Systematic Review and Meta-Analysis

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Comparison of ultrasound scan blood flow measurement versus other forms of surveillance in the thrombosis rate of hemodialysis access

A systemic review and meta-analysis

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Abstract

Background: The benefit of access flow surveillance in preventing vascular access thrombosis and failure remains controversial, as many randomized clinical trials (RCTs) have failed to demonstrate consistent results. The aim of this study was to perform a meta-analysis including newly published RCTs with a subgroup analysis for arteriovenous fistulas (AVFs) and arteriovenous grafts (AVGs).

Methods: A systematic review of the available literature was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. An electronic search was conducted using the MEDLINE, EMBASE, and Cochrane Library databases of RCTs conducted from 1970 to 2017 that involved access flow surveillance. As a result, 9 RCTs met our criteria. The control group was defined by indirect and various surveillance methods such as dynamic venous pressure measurement and physical examination. Conversely, the interventional group was defined as a noninvasive duplex ultrasound scan (USS) or ultrasound dilution that directly measured the flow of vascular access.

Results: The studies included 990 patients comprising 658 native AVFs and 332 AVGs. The prevalence of diabetes was 29.3%and 30.5% in the interventional and control groups, respectively. The estimated overall pooled risk ratio (RR) of thrombosis was 0.782 [95% confidence interval (95% CI), 0.553–1.107; $P = .17$], favoring interventional group, although this was not statistically significant. In the subgroup analysis, the pooled RR of thrombosis was .562 (95% CI, 0.346–0.915; $P = .02$) for AVFs, which significantly favored the interventional group. Conversely, the pooled RR for AVGs was 1.104 (95% CI, 0.672–1.816; $P = .70$).

Conclusion: The surveillance method to measure access flow through USS showed a significant benefit for reducing thrombosis in AVFs. The result encourages adherence to the current guidelines for AVFs. However, no benefit was found regarding AVGs. Recent guidelines with a "one-size-fits-all" approach may be revised to a "tailored-to-risk" approach.

Abbreviations: AVF = arteriovenous fistula, AVG = arteriovenous graft, NKF KDOQI = National Kidney Foundation Kidney Disease Outcomes Quality Initiative, PPV = positive predictive value, Qa = access blood flow, RCT = randomized clinical trial, VA = vascular access, VP = venous pressure.

Keywords: access flow surveillance, arteriovenous fistula, meta-analysis, thrombosis, vascular access

1. Introduction

Vascular access (VA) failure is a leading cause of hospitalization and morbidity in individuals on hemodialysis.[1] The early detection of access stenosis allows preemptive angioplasty or surgical correction in order to prevent access thrombosis and failure, substantially decreasing morbidity and hospitalization.[2,3]

The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKFKDOQI) guidelines[4] recommends that patients with native arteriovenous fistulas (AVFs) and arteriovenous grafts (AVGs) undergo routine monitoring and surveillance for stenosis with preemptive correction. The guidelines recommend access blood flow (Qa) measurement, duplex ultrasonography, and static dialysis venous pressure (VP) measurement as preferred methods for access surveillance for AVGs, and advocate the first 2 methods and physical examination for AVFs. Moreover, the European Best Practice Guidelines[5] recommend that objective monitoring of access function should be performed on a regular basis by measuring access flow (evidence level II).

Although access flow measurement through USS is the most widely preferred surveillance method, its benefit is still under debate. Early studies that supported the clinical practice guidelines[6] were mostly observational studies that compared historical control groups.[5,7–9] Many randomized clinical trials (RCTs)[10–16] were subsequently performed, but these RCTs failed to show consistent results, especially for grafts. Recent

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SDH and JHL contributed equally to this work.

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meta-analyses[17,18] further added to the uncertainty of the usefulness of access flow surveillance for preventing access thrombosis.

Although several additional good quality RCTs have recently been reported, no consensus has been reached regarding the benefit of access flow surveillance. In addition, previous meta-analyses[17,18] showed a modest benefit for native AVFs compared with AVGs. Therefore, we performed a systemic review and meta-analysis of large-scale RCTs, focusing on the difference between AVFs and AVGs.

2. Methods

2.1. Ethics statement

The present review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[19] All analyses were based on previously published studies; thus, ethical approval and patient consent were not required.

2.2. Data sources, searches, and inclusion and exclusion criteria

Two researchers (SDH and JHL) independently performed comprehensive searches of the following databases for studies published from the databases' inception to March 31, 2017: MEDLINE (via PubMed), EMBASE, and the Cochrane Central Register of Controlled Trials in the Cochrane Library. Using a highly sensitive search strategy to identify RCTs, we searched for the following terms: "arteriovenous hemodialysis access" or "arteriovenous fistula" or "arteriovenous graft" or "Doppler ultrasound" or "thrombosis "or "hemodialysis access flow" or "AVF and flow" or "AVG and flow" or "hemodialysis access" or "access flow surveillance" or "hemodialysis access thrombosis" or "hemodialysis patients" and "vascular access surveillance." The study inclusion criteria were as follows: RCTs, access blood flow assessed using ultrasound dilution or ultrasound duplex methods, adult patients (>18 years old), thrombosis reported as either a primary or secondary outcome, hemodialysis approaches with AVFs, AVGs, or both, and data available for extraction. Reviews, observational studies, and clinical trials that did not clearly define outcomes, or that did not have thrombosis as an outcome, were excluded.[18] The search was limited to human studies, but was not restricted to any particular language or publication date. Reference lists from all available review articles and RCTs were manually searched.

2.3. Method of surveillance

A study by Smits et al[10] was separated into 2 studies because it contained 2 substudies [study A: weekly VP measurements (group A1) vs periodic Qa measurements (group A2); and study B: weekly VP measurements (group B1) vs the combination of VP measurements and periodic Qa measurements (group A2)]. Study A was performed in 1 center and study B was performed in 4 centers.

With the exception of 1 study (Scaffaro et al[16]), the included studies used ultrasound dilution to measure Qa. Scaffaro et al[16] estimated Qa using the ultrasound duplex method. The researchers estimated the flow rate of the fistula according to the following formula: $V = \pi r^2 \times V_{average} \times 60$, where V indicates flow in mL/min, r is ray of the segment, and $V_{average}$ is the average of the speeds obtained in cm/s. The flow rate was considered normal when it was greater than 500 mL/min.[16] As this method is different from that used in other trials, a sensitivity analysis was performed to adjust for this inconsistency. Extracted data included the type of access (AVG or AVF), number of patients with thrombosis, and surveillance methods used for the controls.

2.4. Data extraction

Two teams of independent authors extracted the data regarding the baseline studies' characteristics, baseline patients' demographics, studies' quality data, and outcomes of interest. The number of clinical events in each arm was tabulated. The first author (SDH) crosschecked all extracted data, and discrepancies were resolved by consensus among the authors. Outcome events were reported at the longest follow-up duration whenever possible.

2.5. Primary outcomes and definitions

The primary outcome was the development of VA thrombosis. The control group was defined by indirect and various surveillance methods such as dynamic VP measurement and physical examination. Conversely, the interventional group was defined as a noninvasive duplex ultrasound scan or ultrasound dilution that directly measured the flow of VA.

2.6. Risk of bias assessment

Two researchers (SDH and JHL) independently assessed the risk of bias of each trial using the Cochrane Collaboration Risk of Bias tool.[20] We assessed the risk of bias of random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, analysis of incomplete outcome data, selective reporting, and other areas. The risk assessments were categorized as "yes" (low risk of bias), "unclear," or "no" (high risk of bias).[20,21]

2.7. Data synthesis

Comprehensive Meta-Analysis version 2.2.064 (Biostat Inc., Englewood, NJ) was used for the meta-analysis. We calculated the pooled complete resection rate and adverse event rate with 95% confidence intervals (95% CIs) from the enrolled studies. Heterogeneity was determined using the I^2 test, which was developed by Higgins; this test measures the percentage of total variation across studies.[22] I^2 was calculated with the following formula: $I^2\ (\%) = 100 \times (Q\text{-}df)/Q$, where Q is the Cochrane heterogeneity statistic and df signifies the degree of freedom. Negative values for I^2 were set to zero, and an I^2 value greater than 50% was considered substantially heterogeneous (range, 0–100%).[23] Pooled-effect sizes with 95% CIs were calculated using a random-effects model and the DerSimonian and Laird method.[24] These results were confirmed by the I^2 test. A fixed-effects model, which included the inverse variance-weighted (Woolf) method, was used in the sensitivity analyses, including cumulative and 1-study-removed analyses, based on the assumption of a common effect size shared by the studies within each subgroup.[25] Significance was set at $P = .05$ in both models. Publication bias was evaluated using the Begg funnel plot, Egger test of the intercept, Duval and Tweedie trim and fill, and Begg and Mazumdar rank correlation test.[26–29]

2.8. Quality of evidence assessment

We assessed the overall quality of the evidence for our primary outcome using an adapted Grading of Recommendations Assessment, Development, and Evaluation approach.[30] The quality of the evidence for a specific outcome was based on performance versus the limitations of the study design, inconsistency of results, indirectness of evidence, imprecision of results, and publication bias among all studies measuring that particular outcome. The overall quality of the evidence for the outcome was produced by combining assessments from all domains.[31]

3. Results

Overall, 3102 records were initially retrieved from the electronic database search. Of these, 1753 records were excluded based on a review of either the title or abstract. From the remaining screened records, 75 records were retrieved for full-text review (see Fig. 1, PRISMA Flow Diagram). Sixty-six studies were ultimately excluded. Finally, 9 trials reporting outcomes comprising 990 patients (422 women and 568 men) were included in the analysis. Two studies were conducted in the United States,[10,12] 1 in Canada,[13] 1 in Australia,[15] 1 in Brazil,[16] 1 in Spain,[32] 2 in Italy,[14,33] and 1 in the Netherlands.[11] The number of patients ranged from 58 to 196 patients in each study. The mean follow-up period was 25 months (range, 11.5–42.0 months). Please note that the study by Smits et al [11] was broken down into 2 separate studies during the analysis (i.e., Study A and B), as previously described. In addition, the study by Sands et al[10] included both patients with AVFs and AVGs. Therefore, 6 studies consisted of patients with AVFs,[10,14–16,32,33] and 5 studies comprised patients with AVGs.[10–13]

All studies used clinical assessment every dialysis treatment in the access flow surveillance and control groups. The method of access flow measurement was ultrasound dilution in 8 studies[10–15,32,33] and ultrasound duplex in 1 study.[16] The monitoring methods in the control group were dynamic VP[11,13,34] and static pressure.[10,11,35]Table 1 presents other data, including the number of patients, access flow measurement methods, and criteria for intervention.

3.1. Risk of bias in included studies

All of the included studies were described as randomized; however, few authors gave specific details of either the method of randomization or concealment of allocation. The blinding of study subjects and investigators was considered adequate in all but one study. The results are summarized in the risk of bias graphs (Figs. 2 and 3), which present a summary of each risk of bias item for each included study.

3.2. Effect of interventions

Prevalence of diabetes was 29.3% in the interventional group and 30.5% in the control group, and mean patient ages were 60.2 ± 1.00 and 61.9 ± 1.65 years, respectively. A random-effects model pooling of the results showed that the estimated overall pooled risk ratio (RR) of thrombosis favored access blood flow

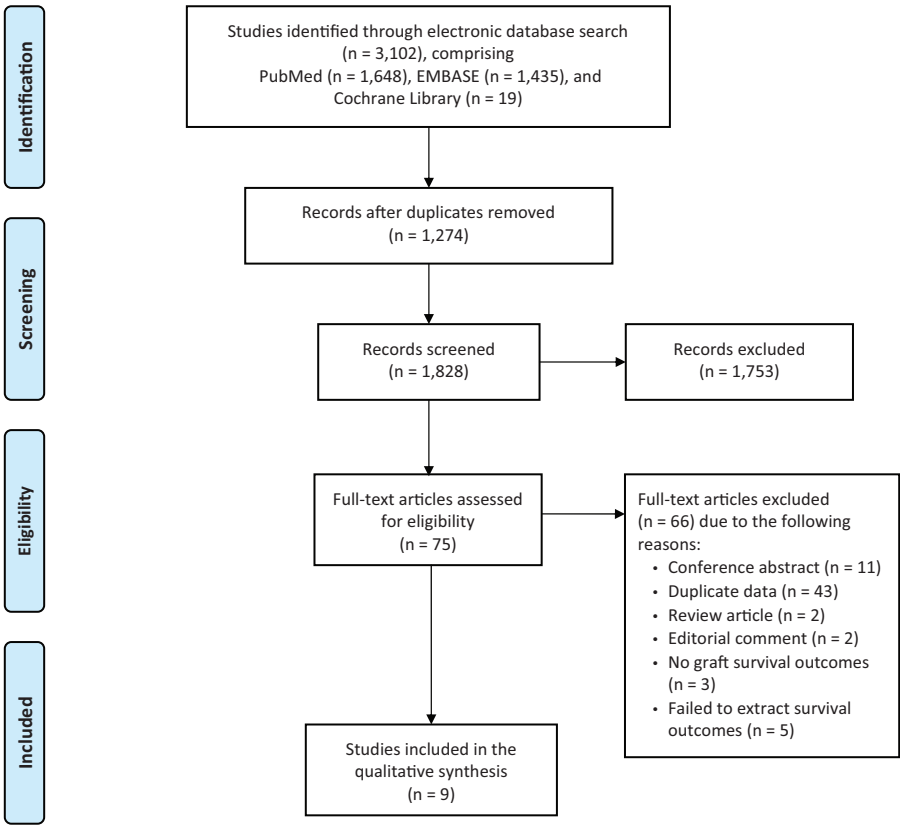

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Figure 1. Flow diagram of the current systematic review (PRISMA Flow Diagram).

Table 1

Important characteristics of the included studies and proportions of patients with thrombosis stratified by groups.

Study	Country/ y	No. of patients	No. of AVFs/ AVGs	Access flow surveillance method	Criteria for intervention, mL/min/% change	Follow-up duration, mo	No. of patients with thrombosis (%)	
							Access flow surveillance group	Control group
Sands et al[10]	USA/1999	112	26/15	US dilution monthly and US duplex every 6 mo	<750/20%	8	14/59	13/53
Smits et al -study A[11]	Netherlands/ 2001	51	0/27	Periodic US dilution	<600/15%	10	4/27 (14.8)	4/24 (24.1)
Smits et al -study B[11]	Netherlands/ 2001	68	0/37	Combination of VP and periodic Qa	<600/15%	12	16/37 (43.2)	10/31 (32.2)
Moist et al[13]	Canada/ 2003	112	0/59	US dilution monthly plus standard surveillance	<650/20%	15	14/59 (23.7)	13/53 (24.5)
Ram et al[12]	US/2003	66	0/32	Monthly Qa measurements by US dilution	<600	15	17/32 (53.1)	16/34 (47.1)
Tessitore et al[14]	Italy/2004	79	43/0	US dilution every 3 mo	<750/25%	60	8/43 (18.6)	16/36 (44.4)
Polkinghorne et al[15]	Australia/ 2006	137	69/0	Monthly Qa surveillance by US dilution	<500/20%	22	6/69 (8.7)	4/68 (5.9)
Scaffaro et al[16]	Brazil/2009	111	53/0	Duplex US surveillance every 3 mo	<500	12	9/53 (17)	14/58 (24.1)
Tessitore et al[33]	Italy/2014	58	28/0	Monthly Qa measurements by US dilution	<750/25	60	2/28 (7.1)	7/30 (23.3)
Aragoncillo et al[32]	Spain/2016	196	98/0	US dilution and duplex US surveillance every 3 mo	<500/25	36	2/98 (2.1)	9/98 (9.1)

AVFs = arteriovenous fistulas, AVGs = arteriovenous grafts, mo = month/s, No. = number, Qa = access blood flow, USA = United States of America, US = ultrasound, VP = venous pressure.

monitoring; however, the result was not statistically significant (Fig. 4). Visual inspection of the forest plot and statistical tests demonstrated considerable heterogeneity among the studies ($P = .08$) (see Figure 1, Supplemental Content, which demonstrates the combined AVG and AVF heterogeneity results, http://links.lww.com/MD/C312). Of the 990 patients, 658 patients had AVFs and 332 had AVGs. In the subgroup analysis of AVGs, the pooled RR of thrombosis was not statistically significant (Fig. 5), and visual inspection of the forest plot and statistical tests demonstrated considerable heterogeneity among the studies in the fixed model (see Figure 2, Supplemental Content, which demonstrates the AVG only heterogeneity results, http://links.lww.com/MD/C312). In contrast, the pooled RR of thrombosis for AVFs was statistically significant (Fig. 6). The forest plot and statistical tests demonstrated considerable heterogeneity among the studies in the fixed model (see Figure 3, Supplemental Content, which demonstrates the AVF only heterogeneity results, http://links.lww.com/MD/C312). Sensitivity analysis was performed to determine whether the different methods used by Scaffaro et al[16] affected the results. When the study by Scaffaro et al[16] was excluded, the pooled RR of thrombosis was 0.535 (95% CI, 0.303–0.946; $P = .031$) for AVF, which was still statistically significant.

4. Discussion

The development of stenosis is the main cause of hemodialysis access thrombosis and failure.[36] The early detection of stenosis enables physicians to perform preemptive angioplasty or surgical correction and decreases the incidence of thrombosis, thus improving patency access rates. The usefulness of access flow surveillance was identified after initial studies reported that it could detect subclinical stenosis, which could not be detected by clinical monitoring.[35,37] Early studies[3,7–9,38–40] showed that

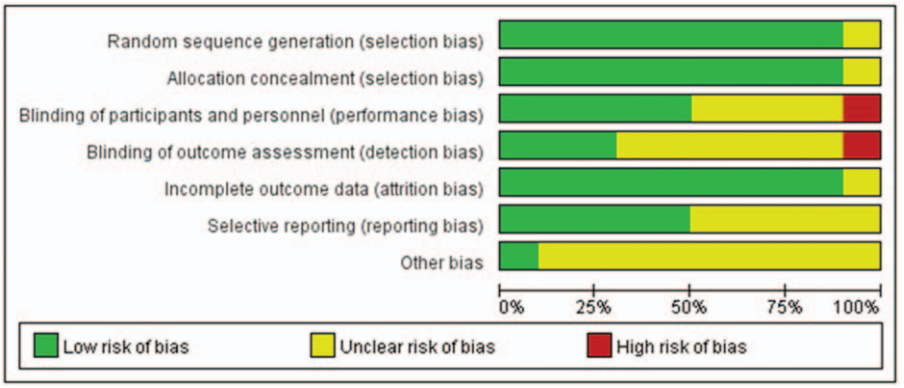

Figure 2. Risk of bias graph. Our assessment of each risk of bias item is presented as a cumulative percentage of all included studies.

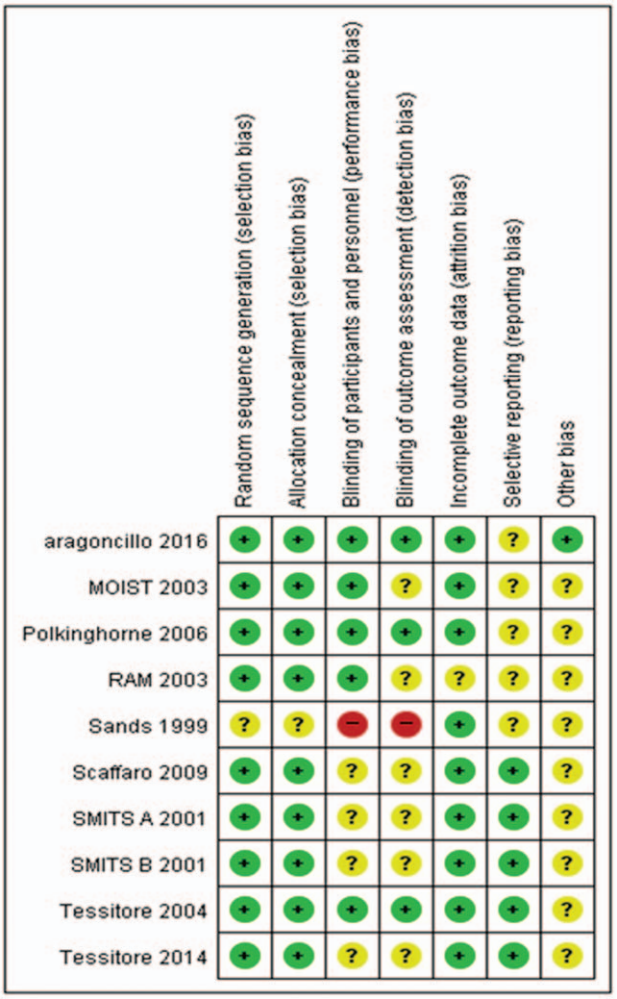

Figure 3. Risk of bias summary. Our assessment of each risk of bias item for each included study. + green circle, good; yellow circle, moderate; - red circle, bad.

low or significantly reduced Qa could be used as a surrogate marker for stenosis and was associated with an increased risk of access thrombosis. These findings led to clinical guidelines[4] suggesting access flow measurement as a surveillance method for AVFs and AVGs. However, early studies were mostly observational studies comparing historical controls, which even included meta-analysis[41]; the inclusion of these studies showed minimal benefit because of the studies' low quality. Subsequently, many RCTs[10–16] were conducted, but they failed to show consistent evidence. The failure of subsequent trials to confirm the benefits made subsequent guidelines[42] tentative or provisional recommendations for access flow surveillance.

The first meta-analysis that included relatively well-designed RCTs was conducted by Tonelli et al[17] in 2008. Four publications of native AVFs and 7 of AVGs met their criteria. The researchers found that AVF flow surveillance reduced the risk of thrombosis by 53%, but AVG flow surveillance showed no benefit. Further, the researchers suggested that access flow surveillance may have differential benefits between AVFs and AVGs and those clinical practice guidelines for graft surveillance might need to be reconsidered. However, the findings of the meta-analysis were only tentatively discussed due to a small sample size in the AVF groups (n = 360 from 4 studies). In addition, it is believed that the strength of the conclusion might have been influenced by the overall quality of the trials analyzed, which was poor to moderate.[43]

Another meta-analysis was reported in 2015 by Muchayi et al,[18] which included 7 studies with 395 AVFs and 332 AVGs. These researchers reported that the risk of thrombosis was 36% lower in fistulas, but 6% higher in grafts, in the access flow surveillance group, yet they failed to detect statistical significance for these associations. The researchers considered the subject number of 395 as underpowered and viewed the result as only hypothesis-generating for future research.

The present study demonstrated that access flow surveillance was effective in the AVF subgroup. The risk of thrombosis was significantly decreased by 43.8% using access flow surveillance. However, no benefit was noted in the AVG subgroups; the risk of thrombosis actually increased by 10.4% using access flow surveillance. These results are in accordance with predictions from previous aforementioned studies. The present study strengthened the statistical power for the analysis of AVFs by adding newly published RCTs[32,33] with relatively good quality. As a result, we analyzed 658 native AVFs, which seemed to contribute to our conclusion regarding fistulas. Our result confirmed the hypothesis that access flow surveillance is beneficial for AVF monitoring. Therefore, we suggest that the current clinical guidelines for AVF flow surveillance be followed.

Apart from our result, there are many reasons why access flow measurement is a reasonable choice for AVF surveillance. In most cases, the method of monitoring to detect AVF stenosis is inaccurate, but physical examination by qualified individuals shows noninferiority as a method of finding dysfunction of VA compared with other surveillance.[44] In a randomized trial,[15] the positive predictive value (PPV) of access flow monitoring for AVF stenosis was twice that obtained with clinical monitoring. This may be due in part to the much lower incidence of stenosis in fistulas than in grafts. In addition, the measurement of static VP showed a lower PPV for stenosis in fistulas.[35] This was likely due to the fistula being a low-pressure system. The disadvantage of VP measurement was also reflected in the NKFKDOQI guidelines.[4]

For AVGs, there is still debate on the usefulness of access flow surveillance, and the recommendation of routine access flow surveillance is still questioned.[45] Favorable results from early studies were not supported by subsequent RCTs.[10–16] The aforementioned meta-analyses reported that AVG flow surveillance reduced thrombosis risk by 6% at best,[17] and it even increased the risk by 6% in 1 study.[18] In the present study, AVG flow surveillance increased the thrombosis risk by up to 10.4%, although these findings were not statistically significant. Of note, the present meta-analysis was unable to improve the statistical power for AVG subgroups, which was the main limitation of our study. This is likely a result of few RCTs having evaluated the benefit of grafts after unfavorable results from early RCTs.

There are several possible reasons for the uncertain or unfavorable effect of AVG flow surveillance. Compared with AVFs, other methods have a relatively good PPV for detecting graft stenosis. For example, an RCT[46] found that clinical monitoring had a 70% PPV for graft stenosis, which is comparable to an 80% PPV for duplex ultrasonography. Moreover, a large prospective study[35] reported that static VP measurement had a 92% PPV for significant stenosis. These high PPVs for clinical monitoring and VP measurement might diminish the advantage of access flow surveillance.

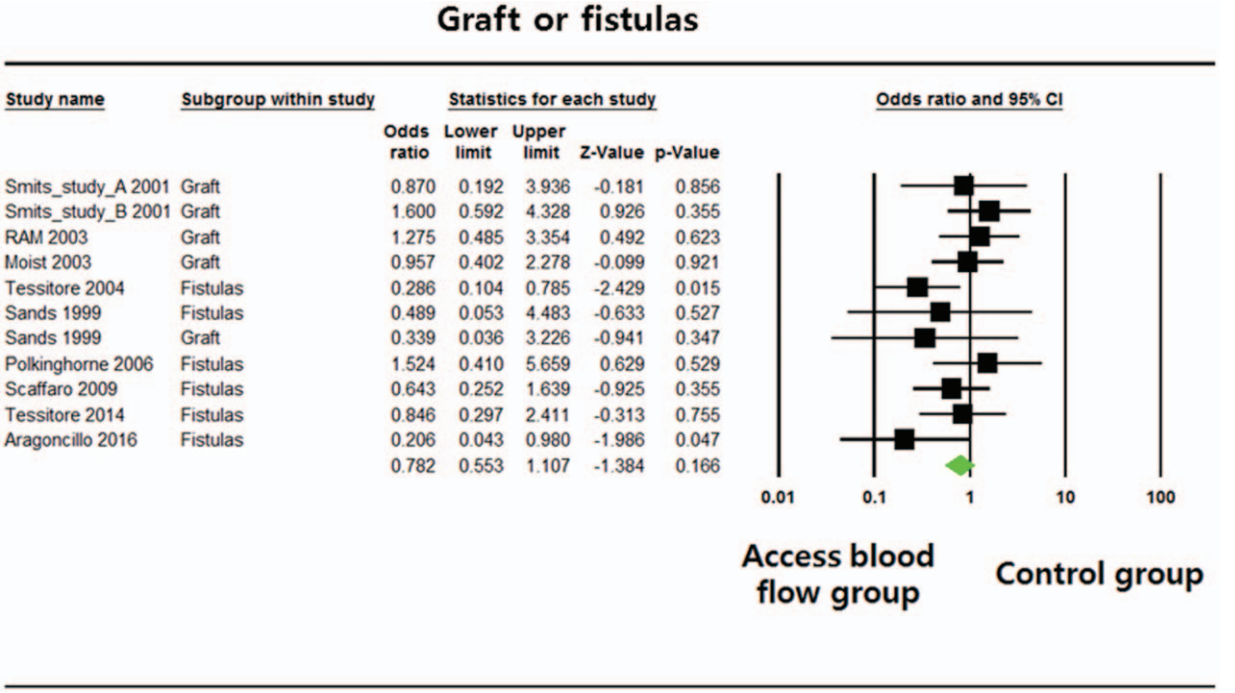

Figure 4. The use of access blood flow monitoring and the risk of thrombosis in end-stage renal disease patients on hemodialysis with grafts or fistulas.

The vessel diameter may also impair the accuracy of access flow surveillance.[47] In the graft model, vessel diameters in the access circuit predominantly control the relationship between Qa and stenosis. As an artery with a narrow diameter mimics stenosis by dominating circuit resistance, the uniform application of the currently recommended cut-off criteria may cause a false-positive interpretation before stenosis is significantly advanced.

Further, the age of grafts may be the most important factor affecting the usefulness of access flow surveillance. A study by Ram et al[48] showed that older grafts were unlikely to thrombosis, even at a low Qa. Large decreases of Qa were also inconsistently associated with thrombosis, suggesting that they were caused by hemodynamic variation rather than by increased stenosis in old grafts. However, new grafts are far more likely to thrombosis earlier. These findings suggest that the benefit of surveillance may be limited to relatively new grafts. This is also supported by a study demonstrating that the benefit of access surveillance and preemptive angioplasty was greatest in grafts less than 3 months old.[49] Thus, the age of grafts should be considered for determining the frequency and method of

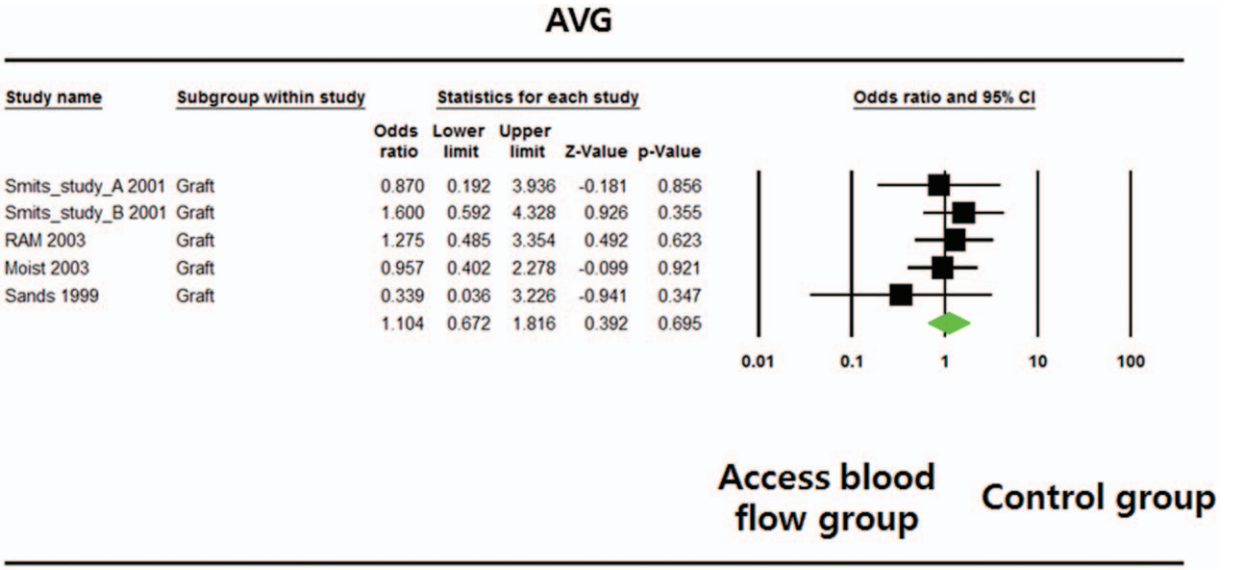

Figure 5. The use of access blood flow monitoring and the risk of thrombosis in end-stage renal disease patients on hemodialysis with grafts only. AVG = arteriovenous graft.

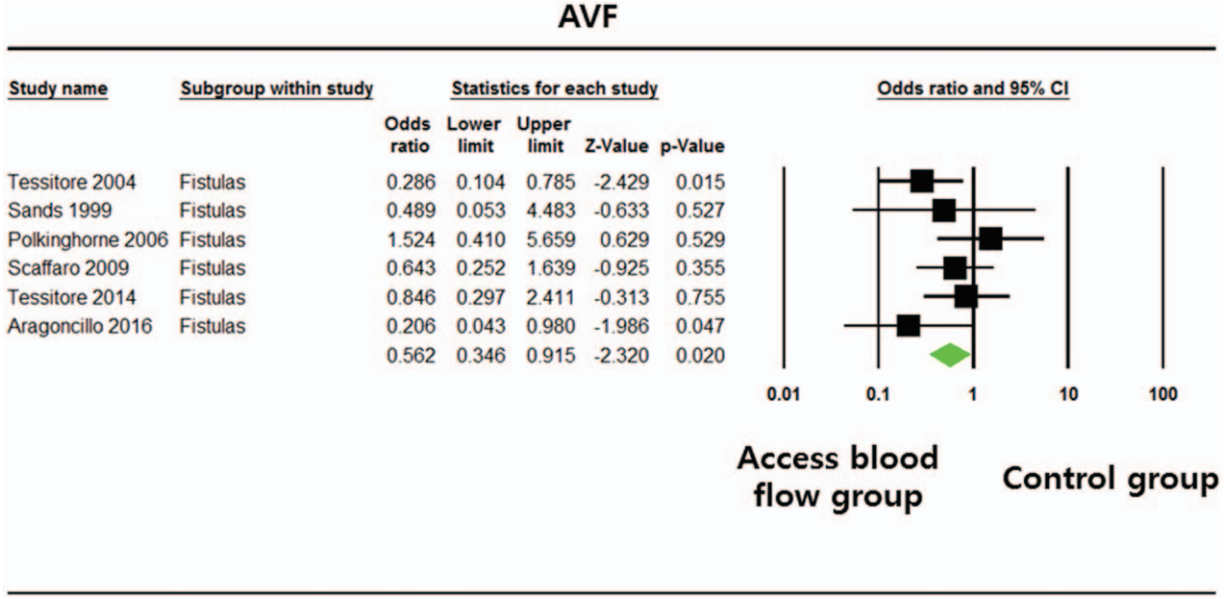

Figure 6. The use of access blood flow monitoring and the risk of thrombosis in end-stage renal disease patients on hemodialysis with fistulas. AVF = arteriovenous fistula.

surveillance. Access flow surveillance may be most valuable for new grafts, but not for old grafts, as there may be frequent false-positive results from old grafts.

Monthly surveillance may not be frequent enough to detect a change before thrombosis occurs. The relationship between Qa and stenosis in grafts is sigmoidal, which means that Qa initially remains unchanged as stenosis progresses, but then rapidly decreases as critical stenosis develops.[50] Relatively narrow arteries dominate circuit resistance and shift the curve to the right, resulting in a longer delay in the decrease of Qa. Assuming stenosis progresses at a constant rate, Qa may change too rapidly to be detected by monthly access flow measurements before thrombosis. Specifically, the window from the decrease of Qa and the development of thrombosis is too fast to be detected by monthly Qa measurement. This is supported by the 20% to 25% false-negative rate observed with graft flow surveillance.[51] The same is true for surveillance with VP measurement.[52]

Numerous studies, including ours, indicate that access flow surveillance lacks the predictive accuracy as a sole surrogate marker for intervention referrals for AVGs. We suggest that the paradigm should be changed for the graft surveillance protocol from a "one-size-fits-all" approach to a "tailored-to-risk" approach. The age of grafts may be an important factor that should be considered in order to determine the frequency and method of surveillance. Depending on the ratio of the artery and vein, the degree of Qa change and the percentage of stenosis are different.[47] The optimal interval of surveillance should also be re-evaluated and tailored to the risk of grafts. It may be better to monitor more frequently than monthly, especially for high-risk grafts, such as new grafts with narrow feeding arteries. The dilution technique is advantageous in that it can be performed during dialysis to reduce time wastage and to identify the problem of the fistula. However, if the dilution technique is used too frequently, the dialysis efficiency may decrease because the blood line is inverted for 10 to 15 minutes during dialysis. Among the noninvasive techniques, there are methods using the reversed position of the blood lines with temperature, dialysate conductivity, or ionic dialysance. Conductivity method measures dialysate conductivity at the dialyzer inlet and outlet.[53] Blood temperature monitors will use the differences in the percentage of recirculation after controlled decrease in temperature in the hemodialysis fluid. The ionic dialysance method is based on ionic dialysance measurements without the need for a saline bolus.[54] Clinical monitoring for every dialysis or VP measurements every week may be more effective than monthly access flow surveillance for high-risk grafts. Duplex ultrasonography with lower frequency may be sufficient for old grafts. We suggest that future studies should focus on surveillance strategies tailored to the risk of grafts.

There are some weaknesses in this study. Other monitoring methods except noninvasive ultrasound dilution or duplex ultrasonography blood flow monitoring were not included in the study. Other instruments can be used to perform blood flow tests directly, but these studies were not included. In addition, the result of treatment according to whether or not thrombosis was detected early or late is unknown.

The present study demonstrated that access flow surveillance was beneficial for reducing the risk of thrombosis in AVFs. This is in agreement with the hypothesis of previous studies.[17,18] The present study's results support the recommendations of the current clinical guidelines for AVF surveillance; however, no benefit was found in the present study for AVGs. The statistical power from our study did not improve for AVGs compared with that in previous studies, which was a limitation of our study. The benefits of graft surveillance may vary according to the different states of grafts. Further studies should stratify the risk of grafts and establish surveillance strategies according to risk. Moreover, we suggest that the current surveillance guidelines for grafts with a "one-size-fits-all" approach may be impractical.

Author contributions

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Statistical analysis: Hwang SD, Lee JH, Lee JH, Song JH.
Drafting of the manuscript: Hwang SD, Lee JH, Song JH.
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Receiving grant: Hwang SD, Song JH.
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