Total | |
|---|---|---|---|---|---|---|
| Access flow >1000 mL/min or 500-1000 with <20% reduction from baseline | N | % | N | % | N | % |
| Access flow <500 mL/min or 500-1000 mL/min with >20% reduction from baseline | N | % | N | % | N | % |
| Total | N | % | N | % | N | 100% |
| | Thrombosis <30 days | | No thrombosis <30 days | | Total | |
| Access flow >1000 mL/min or 500-1000 with <20% reduction from baseline | N | % | N | % | N | % |
| Access flow <500 mL/min or 500- | N | % | N | % | N | % |

| | | | | | | |
|---|---|---|---|---|---|---|
| 1000 mL/min with >20% reduction from baseline | | | | | | |
| Total | N | % | N | % | N | 100% |
| | Loss of vascular access <30 days | | No loss of vascular access <30 days | | Total | |
| Access flow >1000 mL/min or 500-1000 with <20% reduction from baseline | N | % | N | % | N | % |
| Access flow <500 mL/min or 500-1000 mL/min with >20% reduction from baseline | N | % | N | % | N | % |
| Total | N | % | N | % | N | 100% |

| | Intervention for clinical indicators of flow dysfunction <30 days | | No intervention for clinical indicators of flow dysfunction <30 days | | Total | |
|---|---|---|---|---|---|---|
| Mean dynamic venous pressure below threshold | N | % | N | % | N | % |
| Mean dynamic venous pressure above threshold | N | % | N | % | N | % |
| Total | N | % | N | % | N | 100% |
| | Thrombosis <30 days | | No thrombosis <30 days | | Total | |
| Mean dynamic venous pressure below threshold | N | % | N | % | N | % |
| Mean dynamic venous pressure above threshold | N | % | N | % | N | % |
| Total | N | % | N | % | N | 100% |
| | Loss of vascular access <30 days | | No loss of vascular access <30 days | | Total | |
| Mean dynamic venous pressure below threshold | N | % | N | % | N | % |
| Mean dynamic venous pressure above threshold | N | % | N | % | N | % |
| Total | N | % | N | % | N | 100% |

The analysis of diagnostic accuracy of vascular access surveillance is done in the monitoring study group. For diagnostic accuracy of vascular access surveillance to predict clinical signs of flow dysfunction, only measurements without clinical signs of flow dysfunction at the time of

measurement are included. [This leads to exclusion of the sites where clinical signs of flow dysfunction could not be uploaded].
Only flow measurements for surveillance and confirmatory measurements after low flow are included. Flow measurements to evaluate interventions or as random repeats are excluded from analysis. Baseline is the first flow measurement after randomization.
Clinical indicators of flow dysfunction refer to the decision rules for interventions defined in the study protocol (used to send notifications to the study sites).
The threshold for mean dynamic venous pressure will be derived from ROC curve analysis (Figure 10-2)
Calculate sensitivity, specificity, positive predictive value, and negative predictive value.

**Figure 6E: Receiver operator characteristic (ROC) curves for diagnostic accuracy of absolute access flow to predict (A) interventions for clinical indicators of flow dysfunction <30 days, (B) thrombosis <30 days, and (C) loss of vascular access <30 days**
Calculate area under the curve with 95% confidence intervals.

**Figure 6F: Receiver operator characteristic (ROC) curves for diagnostic accuracy of relative access flow compared to baseline to predict (A) interventions for clinical indicators of flow dysfunction <30 days, (B) thrombosis <30 days, and (C) loss of vascular access <30 days**
Calculate area under the curve with 95% confidence intervals.

**Figure 6G: Receiver operator characteristic (ROC) curves for diagnostic accuracy of mean dynamic venous pressure to predict (A) interventions for clinical indicators of flow dysfunction <30 days, (B) thrombosis <30 days, and (C) loss of vascular access <30 days**
Calculate area under the curve with 95% confidence intervals.

**Figure 6H: Scatterplot of (A) absolute access flow to mean dynamic venous pressure, and (B) relative access flow compared to baseline to mean dynamic venous pressure**
Statistical analysis: Pearson correlation coefficient with 95% confidence interval

**Table 6I: Table / Figure 6B: Reproducibility / Inter-session reliability of vascular access monitoring**

| | Inter-session reliability (Cohen's kappa) |
|---|---|
| | Next dialysis session |
| Clinical indicators of flow dysfunction | … |
| Physical examination | … |
| Weak or discontinuous thrill | … |
| High pitched or discontinuous bruit | … |
| Hyperpulsatile vascular access | … |
| Weak vascular access | … |
| No thrill or bruit | … |
| Recurrent problems during dialysis | … |
| Inability to achieve target blood flow | … |
| New cannulation problems | … |
| Prolonged bleeding | … |
| Unexplained fall in dialysis efficiency | … |
| Other findings at inspection | … |
| Aneurysm | … |
| Hand ischemia | … |
| Infection | … |
| Edema | … |
| Skin lesions | … |
| Hematoma | … |

The next dialysis session should be within 7 days of the initial assessment.

**Table 6J: Diagnostic accuracy of vascular access monitoring to predict clinically relevant stenosis**

| | Duplex ultrasound or intervention | | | No significant findings on multidisciplinary review of clinical indicators of flow dysfunction | | |
|---|---|---|---|---|---|---|
| | N | Intervention <30 days (true positive) | No stenosis on imaging <30 days (false positive) | N | No intervention for clinical indicators of flow dysfunction, thrombosis, or loss of vascular access <30 days (true negative) | Intervention for clinical indicators of flow dysfunction, thrombosis, or loss of vascular access <30 days (false negative) |
| Clinical indicators of flow dysfunction | … | % | % | … | % | % |
| Physical examination | … | % | % | … | % | % |
| Weak or discontinuous thrill | … | % | % | … | % | % |
| High pitched or discontinuous bruit | … | % | % | … | % | % |
| Hyperpulsatile vascular access | … | % | % | … | % | % |
| Weak vascular access | … | % | % | … | % | % |
| No thrill or bruit | … | % | % | … | % | % |
| Recurrent problems during dialysis | … | % | % | … | % | % |
| Inability to achieve target blood flow | … | % | % | … | % | % |
| New cannulation problems | … | % | % | … | % | % |
| Prolonged bleeding | … | % | % | … | % | % |
| Unexplained fall in dialysis efficiency | … | % | % | … | % | % |

Clinical indicators of flow dysfunction refer to the decision rules for interventions defined in the study protocol (used to send notifications to the study sites).
The sum of the counts may not add up to the total event rate because patients may have more than one clinical indicator of flow dysfunction.

**Table 7A: Success rate of vascular access interventions for flow dysfunction**

| | All patients (N=…) | | Monitoring (N=…) | | Surveillance (N=…) | | P |
|---|---|---|---|---|---|---|---|
| Technical success (<30% residual stenosis)[a] | % | N | % | N | % | N | … |
| Clinical success | | | | | | | |
| Access flow >500 mL/min | % | N | % | N | % | N | … |
| Resolution of clinical indicators of flow dysfunction[b] | % | N | % | N | % | N | … |
| Functional vascular access[c] | % | N | % | N | % | N | … |

[a] Only for percutaneous interventions

[b] Only for interventions for clinical indicators of flow dysfunction

[c] Functional vascular access is defined as: cannulated with 2 needles for 6 dialysis sessions in 30 days with prescribed dialysis blood flow

Statistical analysis: Chi squared tests

**Figure 7B: Kaplan-Meier curves of (A) primary patency (any access-related intervention), (B) assisted primary patency, and (C) secondary patency after interventions for flow dysfunction**

Include interventions that result in functional vascular access. Censoring after loss of primary patency. Statistical comparison between monitoring and surveillance groups with log-rank tests.

**Table 7C: Success rate of vascular access interventions for thrombosis**

| | All patients (N=…) | | Monitoring (N=…) | | Surveillance (N=…) | | P |
|---|---|---|---|---|---|---|---|
| Percutaneous thrombectomy | % | N | % | N | % | N | … |
| Technical success[a] | % | N | % | N | % | N | … |
| Clinical success[b] | % | N | % | N | % | N | … |
| Recurrent thrombosis in 3 months | % | N | % | N | % | N | … |
| Open thrombectomy | % | N | % | N | % | N | … |
| Technical success[a] | % | N | % | N | % | N | … |
| Clinical success[b] | % | N | % | N | % | N | … |
| Recurrent thrombosis in 3 months | % | N | % | N | % | N | … |
| No thrombectomy | % | N | % | N | % | N | … |
| Vascular access loss in 30 days | % | N | % | N | % | N | … |
| Permanent central venous catheter | % | N | % | N | % | N | … |
| Temporary central venous catheter | % | N | % | N | % | N | … |

[a] Return of thrill and bruit

[b] Successful hemodialysis with the vascular access after thrombectomy: cannulated with 2 needles with prescribed dialysis blood flow

Statistical analysis: Chi squared tests

**Figure 7D: Kaplan-Meier curves of (A) primary patency (any access-related intervention), (B) assisted primary patency, and (C) secondary patency after interventions for thrombosis**

Include interventions that result in clinical success. Censoring after loss of primary patency. Statistical comparison between monitoring and surveillance groups with log-rank tests.

**Table 8A: Duplex ultrasound core lab assessment[a]**

| | All lesions[b] (N=…) | Intimal hyperplasia type (N=…) | Shrinking type (N=…) | No stenosis type (N=…) |
|---|---|---|---|---|
| Inner diameter stenosis (mm) | … + SD | … + SD | … + SD | … + SD |
| Outer diameter stenosis (mm) | … + SD | … + SD | … + SD | … + SD |
| Inner diameter reference vessel (mm) | … + SD | … + SD | … + SD | … + SD |
| Outer diameter reference vessel (mm) | … + SD | … + SD | … + SD | … + SD |
| Intimal hyperplasia rate (%) | … + SD | … + SD | … + SD | … + SD |
| Vascular constriction rate (%) | … + SD | … + SD | … + SD | … + SD |
| Stenosis rate (%) | … + SD | … + SD | … + SD | … + SD |

[a] For multiple stenosis, the most severe stenosis (i.e. highest PSV-ratio) is chosen.
[b] Definitions according to Suemitsu et al. J Endovasc Ther 2025;32(5):1607-1613. No stenosis is defined as <50% stenosis rate and >2 mm inner diameter.

**Table 8B: Duplex ultrasound findings** (selection of duplex ultrasound assessments with available images of the stenosis and subsequent balloon angioplasty of the stenosis)

| | Intimal hyperplasia type (N=…) | | Shrinking type (N=…) | | No stenosis type (N=…) | | P |
|---|---|---|---|---|---|---|---|
| Access flow (mL/min) | … + SD | N | … + SD | N | … + SD | N | … |
| Diameter outflow vein (mm)[b] | … + SD | N | … + SD | N | … + SD | N | … |
| Stenosis | | N | | N | | N | … |
| None | % | N | % | N | % | N | |
| Single | % | N | % | N | % | N | |
| Multiple | % | N | % | N | % | N | |
| Stenosis characteristics[c] | | | | | | | |
| Location | | N | | N | | N | … |
| Fistulas | % | N | % | N | % | N | … |
| Arterial inflow | % | N | % | N | % | N | |
| Juxta-anastomotic vein | % | N | % | N | % | N | |
| Outflow vein | % | N | % | N | % | N | |
| Graft | % | N | % | N | % | N | … |
| Arterial inflow | % | N | % | N | % | N | |
| Juxta-anastomotic arterial | % | N | % | N | % | N | |
| In graft | % | N | % | N | % | N | |
| Juxta-anastomotic venous | % | N | % | N | % | N | |
| Outflow vein | % | N | % | N | % | N | |
| Vessel diameter | | | | | | | |
| Stenosis (mm) | … + SD | N | … + SD | N | … + SD | N | … |
| Reference vessel (mm) | … + SD | N | … + SD | N | … + SD | N | … |
| Diameter reduction (%) | … + SD | N | … + SD | N | … + SD | N | … |
| Peak systolic velocity | | | | | | | |
| Stenosis (cm/s) | … + SD | N | … + SD | N | … + SD | N | … |
| Reference vessel (cm/s) | … + SD | N | … + SD | N | … + SD | N | … |
| PSV ratio | … + SD | N | … + SD | N | … + SD | N | … |
| Hemodynamic significance (yes) | % | N | % | N | % | N | … |

[a] Clinical indicators of flow dysfunction refer to the decision rules for interventions defined in the study protocol (and used to send notifications to the study sites).

[b] Mean of diameter proximal / mid / distal outflow vein.

[c] For multiple stenosis, the most severe stenosis was chosen (i.e. highest PSV-ratio).

Data are presented as proportions or as mean with standard deviation.

Statistical analysis: One-way ANOVA for continuous variables and Chi squared test for categorical variables.

**Table 8C: Angioplasty characteristics**

| | Intimal hyperplasia type (N=…) | | Shrinking type (N=…) | | No stenosis type (N=…) | | P |
|---|---|---|---|---|---|---|---|
| Indication | | | | | | | |
| Clinical indicators of flow dysfunction[a] | % | N | % | N | % | N | … |
| Access flow <500 mL/min without clinical indicators of flow dysfunction[a] | % | N | % | N | % | N | … |
| Vascular access thrombosis | % | N | % | N | % | N | … |
| Stenosis location | | N | | N | | N | … |
| Fistulas | % | N | % | N | % | N | … |
| Arterial inflow | % | N | % | N | % | N | |
| Juxta-anastomotic vein | % | N | % | N | % | N | |
| Outflow vein[b] | % | N | % | N | % | N | |
| Central vein | % | N | % | N | % | N | |
| Graft | % | N | % | N | % | N | … |
| Arterial inflow | % | N | % | N | % | N | |
| Juxta-anastomotic arterial | % | N | % | N | % | N | |
| In graft | % | N | % | N | % | N | |
| Juxta-anastomotic venous | % | N | % | N | % | N | |
| Outflow vein | % | N | % | N | % | N | |
| Central vein | % | N | % | N | % | N | |
| Vessel preparation | | | | | | | |
| Balloon type | | N | | N | | N | … |
| Standard balloon | % | | % | | % | | |
| High pressure balloon | % | | % | | % | | |
| Cutting balloon | % | | % | | % | | |
| Balloon diameter (mm) | … + SD | N | … + SD | N | … + SD | N | … |
| Balloon inflation time (min) | … + SD | N | … + SD | N | … + SD | N | … |
| Balloon inflation pressure (atm) | … + SD | N | … + SD | N | … + SD | N | … |
| Additional treatment | | | | | | | |
| Paclitaxel-coated balloon | % | N | % | N | % | N | … |
| Paclitaxel-coated balloon diameter (mm) | … + SD | N | … + SD | N | … + SD | N | … |
| Stent | % | N | % | N | % | N | … |
| Covera | % | N | % | N | % | N | |
| Viabahn | % | N | % | N | % | N | |
| Wrapsody | % | N | % | N | % | N | |
| Supera | % | N | % | N | % | N | |
| Stent diameter (mm) | … + SD | N | … + SD | N | … + SD | N | … |
| Stent length (mm) | … + SD | N | … + SD | N | … + SD | N | … |
| Treatment effect | | | | | | | |
| Subjective assessment | | | | | | | |
| Luminal loss before treatment (%) | … + SD | N | … + SD | N | … + SD | N | … |
| Luminal loss after treatment (%) | … + SD | N | … + SD | N | … + SD | N | … |
| Core lab assessment | | | | | | | |
| Luminal loss before treatment (%) | … + SD | N | … + SD | N | … + SD | N | … |
| Luminal loss after treatment (%) | … + SD | N | … + SD | N | … + SD | N | … |

[a] Clinical indicators of flow dysfunction refer to the decision rules for interventions defined in the study protocol (and used to send notifications to the study sites).
[b] Outflow vein may be subdivided into cannulation zone / outflow vein / cephalic arch / swing segment when angiography images are available.
Data are presented as proportions or as mean with standard deviation.
Statistical analysis: One-way ANOVA for continuous variables and Chi squared test for categorical variables.

**Figure 8D: Kaplan-Meier curves for (A) primary patency (target lesion), (B) assisted primary patency, and (C) secondary patency after percutaneous balloon angioplasty for 3 stenosis types**
Statistical analysis: log rank test

**Table 8E: Association between duplex ultrasound stenosis type and target lesion primary patency after balloon angioplasty**

| | Target lesion primary patency[a] | |
|---|---|---|
| | HR (95% CI) | P |
| Stenosis type | | … |
| No stenosis | Reference | |
| Intimal hyperplasia | … (…-…) | |
| Shrinking | … (…-…) | |
| Sex (male) | … (…-…) | … |
| Age (/year) | … (…-…) | … |
| Diabetes mellitus (yes) | … (…-…) | … |
| Smoking history (current vs stopped/never) | … (…-…) | … |
| Use of antithrombotics | | … |
| No | Reference | |
| Antiplatelet therapy | … (…-…) | |
| Anticoagulant therapy | … (…-…) | |
| Fish oil supplements (yes) | … (…-…) | … |
| Vascular access type (graft vs fistula) | … (…-…) | … |
| Baseline access flow (/mL/min) | … (…-…) | … |
| Previous vascular access interventions (yes) | … (…-…) | … |
| Study group after treatment (surveillance) | … (…-…) | … |
| Stenosis (multiple vs single) | … (…-…) | … |
| Indication for intervention | | … |
| Clinical indicators of flow dysfunction[a] | Reference | |
| Access flow <500 mL/min without clinical indicators of flow dysfunction[a] | … (…-…) | |
| Vascular access thrombosis | … (…-…) | |
| Balloon diameter (/mm) | … (…-…) | … |
| Balloon inflation time (/min) | … (…-…) | … |
| Balloon inflation pressure (/atm) | … (…-…) | … |
| Paclitaxel-coated balloon (yes) | … (…-…) | … |
| Covered stent (yes) | … (…-…) | … |
| Luminal loss before treatment (/%) | … (…-…) | … |
| Luminal loss after treatment (/%) | … (…-…) | … |

[a] For multiple stenosis, the target lesion is the most severe stenosis (i.e. highest PSV-ratio with duplex ultrasound).
Statistical analysis: all variables will be entered into multivariable Cox regression models
Check for assumptions of statistical model: linearity, multicollinearity, independence of errors, and proportional hazards

**Table 8F: Complications of percutaneous interventions**

| | Intimal hyperplasia type (N=…) | | Shrinking type (N=…) | | No stenosis type (N=…) | | P |
|---|---|---|---|---|---|---|---|
| No complications | % | N | % | N | % | N | … |
| Extravasation after angioplasty | % | N | % | N | % | N | … |
| Balloon dilation | % | N | % | N | % | N | … |
| Covered stent | % | N | % | N | % | N | … |
| Other treatment | % | N | % | N | % | N | … |
| Bleeding from access site | % | N | % | N | % | N | … |
| Compression dressing | % | N | % | N | % | N | … |
| Thrombin injection | % | N | % | N | % | N | … |
| Surgical closure | % | N | % | N | % | N | … |
| Other treatment | % | N | % | N | % | N | … |
| Other complication | % | N | % | N | % | N | … |

Statistical analysis: Chi squared tests

**Table 9A: Cannulation practice – comparison between study groups**

| | All patients (… dialysis sessions) | | Monitoring (… dialysis sessions) | | Surveillance (… dialysis sessions) | | P |
|---|---|---|---|---|---|---|---|
| Cannulation technique | | N | | N | | N | … |
| Rope ladder | % | N | % | N | % | N | |
| Buttonhole | % | N | % | N | % | N | |
| Ultrasound-guided cannulation | | N | | N | | N | … |
| No | % | N | % | N | % | N | |
| Cannulation site determination | % | N | % | N | % | N | |
| Ultrasound-guided puncture | % | N | % | N | % | N | |
| Needle position assessment | % | N | % | N | % | N | |
| Needle type | | N | | N | | N | … |
| Steel | % | N | % | N | % | N | |
| Plastic | % | N | % | N | % | N | |
| Needle size | | N | | N | | N | … |
| 15G | % | N | % | N | % | N | |
| 16G | % | N | % | N | % | N | |
| 17G | % | N | % | N | % | N | |
| Other | % | N | % | N | % | N | |
| Single needle prescription | % | N | % | N | % | N | … |
| Cannulation difficulties[a] | % | N | % | N | % | N | … |
| Cannulation failure[b] | % | N | % | N | % | N | … |
| Arterial punctures | | N | | N | | N | … |
| 1 | % | N | % | N | % | N | |
| 2 | % | N | % | N | % | N | |
| 3 or more | % | N | % | N | % | N | |
| Venous punctures | | N | | N | | N | … |
| 1 | % | N | % | N | % | N | |
| 2 | % | N | % | N | % | N | |
| 3 or more | % | N | % | N | % | N | |
| Hematomas | % | N | % | N | % | N | … |

[a] > 1 attempt to place and secure two needles (or one needle for dialysis sessions with single needle prescription)

[b] inability to place and secure two needles (or one needle for dialysis sessions with single needle prescription)

Statistical analysis: Chi square tests

**Table 9B: Cannulation practice – predictors of cannulation problems**

| | Cannulation difficulties[a] | | Cannulation failure[b] | | Hematoma | |
|---|---|---|---|---|---|---|
| | OR (95% CI) | P | OR (95% CI) | P | OR (95% CI) | P |
| Sex (male) | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Age (/year) | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Body mass index (/kg/m$^2$) | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Use of antithrombotics | | | | | | |
| No | Reference | | Reference | | Reference | |
| Antiplatelet therapy | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Anticoagulant therapy | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Dialysis treatments per week | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Vascular access type | | | | | | |
| Arteriovenous fistula | Reference | | Reference | | Reference | |
| Radiocephalic fistula | Reference | | Reference | | Reference | |
| Brachiocephalic fistula | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Brachiobasilic fistula | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Arteriovenous graft | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Age vascular access (/month) | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Previous vascular access | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Previous vascular access interventions | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Baseline access flow (/100 mL/min) | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Cannulation technique | | | | | | |
| Rope ladder | Reference | | Reference | | Reference | |
| Buttonhole | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Ultrasound-guided cannulation | | | | | | |
| No | Reference | | Reference | | Reference | |
| Cannulation site determination | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Ultrasound-guided puncture | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Needle position assessment | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Needle type | | | | | | |
| Steel | Reference | | Reference | | Reference | |
| Plastic | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Needle size | | | | | | |
| 15G | Reference | | Reference | | Reference | |
| 16G | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| 17G | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Other | … (…-…) | … | … (…-…) | … | … (…-…) | … |
| Single needle prescription | … (…-…) | … | … (…-…) | … | … (…-…) | … |

[a] > 1 attempt to place and secure two needles (or one needle for dialysis sessions with single needle prescription)

[b] inability to place and secure two needles (or one needle for dialysis sessions with single needle prescription)

Statistical analysis: all variables will be entered into multivariable logistic regression models

Check for assumptions of statistical model: linearity, multicollinearity, and independence of errors