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Original Investigation

Patency Rates of the Arteriovenous Fistula for Hemodialysis: A Systematic Review and Meta-analysis

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Background: Advantages of the arteriovenous fistula (AVF), including long patency and few complications, were ascertained more than 2 decades ago and may not apply to the contemporary dialysis population.

Study Design: Systematic review and meta-analysis. Estimates were pooled using a random-effects model and sources of heterogeneity were explored using metaregression.

Setting & Population: Patients treated with long-term hemodialysis using an AVF.

Selection Criteria for Studies: English-language studies indexed in MEDLINE between 2000 and 2012 using prospectively collected data on 100 or more AVFs.

Predictor: Age, AVF location, and study location.

Outcomes: Outcomes of interest were primary AVF failure and primary and secondary patency at 1 and 2 years.

Results: 7,011 citations were screened and 46 articles met eligibility criteria (62 unique cohorts; n = 12,383). The rate of primary failure was 23% (95% CI, 18%-28%; 37 cohorts; 7,393 AVFs). When primary failures were included, the primary patency rate was 60% (95% CI, 56%-64%; 13 studies; 21 cohorts; 4,111 AVFs) at 1 year and 51% (95% CI, 44%-58%; 7 studies; 12 cohorts; 2,694 AVFs) at 2 years. The secondary patency rate was 71% (95% CI, 64%-78%; 10 studies; 11 cohorts; 3,558 AVFs) at 1 year and 64% (95% CI, 56%-73%; 6 studies; 11 cohorts; 1,939 AVFs) at 2 years. In metaregression, there was a significant decrease in primary patency rate in studies that started recruitment in more recent years.

Limitations: Low quality of studies, variable clinical settings, and variable definitions of primary AVF failure.

Conclusions: In recent years, AVFs had a high rate of primary failure and low to moderate primary and secondary patency rates. Consideration of these outcomes is required when choosing a patient's preferred access type.

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INDEX WORDS: Hemodialysis; vascular access; fistula; primary failure; patency; epidemiology and outcomes.

Editorial, p. 384

Clinical practice guidelines endorse the arteriovenous fistula (AVF) as the preferred form of vascular access. Its use is associated with fewer complications, improved access survival, and lower risk of mortality compared to an arteriovenous graft or central venous catheter.[1-3] However, the AVF has a high risk of primary failure resulting from early thrombosis and maturation failure.[4,5] The changing patient demographics and increasing proportion of frail elderly patients may further decrease AVF performance. A total of 58% of Canadian patients starting hemodialysis therapy were 65 years or older in 2011 compared to 33% in 1990.[6] Estimates of primary AVF failure, as well as primary and secondary patency, vary considerably in the literature (standardized definitions of these outcomes are presented in Box 1). Recent reports estimate primary AVF failure and 1-year primary patency to be 30%-70% and 40%-70%, respectively.[7-11]

Knowledge of AVF performance not only informs patient consent and quality improvement initiatives, but more importantly, guides patient and clinician decision making. Better understanding of AVF

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performance will help explain the discrepancy in AVF use between best practice recommendations and current practice and help re-evaluate standards for what is deemed "best practice."[12] In the present study, we conducted a systematic review and pooled estimates of primary failure, as well as primary and secondary patency rates (1 and 2 year), from prospectively collected data published between January 2000 and June 2012. We aimed to improve the precision of AVF performance estimates, as well as explore the influence of study and patient characteristics on overall parameter estimates. In subgroup analyses, we examined the effect of AVF location (lower vs upper arm), age (elderly vs nonelderly), and study location (North America vs Europe) on primary failure, primary patency, and secondary patency rates.

METHODS

Protocol

We conducted and reported this systematic review according to published guidelines using a prespecified protocol; see Table S1 (provided as online supplementary material) for our MOOSE (Meta-analysis of Observational Studies in Epidemiology) reporting guidelines checklist.[13,14]

Studies Eligible for Review

We formulated study inclusion and exclusion criteria a priori. We included any study that collected data prospectively (observational cohort studies or randomized controlled trials) and followed up patients for at least 3 months. We deemed studies eligible only if they described 100 or more AVFs in patients with chronic kidney disease. We included only full-text English-language articles published after December 31, 1999. Studies must have reported information on one or more of the following: (1) primary failure, (2) primary patency (1 and/or 2 years), or (3) secondary patency (1 and/or 2 years). We excluded studies of peritoneal dialysis and children and adolescents (aged <18 years).

Study Definitions

Unless otherwise specified, all vascular access definitions were in accordance with the Society of Vascular Surgery/American Association of Vascular Surgery and the North American Vascular Access Consortium (Box 1).[4,15] When definitions were not in agreement between the 2 documents, we used the consortium definitions. When an outcome definition was unclear, not reported, or different from the mentioned definitions, it was documented within our tables.

Data Sources and Study Selection

We designed and implemented a systematic literature search to identify all relevant published reports in MEDLINE (Ovid and PubMed) from January 1, 2000, to June 30, 2012. The search strategy included a combination of key words and MeSH (Medical Subject Headings) terms (Table S2). We also used the related-articles feature in PubMed. One investigator (A.A.A.) screened all titles and abstracts obtained through the search syntax to identify potentially relevant articles. We retrieved the full text of these articles to further assess their suitability for inclusion in this review. Bibliographies of selected articles were searched manually to identify any additional relevant studies.

Box 1. Outcome Definitions

- Primary failure: immediate failure of AVF within 72 h of surgery, early dialysis suitability failure, or late dialysis suitability failure (NAVAC definition)[4]
  - ◇ Early dialysis suitability failure: this is an AVF for which, despite interventions (radiologic or surgical), it was not possible to use the AVF successfully for hemodialysis by the third month following its creation (NAVAC definition)[4]
  - ◇ Late dialysis suitability failure: this is an access for which, despite interventions (radiologic or surgical), it was not possible to use the AVF successfully for hemodialysis by the sixth month following its creation (NAVAC definition)[4]
- Primary patency: the interval from the time of access creation until first access thrombosis or any intervention to maintain or restore blood flow (NAVAC and SVS definition)[4,15]
- Functional primary patency: the time from the first successful 2-needle cannulation until first intervention or access failure (NAVAC and SVS definition)[4,15]
- Secondary (cumulative) patency: the time from access creation until access abandonment. Secondary patency was not terminated by surgical or interventional radiology procedures to maintain or restore patency (NAVAC and SVS definition)[4,15]
- Functional secondary patency: the interval from first successful 2-needle cannulation for hemodialysis treatment to access abandonment (NAVAC and SVS definition)[4,15]

Abbreviations: AVF, arteriovenous fistula; NAVAC, North American Vascular Access Consortium; SVS, Society of Vascular Surgery.

Data Extraction and Quality Assessment

Two reviewers (A.A.A. and either J.C.Z., S.D.K., or S.M.T.) independently extracted data using a standardized form. This was done in duplicate to increase accuracy and reduce measurement bias. If extracted data differed between the 2 reviewers, we resolved disagreement by consensus or with the help of a third reviewer (J.C.Z., S.D.K., or S.M.T). We extracted data on the following: (1) study characteristics, including year of publication, country, study design, and number of AVFs; (2) methodological characteristics, such as outcome definitions, follow-up period, and loss to follow-up; (3) patient characteristics, including location of upper-extremity AVFs, mean age, mean time between AVF creation and 2-needle cannulation, and proportions of men, whites, and patients with peripheral vascular disease, diabetes, and upper-arm AVFs; (4) assessed risk of bias among included studies, exploring participation, patient selection, attrition, exposure and outcome measurements, confounding, and selective reporting using previously validated methods (Item S1)[16,17]; and (5) primary failure and/or patency rates as defined earlier (Box 1). (Note: The term "rate" is not a true rate [ie, event per person-time] but is used because of convention in the literature.) Most studies reported patency rates using life tables or in text, as opposed to Kaplan-Meier curves. When patency rates were reported using only Kaplan-Meier plot, we estimated the patency rate from the curve.

Data Analysis

Primary outcomes were rates of primary failure, primary patency, and secondary patency. Secondary outcomes were rates of functional primary and secondary patency. We calculated the 95% confidence interval (CI) for each study estimate using the Wilson score method.[18] The Wilson score interval has been shown

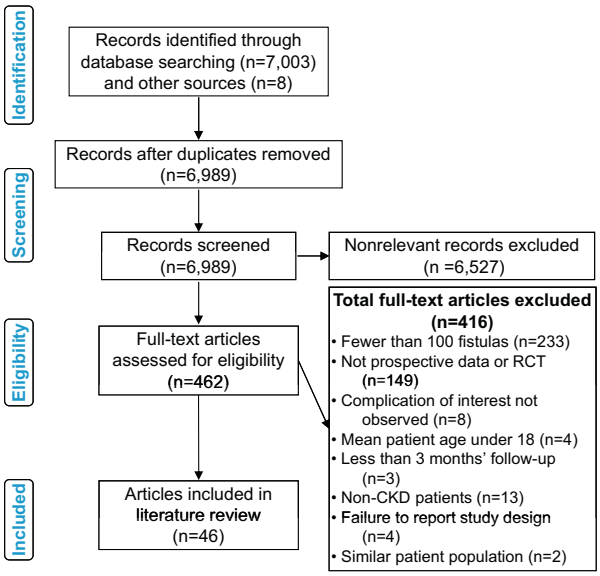

Figure 1. Flow diagram of study eligibility and inclusion. Abbreviations: CKD, chronic kidney disease; RCT, randomized controlled trial.

to provide excellent coverage and has better performance than the standard Wald interval.[19,20]

We pooled rates of primary failure, as well as rates of primary and secondary patency, using a random-effects meta-analysis using a linear mixed model. This method assumes that the observed rates follow a normal distribution. We accounted for correlation between subgroup estimates from the same study, as well as estimates from different articles but from the same dialysis facility. We used the I^2 statistic to measure the proportion of total variation in study estimates that is due to heterogeneity rather than sampling error.[21] When reported, we calculated the pooled estimate for prespecified subgroups, including AVF location (lower vs upper arm), age (elderly vs nonelderly as defined in the selected study), and study location (North America vs Europe). We performed analyses using SAS, version 9.2 (SAS Institute Inc) PROC MIXED procedure. This method allowed us to specify covariates in random-effects univariable metaregression. We explored heterogeneity between risk estimates according to mean patient age; proportions of men, patients with diabetes, and patients with peripheral vascular disease; number of AVFs; proportion of upper-arm AVFs; recruitment start date; and publication year. In sensitivity analyses, we excluded studies that: (1) were published 2000 or later but recruited patients prior to 2000; (2) in which sample size was fewer than 100 AVFs; (3) and in which the study question was asked after data collection (ie, retrospective design). We performed additional sensitivity analyses for patency rate and excluded studies that did not report whether primary failures were included/excluded in the patency calculation. In order to justify our analyses, we required at least 3 independent estimates per subgroup. We used a 2-sided P value and considered $P < 0.05$ to be statistically significant.

RESULTS

Included Studies

We screened 7,011 citations and retrieved 462 full-text articles to assess for eligibility. Forty-two articles met our criteria for review; however, 2 studies were excluded due to insufficient information on study design.[22,23] Three eligible articles were published using data from the US Renal Data System Dialysis Mortality and Morbidity Study (DMMS) Wave 2; however, because study patients in these articles significantly overlapped, we included results from only the study with the largest sample of AVFs.[24-26] Details of the study selection are shown in Fig 1. We identified 8 additional studies through manual search of bibliographies of selected articles. Thus, we included 46 articles (44 studies) reporting on 66 cohorts (62 unique cohorts; n = 12,383 AVFs) published after January 1, 2000, with patient recruitment between 1985 and 2008. Characteristics of each article are described in Tables 1 and 2. Twenty articles reported outcomes from the United States; 7, from Italy; 5, from the United Kingdom; 4 each, from Canada and the Netherlands; 3, from Turkey; and 1 each, from Croatia, Saudi Arabia, and Slovenia. One article by the DOPPS (Dialysis Outcomes & Practice Patterns Study) examined AVF outcomes from European countries in DOPPS in addition to US outcomes.[27] Follow-up was not reported for 18 articles. In the other 28 articles, median loss to follow-up was 2% (range, 0%-22%; interquartile range [IQR], 8%).

Patient Population

Patient demographic data, comorbid conditions, and site of AVF creation were not always reported in the selected studies. However, when reported, median age was 58.9 years (range, 36-74 years; IQR, 9.03 years; 54 of 66 cohorts reported this outcome). The median proportion of men was 58% (range, 34%-82%; IQR, 12%; 63 of 66 cohorts). Within selected studies, median proportions of patients with diabetes and peripheral vascular disease were 43% (range, 0%-81%; IQR, 25%; 62 of 66 cohorts) and 16% (range, 3%-53%; IQR, 12%; 32 of 66 cohorts), respectively. Median proportions of studies with upper-arm AVFs and white patients were 49% (range, 0%-100%; IQR, 68%; 56 of 66 cohorts) and 63% (range, 13%-100%; IQR, 31%; 37 of 66 cohorts), respectively.

Risk of Bias

Many studies reported methods inadequately and definitions were not always consistent across studies. Table S3 lists definitions of primary failure in the included studies when reported. When calculating the primary patency rate, 14 articles included primary failures, 8 articles excluded primary failures, and 5 studies did not report whether primary failures were included or excluded in the definition. Similarly, when calculating secondary patency, 12 articles included primary failures, 6 articles excluded primary failures, and 3 articles did not report the exclusion or

Table 1. Study Characteristics

Study	Country	Recruitment Start	Cohort Subset[a]	Follow-up (mo)	No. of AVFs	Upper Arm[b]	Age (y)	Male Sex	White	DM	PVD
Quintaliani et al[43] (2000)	IT	—	Lower arm	40.8	124	0%	57.5	56%	—	0%	—
Wolowczyk et al[44] (2000)	UK	1985	Lower arm	—	208	0%	63.0	55%	—	14%	—
Allon et al[9] (2001)	US	1998	All	—	138	46%	—	64%	40%	54%	—
Gibson et al[45] (2001)	US	1996	All	11.0	492	—	66.0	53%	66%	54%	—
Dixon et al[10] (2002)	US	1992	Lower arm	—	88	0%	52.0	82%	95%	45%	15%
	US	1992	Upper arm	—	117	100%	59.0	55%	54%	52%	28%
Huber et al[46] (2002)	US	1999	All	—	117	75%	53.0	51%	60%	49%	—
Malovrh[47] (2002)	SI	1993	All	3.0	116	—	51.4	47%	—	—	—
Pisoni et al[27] (2002)	US	1996	US	—	177	—	60.5	53%	62%[f]	46%	23%
	DE, ES, FR, IT, UK	1998	European	—	429	—	60.7	57%	99%[f]	22%	19%
Puskar et al[48] (2002)	HR	1992	All	—	463	5%	—	58%	—	6%	—
Ravani et al[49] (2002)	IT	1995	All	20.4	197	19%	65.7	59%	—	22%	—
Feldman et al[50] (2003)	US	1994	All	—	237	—	56.0	68%	—	34%	—
Bonforte et al[51] (2004)	IT	1991	Lower arm	27.0	112	0%	71.0	50%	—	22%	—
Perera et al[52] (2004)	US	1999	All	—	100	50%	55.0	75%	—	50%	—
Ravani[53] (2004)	IT	1997	All	42.0	513	—	66.3	58%	98%	27%	—
Zeebregts et al[54] (2004)[c]	NL	2000	Clip	14.5	51	0%	58.9	69%	—	19%	—
	NL	2000	Suture	11.4	56	0%	58.9	69%	—	19%	—
Lok et al[55] (2005)	CA	1995	Elderly	—	196	53%	74.0	69%	69%	30%	10%
	CA	1995	Nonelderly	—	248	43%	46.0	65%	63%	29%	8%
Manns et al[56] (2005)	CA	1999	All	—	157	40%	63.6	72%	—	48%	22%
Shahin et al[57] (2005)	US	1992	All[d]	21.0	146	51%	54.9	58%	93%	49%	39%
	US	1999	All[e]	19.0	76	61%	57.6	59%	90%	57%	53%
Vernaglione et al[58] (2005)	IT	1995	Lower arm	42.1	105	0%	63.8	52%	100%	23%	19%
Wells et al[59] (2005)	UK	2002	All	—	136	28%	—	70%	—	17%	—
Zeebregts et al[60] (2005)	NL	1999	Upper arm	20.1	100	100%	59.2	59%	—	24%	—
Elsharawy[61] (2006)	SA	2003	All	—	126	69%	36.0	64%	—	41%	—
Erkut et al[62] (2006)	TR	1995	Lower arm	47.0	298	0%	45.0	75%	—	12%	—
Jennings[63] (2006)	US	2003	All	11.0	134	91%	61.0	39%	—	68%	—
Lok et al[7] (2006)	CA	1995	Derivation cohort	6.0	422	39%	—	—	—	—	16%
	CA	2004	Validation cohort	6.0	445	—	58.0	68%	66%	18%	8%
Korten et al[64] (2007)	NL	2000	Lower arm	—	148	0%	65.0	55%	—	31%	—
Chan et al[24] (2008)	US	1996	All	—	318	—	62.2	53%	58%	53%	22%
Dember et al[65] (2008)[c]	US	2003	Clopidogrel	6.0	385	47%	52.7	62%	50%	49%	4%
	US	2003	Placebo	6.0	373	45%	54.5	63%	54%	47%	3%
Field et al[66] (2008)	UK	2003	Lower arm	—	210	0%	61.7	59%	94%	33%	31%
	UK	2003	Upper arm	—	79	100%	61.0	34%	94%	43%	47%
Huijbregts et al[67] (2008)	NL	2004	All	11.0	491	40%	64.6	62%	78%	33%	10%
Peterson et al[68] (2008)	US	2001	All	—	205	55%	—	60%	14%[f]	52%	15%
Pflederer et al[69] (2008)	US	2004	All	—	321	37%	64.5	65%	—	43%	—
	US	2004	AVF-T	—	161	97%	63.3	61%	—	45%	—
Tessitore et al[70] (2008)[g]	IT	2002	All	—	97	18%	65.1	64%	—	19%	—
	IT	2002	All	—	62	21%	63.4	55%	—	31%	—
Koksoy et al[71] (2009)	TR	2003	AVF-T	28.0	50	100%	54.7	52%	—	32%	—
	TR	2003	Upper arm	28.0	50	100%	54.8	60%	—	24%	—

(Continued)

Table 1 (Cont'd). Study Characteristics

Study	Country	Recruitment Start	Cohort Subset[a]	Follow-up (mo)	No. of AVFs	Upper Arm[b]	Age (y)	Male Sex	White	DM	PVD
Maya et al[72] (2009)	US	2000	AVF-T	—	67	100%	56.0	52%	16%	58%	12%
	US	2000	Upper arm	—	322	100%	56.0	48%	23%	53%	16%
Weber et al[73] (2009)	CA	2003	All	—	125	54%	66.0	58%	54%	44%	—
Ferring et al[74] (2010)[c]	UK	2006	Clinical	—	101	37%	—	66%	67%	34%	22%
	UK	2006	Ultrasound	—	107	41%	—	62%	71%	43%	14%
Gonzalez et al[75] (2010)	US	2007	AVF-T	10.7	33	100%	54.5	46%	70%	81%	6%
	US	2007	Lower arm	10.7	75	0%	54.3	52%	72%	56%	4%
	US	2007	Upper arm	10.7	35	100%	50.2	51%	75%	68%	3%
Korkut & Kosem[76] (2010)	TR	2004	AVF-T	48.0	350	100%	57.8	44%	—	51%	30%
Paul et al[77] (2010)	US	2003	AVF-T	17.8	176	100%	61.0	34%	—	52%	—
Pisoni et al[78] (2010)	US	2000	No statin	—	218	100%	55.0	52%	23%[f]	44%	16%
	US	2000	On statin	—	99	100%	58.0	39%	22%[f]	75%	16%
Ravani et al[79] (2010)	IT	1997	All	42.0	473	18%	66.3	58%	98%	27%	—
Schenk[80] (2010)	US	2008	All	—	131	83%	—	—	—	—	—
Jennings et al[81] (2011)	US	2003	Elderly	17.0	461	38%	73.0	49%	—	60%[h]	—
	US	2003	Nonelderly	—	618	—	53.0	52%	—	56%[h]	—
Lee et al[82] (2011)	US	2005	1 intervention	—	54	70%	—	70%	30%	56%	13%
	US	2005	2+ interventions	—	23	61%	—	52%	13%	70%	39%
	US	2005	0 intervention	—	96	69%	—	82%	26%	43%	19%
Swindlehurst et al[83] (2011)	UK	2000	Elderly	24.6	246	71%	74.0	62%	62%	41%	—
	UK	2000	Nonelderly	27.9	89	71%	49.0	55%	47%	29%	—

Abbreviations: AVF, arteriovenous fistula; AVF-T, transposed arteriovenous fistula; CA, Canada; DE, Germany; DM, diabetes mellitus; ES, Spain; FR, France; HR, Croatia; IT, Italy; NL, the Netherlands; PVD, peripheral vascular disease; SA, Saudi Arabia; SI, Slovenia; TR, Turkey; UK, United Kingdom; US, United States.

[a]All refers to the entire study cohort.

[b]Upper arm (%) refers to the percentage of upper-arm fistulas in each cohort.

[c]Refers to a randomized control trial.

[d]Patients who did not receive access flow monitoring.

[e]Patients who received regular access flow monitoring.

[f]Percentage white was estimated based on 78% of the patient population being African American (ie, not black).

[g]Tessitore et al collected data for 159 hemodialysis patients with mature AVFs, 397 followed up by unsystematic clinical monitoring, and 462, by adding Qa (vascular access flow rate) surveillance to monitoring.

[h]Percentage of patients whose diabetes was the cause of kidney failure. The actual proportion of patients with diabetes in this cohort likely is higher than reported here.

inclusion of primary failures. When studies did not report the inclusion or exclusion of primary failures in the calculation of the patency rate, we assumed that primary failures were excluded. In sensitivity analyses, there were no significant differences in estimates of patency rates when we excluded studies that did not report the inclusion of primary failures. The majority of studies were at moderate or high risk of bias in all domains assessed. The distribution of components that described study quality is summarized in Table 3 (see also tables *a* and *b* of Item S2 for elements of bias by study).

Meta-analysis

Primary Failure

The pooled estimate for primary failure rate was 23% (95% CI, 18%-28%; 37 cohorts; 7,393 AVFs; Fig 2). This estimate must be interpreted cautiously given the high degree of heterogeneity ($I^2 = 97\%$) among studies. In subgroup analyses, the risk of primary failure was 28% (95% CI, 20%-37%; 12 cohorts; 1,447 AVFs) for lower-arm and 20% (95% CI, 12%-28%; 14 cohorts; 1,586 AVFs) for upper-arm AVFs ($P < 0.001$; Fig S1). The risk of primary failure was 37% (95% CI, 32%-41%; 5 cohorts; 723 AVFs) among elderly and 27% (95% CI, 8%-46%; 5 cohorts; 909 AVFs) for nonelderly patients ($P = 0.001$; Fig S2). The risk of primary failure was 22% (95% CI, 11%-33%; 24 cohorts; 4,615 patients) for North American and 26% (95% CI, 19%-33%; 11 cohorts; 2,302 AVFs) for European studies ($P = 0.4$; Fig S3). When sources of heterogeneity were explored in metaregression, we noted an increase in risk of primary failure as sample size increased ($P < 0.001$). However, we found that the risk of primary failure decreased with more recent publication date ($P = 0.002$) and as the proportion of

Table 2. Data Extracted for Each Study

Study	Incident/Prevalent	Study Design	Data Type[a]	PF	1-y Outcome				2-y Outcome			
					PP	SP	FPP	FSP	PP	SP	FPP	FSP
Quintaliani et al[43] (2000)	Prevalent	Retrospective	C	—	—	—	—	X	—	—	—	—
Wolowczyk et al[44] (2000)	Incident	Prospective	T	X	X-	—	—	—	X-	—	—	—
Allon et al[9] (2001)	Incident	Retrospective	C	X	X	X	—	—	—	—	—	—
Gibson et al[45] (2001)	Incident	Retrospective	T	—	X	X	—	—	X	X	—	—
Dixon et al[10] (2002)	Incident	Retrospective	T	X	X	X	—	—	X	X	—	—
Huber et al[46] (2002)	Incident	Prospective	—	X	—	—	—	—	—	—	—	—
Malovrh[47] (2002)	Incident	Prospective	—	X	—	—	—	—	—	—	—	—
Pisoni et al[27] (2002)	Both	Retrospective	T	—	—	—	X	—	—	—	—	—
Puskar et al[48] (2002)	Incident	Prospective	C	X	X	—	—	—	X	—	—	—
Ravani et al[49] (2002)	Incident	Prospective	T	X-	X	X	—	—	X	X	—	—
Feldman et al[50] (2003)	Incident	Prospective	—	X-	—	—	—	—	—	—	—	—
Bonforte et al[51] (2004)	Incident	Prospective	C	—	X-	—	—	—	X-	—	—	—
Perera et al[52] (2004)	Incident	Retrospective	T	X	X-	X-	—	—	X-	X-	—	—
Ravani[53] (2004)	Incident	Retrospective	C	—	—	—	X	—	—	—	X	—
Zeebregts et al[54] (2004)[b]	Incident	Prospective	C	—	X	X	—	—	—	—	—	—
Lok et al[55] (2005)	Incident	Retrospective	T	X	X	X	—	—	X	X	—	—
Manns et al[56] (2005)	Incident	Retrospective	—	X-	—	—	—	—	—	—	—	—
Shahin et al[57] (2005)	Incident	Retrospective	C	—	X	X	—	—	X	X	—	—
Vernaglione et al[58] (2005)	Incident	Prospective	C	—	X-	—	—	—	X-	—	—	—
Wells et al[59] (2005)	Incident	Prospective	T	X-	X-	—	—	—	—	—	—	—
Zeebregts et al[60] (2005)	Incident	Prospective	T	—	X	X	—	—	X	X	—	—
Elsharawy[61] (2006)	Incident	Prospective	—	X	—	—	—	—	—	—	—	—
Erkut et al[62] (2006)	Incident	Retrospective	T	—	X-	—	—	—	X-	—	—	—
Korten et al[64] (2007)	Incident	Retrospective	T	X-	X	X	—	—	—	—	—	—
Lok et al[7] (2006)	Incident	Retrospective	—	X	—	—	—	—	—	—	—	—
Huijbregts et al[67] (2007)	Incident	Prospective	T	X	X	X	X	X	—	—	—	—
Chan et al[24] (2008)	Incident	Retrospective	—	X-	—	—	—	—	—	—	—	—
Dember et al[65] (2008)[b]	Incident	Prospective	—	X	—	—	—	—	—	—	—	—
Field et al[66] (2008)	Incident	Retrospective	T	—	X	—	—	—	X	—	—	—
Peterson et al[68] (2008)	Incident	Retrospective	—	X	—	—	—	—	—	—	—	—
Pflederer et al[69] (2008)	Incident	Retrospective	T	X-	X	X	—	—	X	X	—	—
Tessitore et al[70] (2008)	Prevalent	Retrospective	C	—	—	—	—	X	—	—	—	X
Koksoy et al[71] (2009)	Incident	Prospective	T	—	—	—	X	X	—	—	—	—
Maya et al[72] (2009)	Incident	Retrospective	C	X	—	X	—	X	—	X	—	X
Weber et al[73] (2009)	Incident	Prospective	—	X	—	—	—	—	—	—	—	—
Ferring et al[74] (2010)[b]	Incident	Prospective	C	X	X	—	—	—	—	—	—	—
Gonzalez et al[75] (2010)	Incident	Retrospective	—	X-	—	—	—	—	—	—	—	—
Korkut & Kosem[76] (2010)	Incident	Prospective	T	X-	—	X	X	—	—	X	X	—
Paul et al[77] (2010)	Incident	Retrospective	T	—	X	X	—	—	X	X	—	—
Pisoni et al[78] (2010)	Incident	Retrospective	C	X	—	X	—	—	—	X	—	—
Ravani et al[79] (2010)	Incident	Retrospective	C	—	X	—	—	—	X	—	—	—
Schenk[80] (2010)	Incident	Prospective	—	X-	—	—	—	—	—	—	—	—
Jennings et al[81] (2011)	Incident	Retrospective	T	—	X-	X	—	—	X-	X	—	—
Lee et al[82] (2011)	Incident	Retrospective	T	X-	—	—	—	X	—	—	—	X
Swindlehurst et al[83] (2011)	Incident	Retrospective	T	X	X	X	—	—	—	—	—	—

Abbreviations and definitions: FPP, functional primary patency; FSP, functional secondary patency; PF, primary failure; PP, primary patency; SP, secondary patency; X-, a study that reported outcome of interest; however, the author(s) did not report a definition or the definition was not in accordance with our prespecified definitions.

[a]Patency reported with in-text or table format (T) vs in a Kaplan-Meier curve (C).

[b]Refers to a randomized control trial.

Table 3. Distribution of Components Describing Study Quality for Observational Studies

Component	No. of Studies
Participation bias	
Were participants recruited consecutively, randomly or according to stratified methods?	
Yes	38 (88)
No	0 (0)
Unclear	5 (12)
Was enrollment based on prespecified eligibility criteria?	
Yes	21 (49)
No	21 (49)
Unclear	1 (2)
Selection bias	
Did follow-up begin at fistula creation? (as opposed to the fistula being used prior to study start)	
Yes	36 (84)
No	6 (14)
Unclear	1 (2)
Is it reported whether participants were eligible for different forms of fistulas?	
Yes	25 (58)
No	18 (42)
Attrition bias	
Was loss-to-follow-up treated as censored observations (as opposed to missing)?	
Yes	25 (58)
No	6 (14)
Unclear	12 (28)
Was loss-to-follow-up reported for each cohort?[a]	
Yes	25 (58)
No	18 (42)
Was the proportion lost to follow-up <10%?	
Yes	24 (56)
No	1 (2)
Unclear	18 (42)
Measurement bias	
Was the outcome definition based on published standardized definition[4]?	
Primary failure	
Yes	17 (63)
No	8 (30)
Unclear	2 (7)
Primary patency	
Yes	14 (61)
No	5 (22)
Unclear	4 (17)
Secondary patency	
Yes	12 (67)
No	4 (22)
Unclear	2 (11)
Confounding	
Were at least age, sex, diabetes, and PVD considered or reported?	
Yes	21 (49)
No	22 (51)
Selective reporting	
Are reports of the study free of suggestion of selective outcome reporting?	
Yes	17 (40)
No	10 (23)
Unclear	16 (37)

Note: Values are given as number (percentage). A question that was answered "Yes" was considered as low risk of bias, otherwise it was high risk of bias (answered "No" or "Unclear").

Abbreviation: PVD, peripheral vascular disease.

[a]Corresponds to number of cohorts rather than number of studies.

males ($P = 0.002$) and individuals with upper-arm AVFs increased ($P = 0.004$; Table S4).

Primary Patency

When including primary failure in the calculation for patency rate, the pooled primary patency rate was 60% (95% CI, 56%-64%; 13 studies; 21 cohorts; 4,111 AVFs) at 1 year and 51% (95% CI, 44%-58%; 7 studies; 12 cohorts; 2,694 AVFs) at 2 years (Fig 3). These estimates again must be interpreted cautiously given the high degree of heterogeneity among studies ($I^2 > 80\%$). In subgroup analyses (Table 4), there was a statistically significant difference in primary patency between AVF locations (lower vs upper arm) at 1 year ($P < 0.001$), but not at 2 years ($P = 0.3$). There was no difference between age group (elderly vs non-elderly) at 1 year ($P = 0.3$); however, there was an insufficient number of studies to pool risk estimates at 2 years. Difference by study location (North America vs Europe) was not statistically significant at 1 year ($P = 0.4$). However, we detected a significant difference at 2 years ($P = 0.004$). When sources of heterogeneity were explored in univariable metaregression, we noted a statistically significant decrease in 1- and 2-year patency rates for studies with a higher proportion of diabetic patients ($P = 0.03$ and $P < 0.001$, respectively; tables *a* and *b* of Item S3).

When primary failure was not reported or was excluded from calculation of the patency rate, the pooled primary patency rate was 67% (95% CI, 57%-76%; 12 studies; 18 cohorts; 3,915 AVFs) at 1 year and 51% (95% CI, 40%-62%; 11 studies; 16 cohorts; 3,634 AVFs) at 2 years. The pooled estimate for functional primary patency was 79% (95% CI, 68%-90%; 5 studies; 8

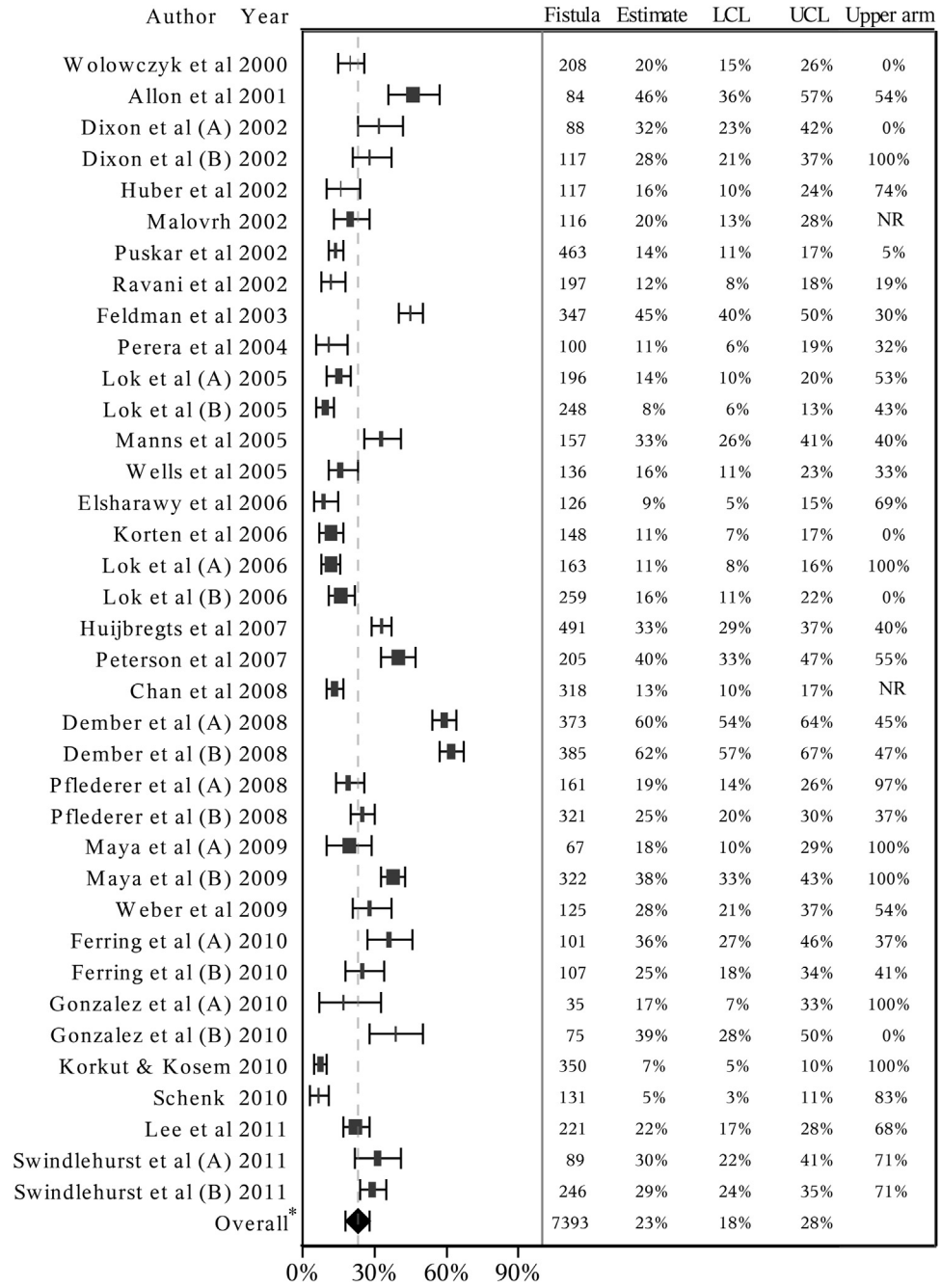

Figure 2. Rates of primary fistula failure. Studies are ordered by ascending publication date. Abbreviations and definitions: Fistulas, number of fistulas in each cohort; LCL, lower confidence limit; UCL, upper confidence limit; Upper arm, percentage of patients using an upper-arm fistula. *Heterogeneity: Q statistics = 1,229.252, $df = 36$, heterogeneity $P < 0.001$, $I^2 = 97\%$. Note: For primary failure: Dixon et al (A) refers to patients with an upper-arm fistula and (B) refers to patients with a lower-arm fistula. Lok et al 2005 reported on (A) elderly and (B) nonelderly patients. Lok et al 2006 reported on (A) upper-arm and (B) lower-arm fistulas. Dember et al conducted a randomized controlled trial and randomly assigned patients to receive either (A) placebo or (B) clopidogrel. Pflederer et al reported on primary failure for (A) transposed arteriovenous fistulas and (B) all other types of fistulas (nontransposed). Maya et al reported on (A) transposed arteriovenous fistulas and (B) upper-arm fistulas (nontransposed). Ferring et al randomly assigned patients to receive either (A) standard care or (B) preoperative ultrasound imaging prior to the surgeon creating the fistula. Gonzalez et al examined primary failure between (A) upper-arm and (B) lower-arm fistulas. Swindlehurst et al examined primary failure between (A) nonelderly and (B) elderly patients.

cohorts; 1,961 AVFs) at 1 year and 73% (95% CI, 57%-88%; 2 studies; 3 cohorts; 764 AVFs) at 2 years. Heterogeneity between studies was high ($I^2 > 96\%$). We noted a statistically significant decrease in 1-year primary patency rates for studies with a higher proportion of males ($P < 0.001$), more recent recruitment date

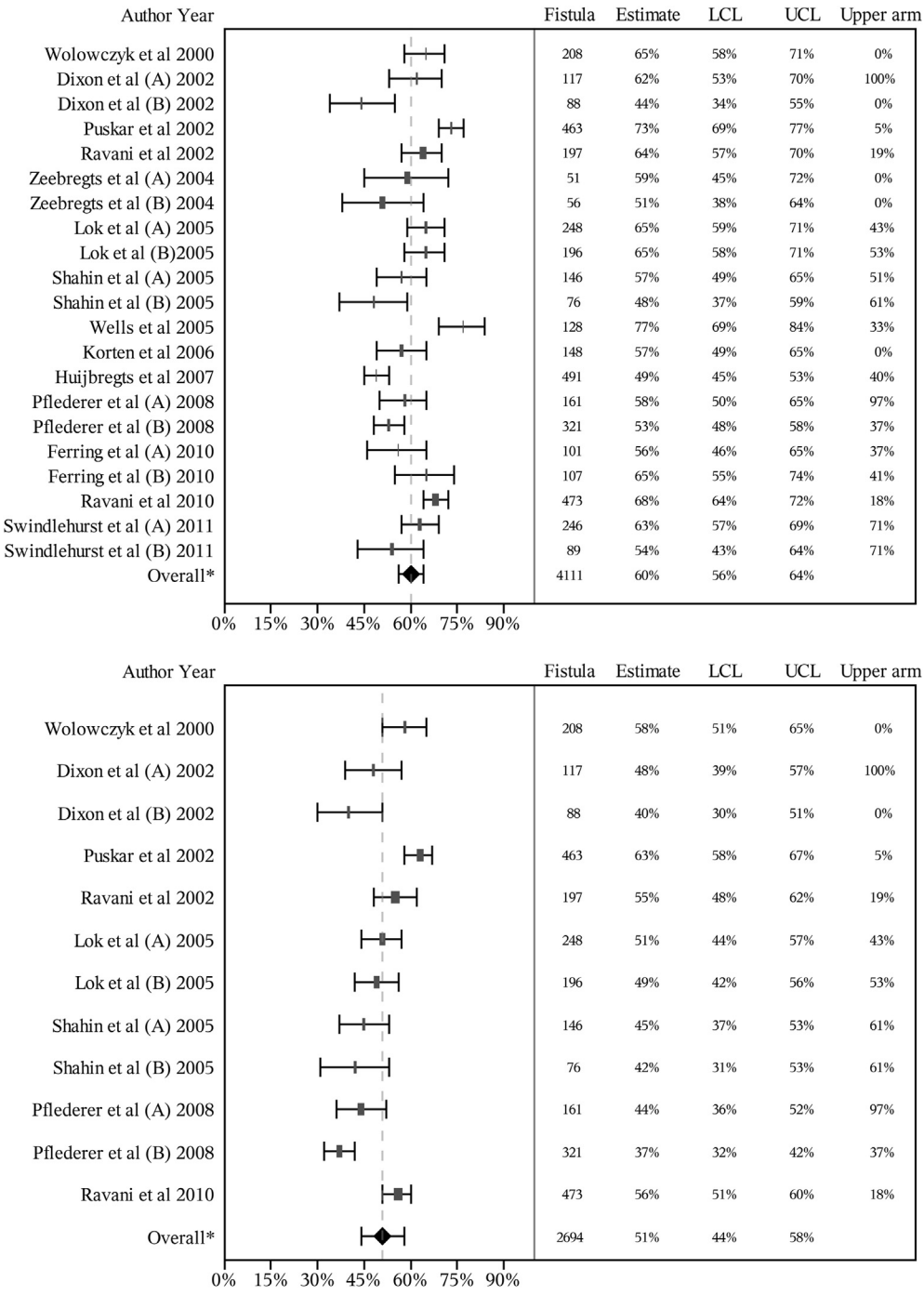

Figure 3. Primary patency rates at 1 (upper panel) and 2 (lower panel) years for fistulas. Primary failures were included in the calculation of patency rate. Studies are ordered by ascending publication date. Abbreviations and definitions: Fistulas, number of fistulas in each cohort; LCL, lower confidence limit; UCL, upper confidence limit; Upper arm, percentage of patients using an upper arm fistula. *(Upper panel) Heterogeneity Q statistic = 139.860, $df = 20$, heterogeneity $P < 0.001$, $I^2 = 86\%$; (lower panel) heterogeneity Q statistic = 87.080, $df = 11$, heterogeneity $P < 0.001$, $I^2 = 87\%$. Note: For primary patency: Dixon et al (A) refers to patients with an upper-arm fistula and (B) refers to patients with a lower-arm fistula. Zeebregts et al conducted a randomized controlled trial and randomly assigned patients to (A) use of sutures or (B) nonpenetrating clips for vascular anastomosis. Lok et al reported on (A) nonelderly and (B) elderly patients. Shahin et al compared patients with (A) standard care and (B) monthly access flow monitoring. Pflederer et al reported on primary patency for (A) transposed arteriovenous fistulas and (B) all other types of fistulas (nontransposed). Ferring et al conducted a randomized controlled trial comparing the efficacy of preoperative ultrasound and randomly assigned patients to (A) standard care or (B) preoperative ultrasound imaging. Swindlehurst et al examined primary patency between (A) elderly and (B) nonelderly patients.

Table 4. Pooled Estimates of Subgroup Analyses

Outcome	1-y	95% CI	No. of Studies	No. of Groups[a]	2-y	95% CI	No. of Studies	No. of Groups[a]
Primary patency rate								
PF included								
Lower arm	55%	49%-61%	7	9 (1,145)	46%	40%-52%	5	6 (890)
Upper arm	65%	58%-72%		5 (483)	49%	39%-59%		5 (483)
Nonelderly	59%	52%-67%	2	2 (337)	—	—		—
Elderly	64%	53%-75%		2 (442)	—	—		—
North America	57%	50%-65%	13	8 (1,353)	45%	40%-49%	7	8 (1,353)
Europe	61%	52%-70%		13 (2,758)	57%	50%-64%		4 (1,341)
PFs excluded or NR								
Lower arm	62%	54%-70%	7	6 (885)	51%	42%-59%	7	6 (885)
Upper arm	68%	53%-82%		5 (506)	52%	36%-67%		5 (506)
North America	64%	49%-79%	11	8 (2,300)	38%	23%-54%	10	6 (2,028)
Europe	68%	47%-88%		8 (1,203)	56%	37%-76%		8 (1,203)
Secondary patency rate								
PFs included								
Lower arm	68%	62%-73%	7	8 (937)	58%	52%-63%	5	5 (682)
Upper arm	70%	62%-78%		7 (872)	59%	53%-73%		7 (872)
Nonelderly	70%	47%-93%	2	2 (337)	—	—		—
Elderly	71%	61%-80%		2 (442)	—	—		—
North America	71%	61%-81%	10	11 (1,880)	63%	55%-71%	6	9 (1,581)
Europe	72%	58%-91%		7 (1,278)	62%	44%-84%		1 (197)
PFs excluded or NR								
Lower arm	—	—	4	—	—	—	4	—
Upper arm	87%	76%-97%		5 (1,505)	75%	63%-87%		5 (1,015)
North America	81%	67%-94%	6	9 (2,251)	73%	57%-88%	6	8 (2,417)
Europe	78%	47%-100%		1 (100)	67%	29%-100%		1 (100)

Note: When not reported, there was an insufficient number of cohorts to pool estimates for elderly and nonelderly patients.

Abbreviations and definitions: CI, confidence interval; Europe refers to studies conducted in Croatia, England, Italy, Netherlands, or Slovenia; North America refers to studies conducted in Canada or United States; NR, not reported; PF, primary failure.

[a]Values given as number of groups (overall number of participants among all groups).

($P = 0.04$), and increase in sample size ($P < 0.001$). However, we observed a statistically significant increase in the 1-year patency rate as the proportion of upper-arm AVFs ($P = 0.002$) and patients with diabetes increased ($P < 0.001$). Similarly, for the 2-year patency rate, we noted a statistically significant increase in patency rate as the proportion of patients with diabetes increased ($P = 0.01$). The 2-year patency rate decreased with more recent recruitment dates ($P < 0.001$; tables *c* and *d* of Item S3).

Secondary Patency

When including primary failure in the calculation of patency rate, the pooled secondary patency rate was 71% (95% CI, 64%-78%; 10 studies; 18 cohorts; 3,558 AVFs) at 1 year and 64% (95% CI, 56%-73%; 6 studies; 11 cohort; 1,939 AVFs) at 2 years (Fig 4). In subgroup analyses (Table 4), we found no difference between AVF locations and study locations. Again, there was an insufficient number of observations reporting on elderly and nonelderly patients to calculate a pooled estimate. Heterogeneity between studies was high ($I^2 > 95\%$). We noted a decrease in 1-year patency rate as the proportion of males increased ($P = 0.009$). However, there was an increase in 1-year patency rate for studies that had a higher proportion of upper-arm AVFs ($P < 0.001$) and more recent recruitment rates ($P = 0.02$). For the 2-year patency rate, we noted a significant decrease in patency rate as sample size ($P < 0.001$) and proportion of males ($P = 0.01$) increased; however, we observed an increase in patency rate as the proportion of upper-arm AVFs increased (tables *a* and *b* of Item S4).

When primary failure was not reported or was excluded from calculation of the patency rate, the pooled secondary patency rate was 82% (95% CI, 71%-92%; 7 studies; 11 cohorts; 3,001 AVFs) at 1 year and 73% (95% CI, 61%-85%; 7 studies; 10 cohorts; 2,867 AVFs) at 2 years. Pooled functional secondary patency was 81% (95% CI, 63%-99%; 5 studies; 11 cohorts; 1,436 AVFs) at 1 year and 80% (95% CI, 57%-100%; 3 studies; 7 cohorts; 721 AVFs) at 2 years. Heterogeneity between studies was high ($I^2 > 95\%$). In metaregression analyses, we noted a statistically significant decrease in 1-year

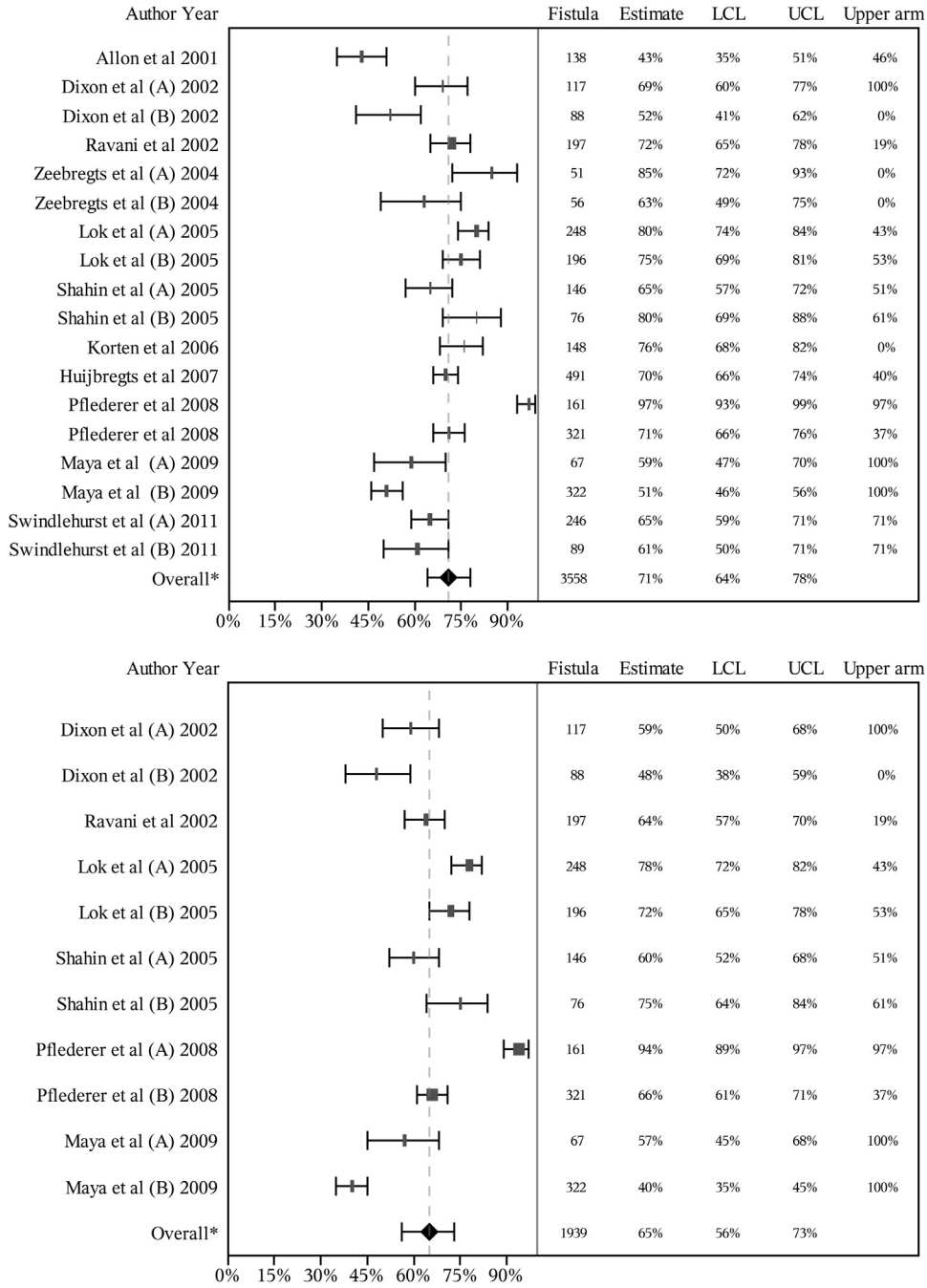

Figure 4. Secondary patency rates at (A) 1 and (B) 2 years for fistulas. Primary failures were included in the calculation of patency rate. Studies are ordered by ascending publication date. Abbreviations and definitions: Fistulas, number of fistulas in each cohort; LCL, lower confidence limit; UCL, upper confidence limit; Upper arm, percentage of patients using an upper-arm fistula. *(Upper panel) Heterogeneity Q statistic = 651.171, $df = 17$, heterogeneity $P < 0.001$, $I^2 = 97\%$; (lower panel) heterogeneity Q statistic = 425.382, $df = 10$, heterogeneity $P < 0.001$, $I^2 = 98\%$. Note: For secondary patency: Dixon et al (A) refers to patients with an upper-arm fistula and (B) a lower-arm fistula. Zeebregts et al conducted a randomized controlled trial and randomly assigned patients to (A) nonpenetrating clips for vascular anastomosis or (B) use of sutures. Lok et al reported on (A) nonelderly and (B) elderly patients. Shahin et al compared patients with (A) standard care and (B) monthly access flow monitoring. Pflederer et al reported on secondary patency for (A) transposed arteriovenous fistulas and (B) all other types of fistulas (nontransposed). Maya et al compared secondary patency between (A) transposed arteriovenous fistulas and (B) upper-arm fistulas (nontransposed). Swindlehurst et al examined primary patency between (A) elderly and (B) nonelderly patients.

secondary patency rates for studies with a higher proportion of men ($P < 0.001$) and patients with diabetes ($P < 0.001$). However, there was a statistically significant increase in 1-year secondary patency rate for studies with more recent recruitment start dates and larger sample size ($P = 0.002$ and

$P < 0.001$, respectively). At 2 years, we noted a decrease in secondary patency rate as the proportion of males increased. Conversely, we observed an increase in the 2-year patency rate for studies with more recent recruitment start dates (tables *c* and *d* of Item S4).

Sensitivity Analyses

Our estimates of primary failure were unchanged when we analyzed cohorts that had 100 or more AVFs, had recruitment start date at or after 2000, and when the study question was asked before data collection (ie, prospective design). Table S5 shows sensitivity analyses for estimates of primary and secondary patency rates.

DISCUSSION

We conducted a comprehensive review of recent studies describing rates of AVF primary failure, primary patency, and secondary patency according to standardized definitions. We report 2 important findings: (1) approximately one-quarter to one-third of created AVFs failed to ever be used, with even higher risk in the elderly and those using a lower-arm AVF; and (2) by 1 year, 40% of all AVFs failed or required at least one intervention. Our results show a significant decrease in AVF performance over time (except for secondary patency), with more current data highlighting a higher risk of primary failure and low to moderate primary and secondary patency rates.

Prior to 2000, AVFs tended to have an acceptable risk of primary failure, ranging from 10%-24%,[28-31] and 1-year primary and secondary patency rates of 65%-94%[30,32-34] and 85%-90%,[35] respectively. Using data from 1970-2002, Rooijens et al[36] reported a primary failure risk of 15% (95% CI, 13%-18%), a 62.5% (95% CI, 54%-70%) primary patency rate, and a 66% (95% CI, 58%-73%) secondary patency rate at 1 year for radiocephalic (lower-arm) AVFs. We obtained a higher risk of primary failure and lower primary patency rates among lower-arm AVFs (when primary failures were included). However, when we excluded primary failures from calculation of the patency rate, we obtained a similar pooled estimate for 1-year primary patency and similar 1-year secondary patency (primary failures included). In contrast to Rooijens et al,[36] we examined all AVF locations and included only prospectively collected data.

Given the significant statistical heterogeneity in study results, the pooled estimates must be applied judiciously to different types of patients and AVF procedures. We conducted metaregression to examine the sources of heterogeneity and found that in general, parameter estimates depended significantly on the proportions of males, upper-arm AVFs, and patients with diabetes and study recruitment date. At the study level, we could not attribute study differences in AVF outcomes to other patient factors (age and peripheral vascular disease). There are other important factors not available in our data sources, such as vessel diameter and quality, surgical expertise, and differences in vascular access practices across programs, which may account for some of the differences in AVF outcomes across studies.[37-39] For example, a higher emphasis of vascular access surgical training and facility practices have been shown to be associated with the likelihood of creating a successful AVF.[37,40,41] Using DOPPS data, Saran et al[37] reported a 34% lower risk of primary failure when an AVF was created by a surgeon with at least 25 AVF creations during surgical training, compared to those with fewer than 25 AVF creations.

This review serves as a call to action to improve several key factors that affect vascular access choice, evaluation, and management. First, the quality of reporting in future studies requires refinement and consistent application of standardized definitions. We found inconsistent reporting of definitions across studies and a high risk of potential bias. However, study definitions not only had inconsistent reporting, but also a lack of an objective definition that is easily benchmarked across studies and programs. For example, time of AVF use was not clearly defined across studies. Many definitions were used, including single-needle versus 2-needle cannulation, consistency of cannulation (eg, 3 successive cannulations), having blood flow > 350 mL/min, and catheter removal. Because one objective of using an AVF is to avoid catheter use, the success of an AVF could be indicated by the time the catheter is removed or by not using a catheter at hemodialysis therapy initiation.[4] However, there are limitations in the precision of even this definition because catheter removal may depend on other factors, such as available resources, which then potentially falsely lengthens the time of catheter dependence and delays AVF use time.

Our review has a number of strengths, including rigorous methodology, consistency of 1- and 2-year parameter estimates for patency rates, and its relevance to current practice and informing practice guidelines. Our review also has limitations. Screening of articles was conducted by a single individual, possibly contributing to study selection bias. We searched MEDLINE only and may be missing relevant studies captured in only EMBASE and/or Google Scholar. We restricted this review to articles published in English, and whether this introduced some bias is controversial.[42]

In conclusion, we report a high risk of primary failure and low to moderate primary and secondary

patency rates. There has been a significant decrease in AVF performance over time. These results may explain in part the decrease in AVF use in some countries. However, these results should be used judiciously because the quality of evidence for AVF performance is low and susceptible to bias.

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SUPPLEMENTARY MATERIAL

Table S1: MOOSE checklist.
Table S2: Search strategy (Ovid).
Table S3: Reported definition of primary access failures.
Table S4: Metaregression analysis for primary failures.
Table S5: Sensitivity analyses.
Figure S1: Rates of primary failure in upper- and lower-arm fistulas.
Figure S2: Rates of primary failure among elderly and non-elderly patients.
Figure S3: Rates of primary failure in North American and European studies.
Item S1: Risk-of-bias assessment.
Item S2: Elements of risk of bias.
Item S3: Metaregression analysis for 1- and 2-year primary patency.
Item S4: Metaregression analysis for 1- and 2-year secondary patency.

Note: The supplementary material accompanying this article (http://dx.doi.org/10.1053/j.ajkd.2013.08.023) is available at www.ajkd.org

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