

Dialysis

Ultrasound Monitoring to Detect Access Stenosis in Hemodialysis Patients: A Systematic Review

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Background: Observational studies indicate that routine measurements of access blood flow and use of Doppler ultrasound improve vascular access outcomes in hemodialysis patients, but randomized trials reached conflicting conclusions.

Study Design: Systematic review and meta-analysis.

Setting & Population: Adult hemodialysis patients with arteriovenous accesses. Selection Criteria for Studies: Randomized trials.

Intervention: Screening with access blood flow measurements or Doppler ultrasound.

Outcomes: Thrombosis, access loss, and resource use.

Results: Of 1,613 identified citations and abstracts, 69 full articles were retrieved, and 12 randomized controlled trials comparing access screening (using access blood flow- or ultrasound-based screening) with standard care in a total of 1,164 participants were included. In meta-regression, vascular access type was significantly associated with the relative risk of thrombosis associated with screening ($P < 0.01$), supporting the need to stratify analyses on access type. In the 4 trials that studied arteriovenous fistulas, access blood flow- or ultrasound-based screening significantly decreased the risk of access thrombosis (relative risk [RR], 0.47; 95% confidence interval [CI], 0.28 to 0.77; 360 participants; $I^2 = 8\%$), but not the risk of fistula loss (RR, 0.65; 95% CI, 0.28 to 1.51, $I^2 = 0\%$) or resource use. Conversely, no decrease in risk of thrombosis (RR, 0.94; 95% CI, 0.77 to 1.16; 446 participants; $I^2 = 0\%$) or access loss (RR, 1.08; 95% CI, 0.83 to 1.40; $I^2 = 0\%$) was identified in trials studying grafts.

Limitations: Overall trial quality was moderate to poor, many trials did not report all clinically or economically relevant outcomes, and statistical power generally was low.

Conclusions: There was no evidence that screening with access blood flow measurements or Doppler ultrasound is of benefit to patients with grafts. Access blood flow screening may prevent access thrombosis in arteriovenous fistulas, but may not reduce the risk of access loss or extent of resource use. These findings have implications for clinical practice guidelines and for future research.

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INDEX WORDS: Hemodialysis; vascular access; diagnostic test; meta-analysis.

Because early observational data indicating that routine Doppler ultrasound studies and measurements of access blood flow could detect subclinical stenosis in hemodialysis vascular access, there has been considerable interest in vas-

cular access screening.^{1,2} Although multiple observational studies and economic analyses of access monitoring with access blood flow monitoring or Doppler ultrasound seemed to support implementation of these screening strategies,³⁻⁶ subsequent randomized trials reached conflicting conclusions.

Although created to serve a common purpose, fistulas and grafts have important structural and functional differences that might affect the diagnostic properties of screening or influence the capacity of screening-based intervention to improve clinically relevant outcomes. For example, the high rate of postangioplasty restenosis in grafts compared with fistulas might suggest that even a highly sensitive screening strategy would be of limited clinical benefit in grafts.⁷ These differences argue in favor of evaluating the clinical benefits of screening for fistulas and grafts separately.

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Current clinical practice guidelines recommend routine screening of permanent arteriovenous (AV) access by using regular access blood flow measurements or Doppler ultrasound studies,^{8,9} but several important trials have appeared since these guidelines were last updated. Given the considerable costs and adverse clinical consequences of vascular access dysfunction (and the potential costs of implementing an ineffective screening strategy), this issue is important for patients, clinicians, and policy makers. We performed a systematic review and meta-analysis of randomized trials that examined the clinical utility of access blood flow- or Doppler-based screening for AV hemodialysis access. Our primary objective was to determine whether screening improves clinically relevant outcomes in hemodialysis patients. Our secondary objective was to determine whether any clinical benefits of screening are greater for fistulas than for grafts.

METHODS

This systematic review is reported according to published guidelines.¹⁰ We conducted a comprehensive search to identify all relevant randomized controlled trials of access blood flow and Doppler surveillance in hemodialysis patients with permanent AV access regardless of language or publication status. Five electronic databases, MEDLINE (1966 to May 25, 2007), EMBASE (1988 to May 25, 2007), the Cochrane Library (May 28, 2007), PASCAL (1987 to May 25, 2007), and SCOPUS (May 28, 2007), were searched. The detailed search strategies are provided as supplementary material available with this article at www.ajkd.org. Each citation or abstract was screened by a subject specialist and a methodologist. Any study considered potentially relevant by at least 1 reviewer was retrieved for further review.

The full text of each potentially relevant study was independently assessed by 2 reviewers for inclusion in the review by using predetermined eligibility criteria on a pre-printed form. Studies were eligible for inclusion if they were parallel randomized or quasi-randomized controlled trials including adult hemodialysis patients with permanent AV access (fistulas or grafts) that compared surveillance by means of access blood flow measurements or Doppler ultrasound with another (eg, static venous pressure, dynamic venous pressure, or clinical monitoring) or no form of access surveillance. Additionally, the studies had to report one of the following outcomes: access loss (defined as abandonment of the access), thrombosis (regardless of whether it resulted in access loss), primary patency, secondary patency, resource use (eg, number of procedures and number of hospital days), and adverse events (eg, reaction to contrast media and bleeding). The primary outcome was access thrombosis. Disagreements were resolved by discussion and consultation with a third party.

We assessed the study quality of included trials by using characteristics associated with internal validity (method of allocation concealment,¹¹ randomization technique, double blinding, and description of withdrawals¹²). Allocation concealment was deemed adequate if the study used an off-site or independent source to assign treatment or coded, opaque, sealed envelopes. We also extracted data about funding source given its potential to introduce bias.¹³ Two reviewers assessed each included study independently. Disagreements were resolved with a third party through consensus.

The following properties of each trial were recorded in a database: trial characteristics (country, design, eligibility criteria, sample size, and duration of follow-up), descriptions of access (type, location, age, and prior interventions), surveillance strategy (technique, device, schedule, and criteria for referral for angiography), angiography (technique, reader, and definition of stenosis), type of interventions, and demographics (age, sex, cause of end-stage renal disease, comorbidities, baseline access blood flow, and medications). One reviewer extracted the data. A second reviewer checked the data for accuracy.

We analyzed data using Review Manager 4.2.7 (The Nordic Cochrane Centre, The Cochrane Collaboration, Oxford, England) and Stata 8.2 (StataCorp, College Station, TX). Results were pooled in the primary analysis and then stratified by whether venous pressure monitoring (VP) was or was not used as a cointervention in sensitivity analysis. We calculated the relative risk (RR) and relative rate (treatment rate divided by control rate) to summarize dichotomous and rate data (for outcomes, eg, number of interventions, for which each participant can experience > 1 event), respectively. We assumed a Poisson distribution for the rates, which gave us a method to estimate the natural logarithm for the variance of the relative rates ($1/[\text{number of events in the intervention group} + 0.5] + 1/[\text{number of events in the control group} + 0.5]$).¹⁴ Hazard ratios (HRs) for time-to-event data were extracted directly from the articles. Because of the differences expected between trials, we decided a priori to combine results by using a random-effects model.¹⁵ This method weights each trial by using the inverse sum of each trial's variance and an estimate of between-study variance (τ^2). Statistical heterogeneity was quantified by using the I^2 statistic.^{16,17} The I^2 statistic approximates the percentage of total variability (within and between study) caused by between-study variability. Given our primary hypothesis, we decided a priori to use meta-regression¹⁸ to examine whether access type influenced the association between access blood flow- or Doppler-based surveillance and access thrombosis and to analyze results separately by access type if results of meta-regression were significant. In a sensitivity analysis, we stratified results by method of surveillance. Publication bias¹⁹ was not assessed because of the relatively low number of trials available.

RESULTS

From a total of 1,613 identified citations and abstracts, 69 full articles were retrieved for detailed evaluation (Fig 1). Two of the included studies^{20,21} published multiple reports^{22,23} and thus were in-

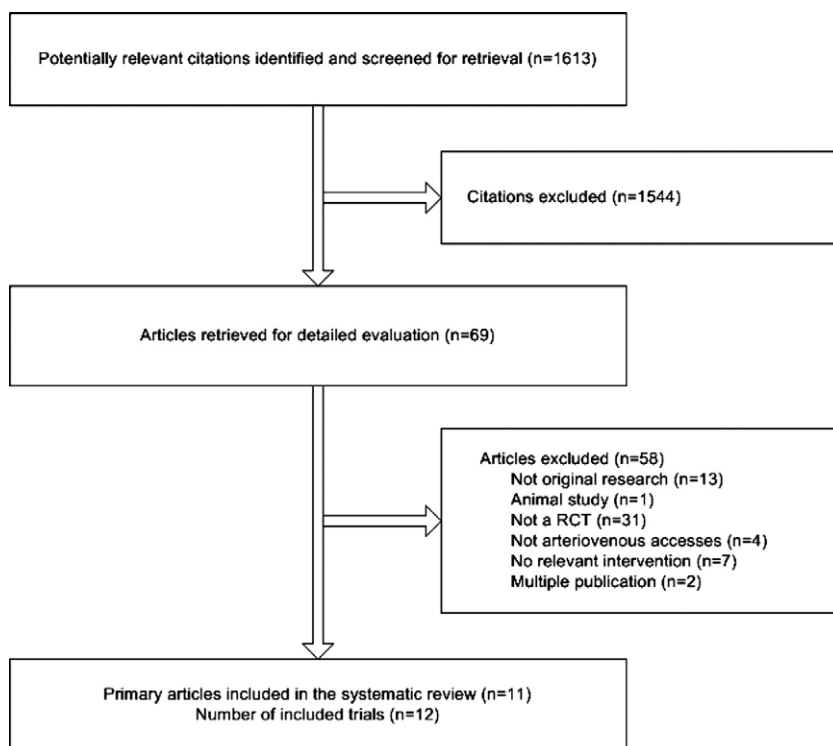


Figure 1. Flow diagram of study selection. Abbreviation: RCT, randomized controlled trial.

cluded only once in the final tally. Last, 5 studies were excluded because they compared different types of accesses²⁴⁻²⁷ or considered VP alone.²⁸

Study Design

Characteristics of included trials are listed in Tables 1 and 2. In total, from 11 primary articles^{7,20,21,29-36} (a total of 1,164 participants), we reported findings from 12 trials after distinguishing between the 2 comparisons reported in Smits et al.³³ Our κ score for agreement was 0.9. All these studies compared access screening (using regular access blood flow measurements or Doppler ultrasound) with standard care during follow-up ranging from 6 to 30 months (median, 15 months). In most studies, participants in both arms received clinical monitoring for access dysfunction as a cosurveillance technique, although 1 study³⁵ used clinical monitoring in only the control group and 1 study²¹ did not report its use. In 5 of 12 trials,^{7,20,30,33,36} standard care also included dynamic venous pressure for both groups. Furthermore, both comparisons in Smits et al.³³ used static VP in addition to dynamic VP. In 2 studies, surrogates of access blood flow (decrease in prescribed blood flow and urea

recirculation) were used for screening during earlier periods of the trial, and ultrasound dilution techniques were introduced later.^{31,32} Finally, 1 trial performed access blood flow surveillance by using Doppler ultrasound in all 3 of its treatment groups every 6 months, but used ultrasound dilution every month in 1 intervention group and venous pressure every month in the other intervention group.³⁴ Last, 2 trials (Smits et al.³³ and Sands et al.³⁴) compared access blood flow–based screening directly with dynamic VP.

Techniques for Access Screening and Interpretation of Angiography

Access blood flow was measured by using ultrasound dilution in 7 trials^{7,31-34,36} (both trials from Smits et al.³³). Doppler ultrasound alone was used in 4 trials,^{21,29,30,35} and a fifth trial used both techniques, but in 2 separate arms.²⁰ All trials that used Doppler ultrasound were conducted solely in grafts. Baseline mean access blood flow was reported in 7 of 12 trials^{7,20,21,30-32,36} (range, 442 to 1,801 mL/min; median, 1,108 mL/min). All trials defined stenosis as a 50% or greater decrease in luminal diameter, except for 1 trial³⁰ that did not provide a definition. Four trials^{7,29,31,36} reported

Table 1. Description of Included Trial Populations

Reference	Country	Type of Access/Criteria for Eligibility	Ultrasound Group				Control Group			
			Access Location/ Mean Access Time (mo)	Mean Baseline Access Blood Flow (mL/min)/Accesses With Prior Interventions (%)	Mean Age (y)/Men (%)	DM (%)/ CVD (%)	Access Location/ Mean Access Duration (mo)	Mean Baseline Qa (mL/min)/Accesses With Prior Interventions (%)	Mean Age (y)/Men (%)	DM (%)/ CVD (%)
Polkinghorne et al, ³⁶ 2006	Australia	Fistula/stable HD for 4 wk & Qa > 500 mL/min	61% FA/36% UA/3% other/23*	1,243/NR*	60/65*	35/28†	62% FA/34% UA/4% other/29*	1,145/NR*	56/71*	28/29†
Tessitore et al, ³¹ 2004	Italy	Fistula/native mature functioning, Kt/V > 1.2, & no prior interventions	FA/17	445/0	58/53	23/40	FA/22	438/0	62/58	23/49
Tessitore et al, ³² 2003	Italy	Fistula/virgin mature functioning & Kt/V > 1.2	FA/10*	451/NR	57/60	23/40	FA/16*	473/NR	62/67	27/33
Sands et al, ³⁴ 1999‡	United States	66% Fistula, 34% graft/NR	NR/18	NR/NR	56/NR	26/NR	NR/28	NR/NR	60/NR	30/NR
Robbin et al, ²⁹ 2006	United States	Graft/no prior interventions in previous mo	17% FA/83% UA/9	NR/52	57/48	52/21†	30% FA/70% UA/9	NR/57	58/34	70/25†
Malik et al, ³⁰ 2005	Czech Republic	Graft/virgin	78% FA/20% UA/2% SC/NR§	769/>0	59/43	47/NR	78% FA/20% UA/2% SC/NR§	NR/>0	58/45	49/NR
Moist et al, ⁷ 2003	Canada	Graft/functioning & Qa > 650 mL/min	68% FA/24% UA/8% L/21	1,116/>0	63/48	36/57†	76% FA/24% UA/24	1,100/>0	66/53	40/68†
Ram et al, ²⁰ 2003	United States	Graft/NR	NR/16/14	1,219/1,253/41/26	55/59/34/51	38/49/NR	NR/9	1,333/35	53/38	56/NR
Smits et al, ³³ 2001 A#	The Netherlands	Graft/NR	93% FA/7% UA/8	NR/NR	61/67	NR/NR	92% FA/8% UA/13	NR/NR	61/38	NR/NR
Smits et al, ³³ 2001 B†	The Netherlands	Graft/NR	90% FA/10% UA/16	NR/NR	60/43	NR/NR	100% FA/18	NR/NR	62/48	NR/NR
Lumsden et al, ²¹ 1997	United States	Graft/functioning & stenosis > 50%	25% FA/72% UA/3% L/NR	1,716/>0	56/53	41/28†	28% FA/72% UA/NR	1,886/>0	58/44	38/19†
Mayer et al, ³⁵ 1993	United States	Graft/NR	57% FA/43% UA/NR	NR/NR	NR/NR	NR/NR	46% FA/54% UA/NR	NR/NR	NR/NR	NR/NR

Abbreviations: HD, hemodialysis; FA, forearm; UA, upper arm; SC, subclavian; L, leg; Qa, access blood flow; DM, diabetes mellitus; CVD, cardiovascular diseases; NR, not reported.

*Median

†Just coronary artery disease.

‡Sands et al compared 3 groups: 1 access blood flow screening group, 1 venous pressure monitoring (VP) screening group, and 1 control group. Because the primary investigators presented this table's data combined for the access blood flow and VP screening groups, we also present this information combined under the ultrasound group heading.

§Pooled results for both groups.

||Ram et al compared 3 groups: 2 access blood flow intervention groups (1 using ultrasound dilution and the other using Doppler ultrasound) and 1 control group. The ultrasound dilution and Doppler ultrasound group data are presented together separated by a virgule.

#Smits et al had 2 trials: 1 used VP as a singular intervention and the other used VP as a cointervention.

Table 2. Description of Included Study Design Characteristics

Reference, Year	Study Design/ Mean Follow-up (mo)	No. of Patients (US/control groups)	US Description/Technique Schedule	US Criteria for Angiography Referral (mL/min)	Control/ Cointervention(s)	CM Criteria for Angiography Referral*	Type of Intervention (% percutaneous/ % surgical)	Thrombosis	Access Loss	Resource Use
Polkinghorne et al, ³⁶ 2006	RCT/18†	69/68	US dilution/every 1 mo	<500 or decrease >20% when Qa < 1,000	None/CM and dVP	Clinical signs, dVPpresc, dQb, dClear	33/66	✓		✓
Tessitore et al, ³¹ 2004	RCT/30†	44/39	US dilution/every 3 mo; Qb monitoring/every dialysis session‡	<750 or >25% decrease	None/CM	dQb > 40 mL/min, recirc urea > 5%	79/21	✓	✓	
Tessitore et al, ³² 2003	qRCT/15†	30/30	US dilution/every 3 mo; Qb monitoring/every dialysis session‡	<850	None/NR	dQb >30 mL/min, Recirc urea >5%	NR/>0	✓	✓	✓
Sands et al, ³⁴ 1999	RCT/6	63/40	US dilution, sVP/every 1 mo	≤600 for fistulas, ≤800 for grafts	None/Qa every 6 mo using Doppler US	sVP	NR/NR	✓		
Robbin et al, ²⁹ 2006	RCT/38†	65/61	Doppler US/every 4 mo	Peak systolic velocity ratio ≥2	None/CM	Clinical signs, dQb dClear	100/0	✓	✓	
Malik et al, ³⁰ 2005	RCT/13	97/92	Doppler US/every 3 mo	Peak systolic velocity ratio >2 or >25% decrease	None/CM and dVP	Clinical signs, dVP200, Recirc urea, dClear	96/4		✓	✓
Moist et al, ⁷ 2003	RCT/<15	59/53	US dilution/every 1 mo	<650 or >20% decrease	None/CM and dVP	dVP200, clinical signs	NR/NR		✓	✓
Ram et al, ²⁰ 2003	RCT/≤28	32/34	US dilution/every 1 mo	<600	None/CM and dVP	Clinical signs, dQb, dVPpresc	NR/NR	✓	✓	✓
Smits et al, ³³ 2001 A	RCT/9	27/24	US dilution/every 2 mo	<600	sVP and dVP/none	sVP, dVP200	87/13	✓		✓
Smits et al, ³³ 2001 B	RCT/8	37/31	US dilution/every 2 mo	<600	None/sVP and dVP	sVP, dVP200	89/11	✓		✓
Lumsden et al, ²¹ 1997	RCT/15	32/32	Doppler US/every 2 mo	≥50% stenosis	None/NR	Recirc urea >15%, dVPpresc	NR/NR		✓	✓
Mayer et al, ³⁵ 1993	RCT/21†	35/35	Doppler US/at 3, 6, 12, and 24 mo	NR	CM/NR	NR	0/100		✓	

Abbreviations: RCT, randomized controlled trial; qRCT, quasi-randomized controlled trial; US, ultrasound; CM, clinical monitoring; dVP, dynamic venous pressure; dVP200, dVP at blood flow of 200 mL/min; dVPpresc, dynamic venous pressure monitoring at prescribed/actual blood flow; sVP, static venous pressure; Recirc urea, access recirculation; Qa, access blood flow; Qb, blood flow; dQb, reduction in Qb; dClear, reduction in urea clearance; this would include decrease in Kt/V and urea reduction ratio; NR, not reported.

*Clinical monitoring criteria for angiography referral: (1) clinical signs, such as loss of thrill, change in bruit/auscultation abnormality, extremity edema, and prolonged bleeding; (2) sVP; (3) dVP200; (4) dVPpresc; (5) dQb; (6) recirc urea; and (7) dClear.

†Median.

‡A small proportion of participants enrolled early in the trial initially were screened by using urea-based access recirculation rather than access blood flow surveillance.

that a radiologist interpreted results of angiography. Thirty-three percent to 100% (median, 87%) of interventions were percutaneous.

Trial Participants

Sample sizes of the individual trials ranged from 51 to 189 participants (median, 92). Mean age of participants ranged from 56 to 65 years, and the proportion of men ranged from 41% to 68%. Most trials (8 of 12) included only patients with AV grafts, usually in the forearm. One trial³⁴ included patients with either fistulas (66%) or grafts (34%). Mean age of AV accesses in study participants ranged from 9 to 26 months at the time of enrollment (median, 17 months). Nine and 6 trials reported baseline prevalences of diabetes mellitus (range, 22% to 61%) and coronary artery disease (range, 23% to 62%), respectively. Only 2 trials^{7,36} reported the proportion of participants who used aspirin, erythropoietin, or warfarin. Six studies reported information for prior access interventions, such as angioplasty or surgical revision. Four of 6 trials reported the percentage with prior access interventions, but only 2 trials^{20,29} reported the specific percentage (38% and 60%). Two trials^{7,31} included participants with virgin accesses.

Trial Quality

Quality assessment of included trials is listed in Table 3. Of these 12 trials, only 3 trials^{7,29,36} used an adequate concealment method of treat-

ment allocation. All were fully randomized except for 1 trial³² that initially assigned blocks of patients, rather than individual patients. Few trials reported blinding patients or investigators; 2 trials^{7,20} blinded participants and 1 trial³⁶ blinded both participants and the individuals who ascertained outcomes. An intention-to-treat design was used in 3 of 12 trials.^{7,20,29} Most (10 of 12) reported some information for withdrawal and loss to follow-up. Of these, only 1 trial³⁵ had a percentage of loss to follow-up greater than 10%. Most trials reported public funding sources, except for 1 trial²⁰ that reported a private source and 3 trials^{31,32,35} that reported no information for funding sources. Agreement on assessment of quality items ranged from 73% to 100%.

Screening Versus No Screening

In meta-regression, vascular access type was significantly associated with the RR of thrombosis associated with screening ($P < 0.01$), indicating that analyses should be performed separately for fistulas and grafts. In a sensitivity analysis, the apparent benefit of screening remained more pronounced in fistulas ($P < 0.05$) when only trials that used access blood flow–based screening were included.

In the primary analysis, trials that evaluated screening with either access blood flow or Doppler were analyzed together after stratification for access type. Three trials of AV fistula screening reported reasons for angiography

Table 3. Quality Assessment of Included Trials

Reference, Publication Year	Concealed Treatment Allocation	Randomized	Double-Blind	Intention to Treat	Description of Loss to Follow-up	Loss to Follow-up (%)	Funding
Robbin et al, ²⁹ 2006	Yes	Yes	No	Yes	Yes	0.8	Public
Polkinghorne et al, ³⁶ 2006	Yes	Yes	Yes	No	Yes	7	Public
Malik et al, ³⁰ 2005	NR	Yes	No	No	Yes	0	Public
Tessitore et al, ³¹ 2004	No	Yes	No	No	Partial	5	NR
Moist et al, ⁷ 2003	Yes	Yes	S	Yes	Yes	0.9	Public
Ram et al, ²⁰ 2003	NR	Yes	S	Yes	Partial	0	Private
Tessitore et al, ³² 2003	No	Q	No	No	No	NR	NR
Smits et al, ³³ 2001A	NR	Yes	No	No	Partial	4	Public
Smits et al, ³³ 2001B*	NR	Yes	No	No	Partial	0	Public
Sands et al, ³⁴ 1999	NR	Yes	No	No	No	NR	Public
Lumsden et al, ²¹ 1997	NR	Yes	No	No	Yes	5	Public
Mayer et al, ³⁵ 1993	NR	Yes	No	No	Yes	11	NR

Abbreviations: NR, not reported or unclear; Q, quasi-randomized; S, single-blind.

*Smits et al had 2 comparisons: 1 used venous pressure monitoring (VP) as a singular intervention and the other used VP as a cointervention.

Table 4. Overall Outcome Summaries in Fistula Trials

Outcomes	No. of Trials	No. of Participants	Overall Summary	I ² (%)
Access blood flow surveillance v none				
Thrombosis	4	360	RR, 0.47* (0.28-0.77)	8
Time to thrombosis	2	158	HR, 0.30* (0.16-0.56)	0
Access loss	2	141	RR, 0.65 (0.28-1.51)	0
Time to access loss	1	60	HR, 0.38* (0.14-0.99)	—
Resources				
No. of angiographies	1	137	RRt, 1.90 (0.95-3.79)	—
No. of PTAs	1	137	RRt, 5.88 (0.69-50.34)	—
No. of surgeries	1	137	RRt, 1.70 (0.71-4.05)	—
No. of revisions	1	60	RRt, 0.80 (0.09-7.43)	—
No. of catheter insertions	1	60	RRt, 0.20* (0.04-0.88)	—
No. of hospitalizations	1	60	RRt, 0.37* (0.16-0.87)	—

Note: Values in parentheses are 95% confidence intervals.

Abbreviations: RR, relative risk; HR, hazard ratio; RRt, relative rate; PTA, percutaneous transluminal angioplasty.

*Statistically significant ($P \leq 0.05$).

referral other than abnormal ultrasound screening results in patients with access blood flow surveillance (24%,³¹ 24%³² [not including 20 participants for whom results of access blood flow screening were unavailable], and 71%³⁶). Nine trials reported the frequency of thrombosis during follow-up, ranging from 6 to 38 months. In the 4 trials that studied fistulas (including two thirds of patients from the trial by Sands et al³⁴), access blood flow surveillance significantly decreased the risk of access thrombosis (RR, 0.47; 95% confidence interval [CI], 0.28 to 0.77; 18% event rate; Table 4; Fig 2). Of 3 trials that reported time to thrombosis, 2 studied AV fistulas. Time to thrombosis in patients with AV fistulas was significantly longer in the surveillance group than in the

control group (HR, 0.30; 95% CI, 0.16 to 0.56). Two fistula trials reported the frequency of access loss by treatment group. In contrast to the findings for access thrombosis, risk of fistula loss was not significantly different in the surveillance and control groups (RR, 0.65; 95% CI, 0.28 to 1.51; 13% event rate; Fig 3). One trial reported time to access loss in patients with fistulas and found a significant benefit of access blood flow surveillance (HR, 0.38; 95% CI, 0.14 to 0.99). Pooled analyses did not suggest that access screening significantly influenced resource use in patients with AV fistulas (Table 4), with the exception of less frequent dialysis catheter insertion and hospitalization (which were reported in a single trial). Only 1 trial³⁶ reported an adverse event

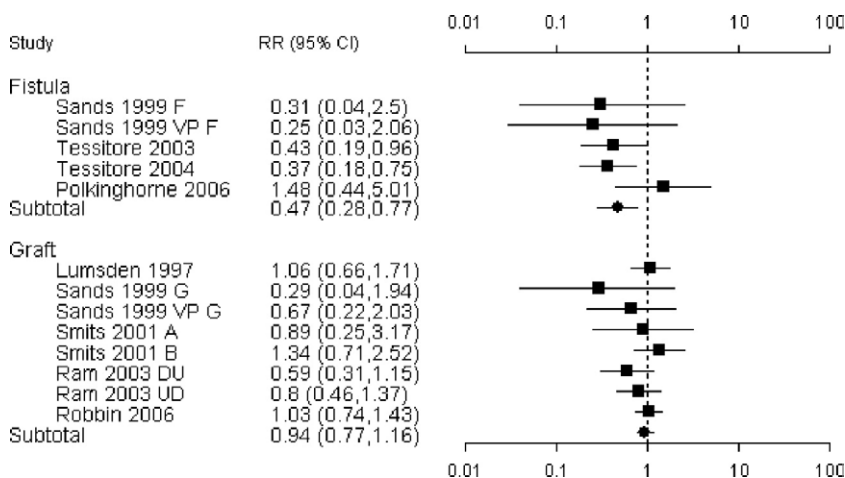


Figure 2. Thrombosis with access blood flow surveillance versus standard care. Standard care could consist of either venous pressure monitoring or no access surveillance. Abbreviations: RR, relative risk; CI, confidence interval; F, fistula; VP, venous pressure; G, graft; DU, Doppler ultrasound; UD, ultrasound dilution.

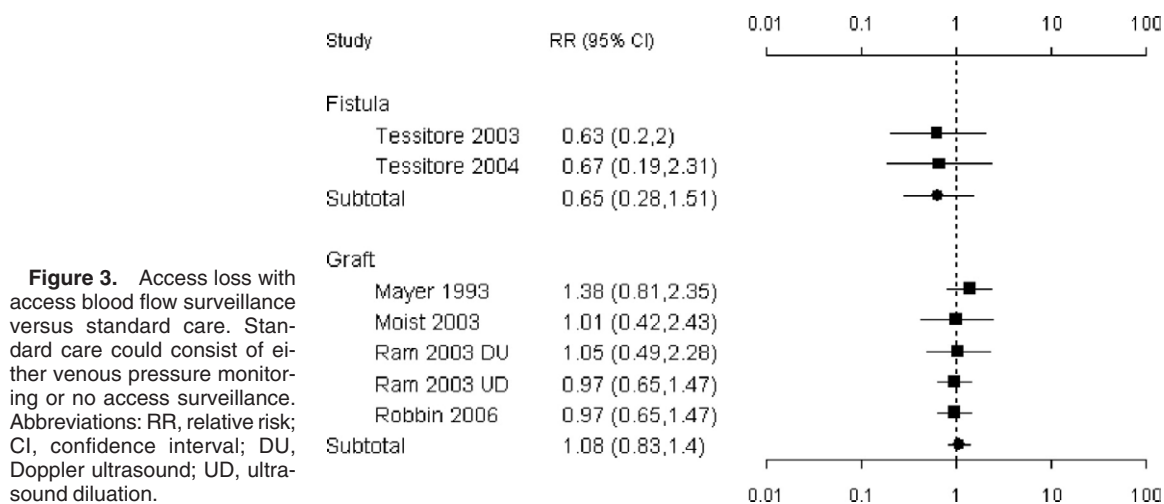


Figure 3. Access loss with access blood flow surveillance versus standard care. Standard care could consist of either venous pressure monitoring or no access surveillance. Abbreviations: RR, relative risk; CI, confidence interval; DU, Doppler ultrasound; UD, ultrasound dilution.

in a patient with a fistula that plausibly was caused by access blood flow surveillance (excess bleeding postdialysis).

Conversely, no decrease in risk of thrombosis (RR, 0.94; 95% CI, 0.77 to 1.16; 43% event rate; Table 5; Fig 2) or time to thrombosis (HR, 1.13; 95% CI, 0.71 to 1.80) was identified in trials studying grafts. Risk of graft loss was not influenced by treatment group assignment (RR, 1.08; 95% CI, 0.83 to 1.40; 35% event rate; Fig 3). Two trials measured time to access loss in patients with grafts and again found no benefit of screening (HR, 0.51; 95% CI, 0.15 to 1.74). Available data suggested that access screening significantly increased certain types of resource use (number of percutaneous interventions; relative rate, 1.29; 95% CI, 1.04 to 1.60) in patients

with grafts while decreasing others (risk of dialysis catheter insertion; relative rate, 0.59; 95% CI, 0.37 to 0.93; Table 5).

In sensitivity analyses, we considered only trials that considered access blood flow–based screening in grafts. We found no significant differences for the outcomes for which data were available: the RR of thrombosis was 0.82 (95% CI, 0.60 to 1.13), and results for resource consumption were unchanged. No trials reported the effect of access blood flow–based screening on graft loss. Results were similar when only trials that studied Doppler-based screening in grafts were considered (data not shown).

Three trials of AV graft screening reported reasons for angiography referral other than abnormal ultrasound screenings in patients with access

Table 5. Overall Outcome Summaries in Graft Trials

Outcomes	No. of Trials	No. of Participants	Overall Summary	I ² (%)
Access blood flow surveillance v none				
Thrombosis	6	446	RR, 0.94 (0.77-1.16)	0
Time to thrombosis	1	126	HR, 1.13 (0.71-1.80)	—
Access loss	4	381	RR, 1.08 (0.83-1.40)	0
Time to access loss	2	315	HR, 0.51 (0.15-1.74)	85
Resources				
No. of angiographies	4	332	RRt, 1.23 (0.94-1.61)	47
No. of PTAs	5	521	RRt, 1.29* (1.04-1.60)	42
No. of surgeries	2	119	RRt, 1.15 (0.79-1.67)	—
No. of catheter insertions	1	101	RRt, 0.59* (0.37-0.93)	—
No. of hospitalizations	1	101	RRt, 0.74 (0.24-2.30)	—

Note: Values in parentheses are 95% confidence intervals.

Abbreviations: RR, relative risk; HR, hazard ratio; RRt, relative rate; PTA, percutaneous transluminal angioplasty.

*Statistically significant ($P \leq 0.05$).

blood flow surveillance (30%,⁷ 33%,²⁰ and 47%³³). Two trials of AV graft screening reported reasons for angiography referral other than abnormal ultrasound screening results in patients screened by using Doppler ultrasound (4%²⁰ and 24%²⁹).

Venous Pressure Monitoring

Stratifying trials by dynamic VP involvement did not significantly affect results. In fistula trials, the RR of thrombosis was 0.39 (95% CI, 0.23 to 0.65) when dynamic VP was not used and 0.25 (95% CI, 0.03 to 2.06) when access blood flow surveillance was compared directly with dynamic VP surveillance. Similarly, in graft trials, the RR of thrombosis was 1.01 (95% CI, 0.77 to 1.32) when dynamic VP was not used and 0.76 (95% CI, 0.33 to 1.74) when access blood flow- or Doppler-based surveillance was compared directly with dynamic VP.

DISCUSSION

Our systematic review identified 12 randomized trials with a total of 1,164 participants. Together, these trials suggest that screening with access blood flow measurements decreases the risk of access thrombosis in AV fistulas, but that neither access blood flow-based nor Doppler-based screening prevents access thrombosis in AV grafts. There was no conclusive evidence that screening with access blood flow prevents access loss in either fistulas or grafts. Although prevention of thrombosis might still be a worthwhile goal if this decreased resource use or improved quality of life in hemodialysis patients, the pooled evidence base does not suggest that access screening achieves these objectives. Given that the efficacy of screening appears to differ for grafts and fistulas, we next discuss the implications of these findings separately for each access type.

We and others have been proponents of vascular access screening based on observational studies indicating that access blood flow monitoring safely detects subclinical stenosis and that stenoses identified in this way are amenable to angioplasty.^{1-3,5} The finding that screening prevents fistula thrombosis is promising and suggests that access blood flow screening is worthy of further evaluation in a large-scale randomized trial with statistical power to detect decreases in the risk of

fistula loss and in resource use (cost and hospitalization). A trial of 850 patients (balanced groups) would have 90% power to detect a beneficial effect of screening consistent with that reported in our meta-analysis (HR, 0.65 for fistula loss), assuming overall fistula loss of 35% during 3 years³⁷ and 10% loss to follow-up in each year. Until such data are available, clinicians and policy makers may choose to offer routine access blood flow screening for patients with fistulas, recognizing that available data suggest only that screening decreases the risk of an intermediate clinical outcome (fistula thrombosis) rather than a more definitive outcome, such as fistula loss. However, given the absence of proven benefit, choosing not to offer routine screening is also reasonable at present.

Screening with either access blood flow measurements or Doppler studies can detect stenosis in AV grafts, but available data do not suggest that this technique decreases the risk of a clinically relevant outcome in this patient population. Findings were similar when no-screening and static-VP strategies were selected as the comparator and in analyses that considered each screening technique separately. Why screening apparently does not benefit patients with grafts despite efficiently detecting stenosis is unclear. However, there is substantial literature about the failure of screening to improve outcomes in other disease conditions, which suggests that such factors as lead-time bias, length-time bias, and ineffective interventions may explain the disparities between results of screening strategies in clinical practice compared with observational studies.³⁸ In the case of grafts, this may translate to the detection of indolent lesions (rather than more clinically relevant stenoses that lead to access loss) or to lack of durable benefit from angioplasty. Either way, presently available data do not support routine screening for patients with AV grafts, a finding that should be considered in future clinical practice guidelines. The lack of benefit from screening despite detection of stenosis, as well as the well-documented risk of recurrent restenosis after angioplasty, suggests that future research should investigate how to improve the efficacy of percutaneous intervention in grafts.

The available literature has several important limitations. First, overall trial quality was moder-

ate to poor. Although it would be difficult, if not impossible, to conduct fully blinded studies of screening strategies, the requirement that personnel assessing outcomes (including angiograms) are unaware of results of screening studies appears feasible. In addition, allocation concealment and intention-to-treat analyses are implemented easily and would materially improve trial quality. Second, our findings suggest that future trials should be restricted to a single access type (either grafts or fistulas, but not both). Although access blood flow is the logical modality for additional study of fistulas, current data do not allow us to determine which (if either) of access blood flow– or Doppler-based screening would be preferable in grafts. Third, many trials did not report all clinically or economically relevant outcomes. We suggest that future studies report thrombosis, access loss, costs, and hospitalization rates by treatment group to facilitate the interpretation of results. Finally, the biggest limitation of the available studies is inadequate statistical power, especially for analyses relating to the effect of screening on fistula loss (which were based on 2 studies with a total of 141 participants). Given the high cost of maintaining vascular access for hemodialysis, as well as the potential consequences of implementing a potentially ineffective screening strategy, we believe that a definitive clinical trial is justified despite its inevitable challenges.

Although systematic reviews have potential limitations, we conducted and reported this analysis according to published guidelines aimed at reducing bias.¹⁰ Nonetheless, as with all systematic reviews, the strength of our conclusions is influenced by the quality of the studies on which they are based. The method limitations noted tend to bias toward type I error (finding an apparent benefit of screening when none exists). Together with the point estimates for the effect of screening on thrombosis and access loss that were close to unity, our conclusions are unlikely to be incorrect for grafts. However, we cannot exclude the possibility that screening does not truly decrease the thrombosis rate in fistulas, supporting our contention that a definitive trial is required to support existing guidelines and inform clinical practice.

In conclusion, there was no evidence that screening with either access blood flow or Dopp-

ler ultrasound is of benefit to patients with AV grafts. Although access blood flow screening appears to prevent access thrombosis in AV fistulas, there was no evidence that screening with access blood flow prevents access loss in patients with fistulas. These findings have implications for clinical practice guidelines and future research.

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SUPPLEMENTARY DATA

Item S1: Description of detailed search strategies.

Note: Supplementary data accompanying this article (doi: 10.1053/j.ajkd.2007.11.025) is available at www.ajkd.org.

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