Outcomes of arteriovenous graft vs. fistula for haemodialysis access in the elderly: A systematic review and meta-analysis

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Abstract. The impact of the type of vascular access on the outcomes in the elderly haemodialysis patients is still unclear. The goal of the present study was to compare survival outcomes in elderly haemodialysis patients who received either arteriovenous graft (AVG) or arteriovenous fistula (AVF). A systematic literature search was performed in EMBASE, Cochrane, MEDLINE, ScienceDirect and Google Scholar databases for papers published from January 1954 until January 2022. Risk of bias in the selected publications was assessed by Newcastle Ottawa scale or Cochrane risk of bias tool depending on the study design. Meta-analysis was carried out using the random-effects model. Data were reported as pooled odds ratio (OR) or hazard ratio (HR) with 95% confidence interval (CI). A total of 12 studies were included in the analysis. The majority of the studies had poor quality. Elderly patients receiving AVG had significantly worse survival rate compared with patients that received AVF for the haemodialysis access, with a pooled HR of 1.38 (95% CI, 1.24-1.53; I^2=79.9%). Pooled HR for access survival was 1.60 (95% CI, 1.54-1.66; I^2=0%). Pooled OR for primary patency rate, maturation failure and infections were 1.81 (95% CI, 0.73-4.49; I^2=79.2%), 0.33 (95% CI, 0.12-0.91; I^2=70.4%) and 9.74 (95% CI, 2.60-36.49; I^2=52.4%), respectively. These results suggested that in elderly patients undergoing haemodialysis, AVG was associated with reduced overall survival and access survival, and higher infection rate, compared with AVF. Notably, AVG was also associated with a lower risk of maturation failure, presenting a potential advantage in specific patient populations (study registration: PROSPERO, no. CRD42022313199).

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Introduction

Almost 3 million people worldwide receive haemodialysis treatment every year, and this number is expected to double by the year 2030 (1). More than half of all haemodialysis patients are elderly (aged ≥65 years) (1). For this population, well-timed placement of an arteriovenous (AV) vascular access by AV graft (AVG) or AV fistula (AVF) may limit the usage of a tunnelled central venous catheter (CVC) (2). This is important as a well-timed placement of AV access in elderly haemodialysis patients may reduce the risk of complications, such as infection and thrombosis, that are associated with prolonged use of tunnelled CVCs, thereby improving the quality of care and overall prognosis of the patient (2). Currently, the general guidelines for selecting a dialysis vascular access include a categorized preference order, where AVF, AVG and CVC are the first, second and last choice, respectively (3). AVFs are often selected as the first choice due to their longer patency and lower infection rates. However, AVF maturation process can be slow and unpredictable, posing unique challenges for elderly patients. On the other hand, AVGs, while quicker to mature, are traditionally associated with a higher rate of complications, which often makes them a less preferred method of dialysis vascular access (3).

This categorized preference order for the placement of vascular access has become a major point of debate worldwide (4,5). For decades, AVF placement was considered a preferred method of choice for the majority of patients that required haemodialysis for treating end-stage kidney disease (ESKD). However, recent advances in the treatment of ESKD led to the changes in the incidence and prevalence of patients with advanced renal conditions (6). Changes in the treatment of ESKD have also changed our understanding of the pros and cons associated with different vascular access options. With increasing complexity of the health profiles of patients, particularly among elderly populations, it is necessary to reassess the efficacy and safety of AVGs and AVFs.

Haemodialysis is now offered to elderly ESKD patients with various comorbidities, such as diabetes mellitus, hypertension, cardiovascular disease, chronic respiratory conditions, osteoporosis, and autoimmune disorders such as lupus. Age is a major biological variable that can affect the outcomes of vascular access (7). The optimal vascular access (VA) strategy in elderly dialysis patients is still unclear due to their shorter life expectancy, difficulties in VA maturation and significantly

higher risk of primary AVF failure compared to younger adults (8). Recent studies in elderly patients suggest that AVF may not demonstrate clear advantage over AVG in terms of patency. Therefore, patients can still benefit from AVG, as it is associated with a shorter time to maturation (9-11). To the best of our knowledge, there are no reviews that pool data on the difference in outcomes, such as overall survival, mortality rates, access survival, primary patency, maturation failure and risk of infection in elderly patients. The goal of the present study is to summarize data from individual studies to compare the outcomes of AVG versus AVF for haemodialysis access in elderly patients.

Materials and methods

Eligibility criteria
Study design. Randomized controlled trials/non-randomized trials/cross-sectional/cohort/case-control studies were included if they satisfied the inclusion criteria listed below.

Study participants. Studies containing data of elderly patients (≥60 years) requiring haemodialysis access were incorporated.

Exposure. Studies evaluating the difference in outcomes between AVF and AVG access for elderly patients were included.

Outcomes. Studies reporting any of the following outcomes: Overall survival/mortality rates, access survival, primary patency, maturation failure and infection, were eligible for inclusion.

Exclusion criteria. Case reports, case series, conference abstracts, letters to editors, commentaries and studies not reporting any of the aforementioned outcomes were excluded from the analysis.

Search strategy. Systematic literature search was conducted in EMBASE (https://www.embase.com/), Cochrane library (https://www.cochranelibrary.com/search), MEDLINE (https://pubmed.ncbi.nlm.nih.gov/), Google Scholar (https://scholar.google.com/) and ScienceDirect (https://www.sciencedirect.com/) databases and search engines (Appendix S1). The search strategy used a combination of medical subject headings (MeSH) and free-text terms using the suitable Boolean operators ('AND' and 'OR'). The following filters were applied during the search: Time point (January 1954 to January 2022), language (English only). Bibliography of the retrieved articles was also searched to find additional relevant studies (Data S1).

Study selection process. The title and abstract were screened by two independent investigators (JL and HL). Full text of the studies that met the inclusion criteria were retrieved and further screened by the same investigators (JL and HL) for studies that satisfied the inclusion criteria. Disagreements were solved by discussion with the third investigator (ZX). The review was reported based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement 2020 (12).

Data extraction process. Data was manually extracted using a pre-defined structured data extraction form and included authors, title of study, year of publication, study period, study design, setting, country/region, total sample size, outcome assessment details, average age, primary and secondary outcomes in each group. Data entry was done by the first author (JL) and checked for any potential errors by the second author (HL).

Risk of bias assessment. Two independent authors (ZX and QL) carried out assessment of the risk of bias using Newcastle Ottawa (NO) scale for observational studies and Cochrane Risk of bias 2 (RoB 2 tool) for randomized controlled trials. NO scale included the following domains: Selection (four stars), comparability (two stars) and outcome (three stars). The final score ranged from zero to eight stars. Studies ranging from 7-9 stars indicated 'good quality'. Quality of the studies with 5-6 stars were considered 'satisfactory', and studies with 0-4 stars were considered 'unsatisfactory' (13).

The RoB-2 tool was structured into a following domains of bias: Process of randomization, variation from the intended intervention, missing data on outcomes, outcome measurements and selection of the reported results.

Based on results of the NO scale and RoB2 tool assessment, quality of evidence of each study was then categorised as having 'low bias risk', 'high bias risk', and 'some concerns' (14).

Statistical analysis. Meta-analysis was performed using STATA version 14.2 (StataCorp LLC). For the binary outcomes, the data were reported as pooled odds ratio (OR) with 95% confidence interval (CI). For time to event data (mortality and access free survival), pooled estimate were calculated using natural logarithm of hazard ratio (ln{HR}) and standard error of ln(HR). First, HR with 95% Confidence interval (CI) was retrieved from the included studies. Natural logarithm of HR was calculated for each of the HR estimate. Standard error of ln(HR) was calculated using the following equations (15):

Variance of logarithmic HR was calculated as follows: Variance (ln{HR})=[ln(upper CI of HR)-ln(lower CI of HR)/2x1.96]

Standard error (SE) of logarithmic HR was calculated as follows: SE (ln{HR})=√Variance (ln{HR})

Values of ln(HR)and SE were then entered into the STATA software to estimate the pooled effect. Random effects model was applied, and the data were reported as pooled HR with 95% CI for both outcomes. Visual representation of the pooled estimates were performed using Forest plots.

Heterogeneity was evaluated using χ^2 test and I^2 statistic. $I^2 < 25\%$ indicated mild heterogeneity; 25-75% indicated moderate heterogeneity; and >75% indicated substantial heterogeneity (16). Sensitivity analysis was performed to evaluate the robustness of pooled estimate. Assessment of publication bias through funnel plot and Egger's test could not be performed for any of outcomes due to an insufficient (<10) number of studies reporting each outcome.

Results

Study selection. Literature search identified 3,489 papers. Of them, 145 studies were eligible for full text evaluation. In addition, six more articles were retrieved by screening the references of the full texts during primary screening. After
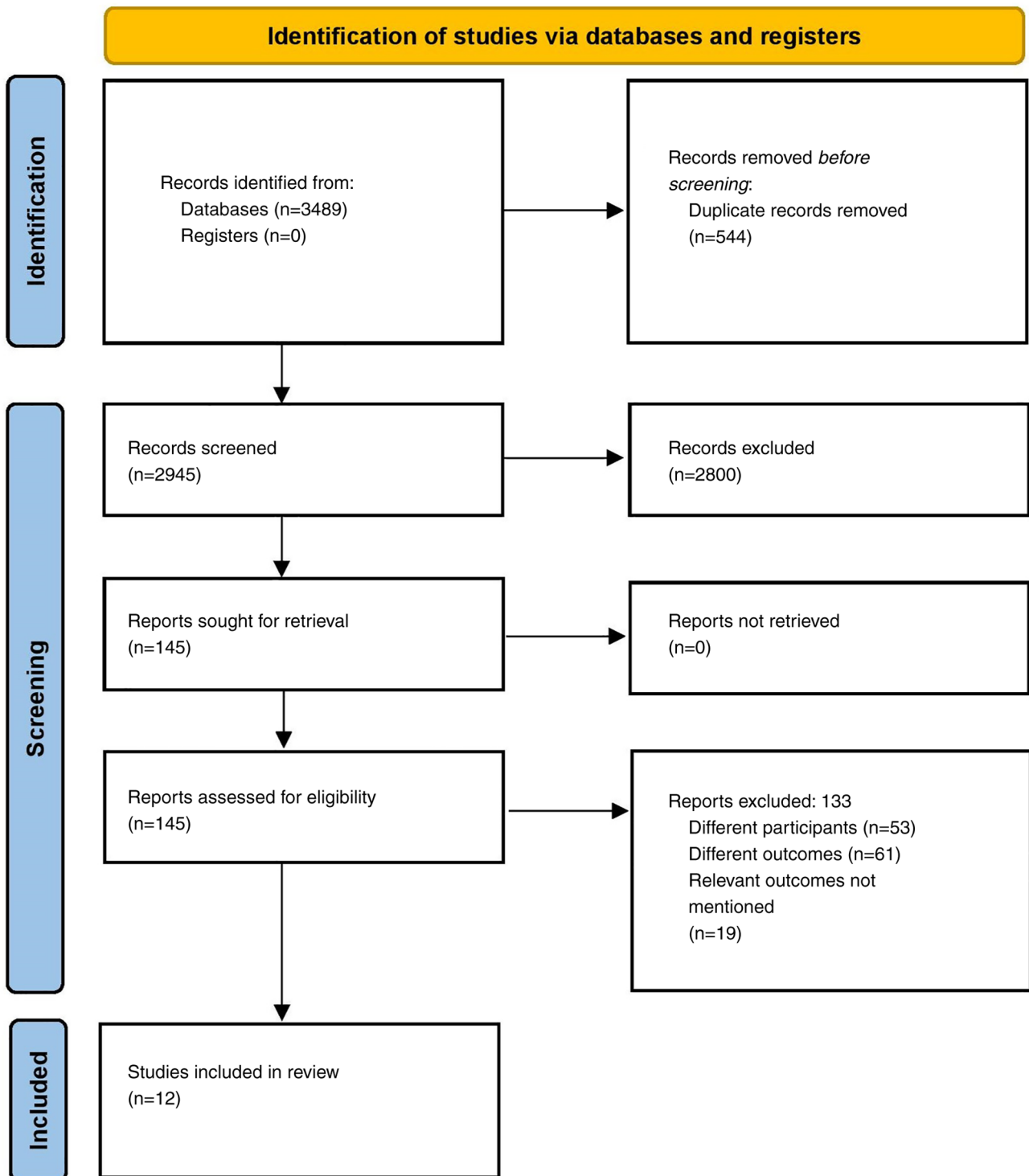
Figure 1. PRISMA flowchart.

the final screening, 12 studies containing 95,449 participants met the eligibility criteria and were included in the analysis (Fig. 1) (9-11,17-25).

Characteristics of the included studies. All studies, except Murea *et al* (17) and Robinson *et al* (18), were retrospective. Most (eight out of 12) were conducted in the USA followed by South Korea (3 studies). The range of sample sizes was 29 to 25,226. The majority of the studies were conducted in patient cohorts with >65 years cut-off followed by >75 years cut-off.

The follow-up duration ranged from 215 days to 5 years (Table I). Overall, nine out of 12 studies had higher risk of bias (Table II and III).

Overall survival. Firstly, five studies (9,10,20,23,25) reported the difference in overall survival between elderly patients that received AVG and AVF for haemodialysis access. The pooled HR was 1.38 (95% CI, 1.24-1.53; I^2=79.9%), which suggested that AVG was associated with significantly decreased survival compared with AVF in elderly patients (Fig. 2).

Table I. Characteristics of the included studies (n=12).

First author, year	Country	Study design	Sample size	Age cut-off, years	Mean age, years	Males, %	Mean BMI, kg/m²	DM, %	HTN, %	CAD, %	Cancer, %	Follow-up duration	Outcomes measured	(Refs.)
Arthuidese et al, 2019	USA	Retrospective	23,653	>75	AVG=82.2 AVF=82.0	AVG=45.4 AVF=65.8	AVG=26.9 AVF=26.8	AVG=48 AVF=43	AVG=87.3 AVF=88.9	AVG=28 AVF=29.5	AVG=10.7 AVF=11.7	5-year	Overall survival, infection, primary patency	(9)
Bae et al, 2018	South Korea	Retrospective	361	>65	AVG=74.9 AVF=74.2	AVG=57.7 AVF=54.8	AVG=22.7 AVF=22.8	AVG=55.7 AVF=55.4	AVG=72.2 AVF=78	AVG=28.9 AVF=19	AVG=18.3 AVF=23.2	5-year	Overall survival, Maturation failure	(10)
Choi et al, 2020	South Korea	Retrospective	878	>65	AVG=61 AVF=59	AVG=52.9 AVF=60.9	NR	AVG=71.2 AVF=62.7	NR	AVG=20.4 AVF=16	NR	NR	Access free survival	(11)
Cui et al, 2016	China	Retrospective	182	>75	NR	AVG=56.8 AVF=65.2	NR	AVG=56.8 AVF=47.1	AVG=93.2 AVF=93.5	AVG=52.3 AVF=55.8	NR	2-year	Maturation failure	(22)
Jadlowiec et al, 2016	USA	Retrospective	186	>70	AVG=78 AVF=78.8	AVG=42.9 AVF=59.7	NR	AVG=59.5 AVF=57	AVG=89.2 AVF=94	AVG=75.7 AVF=73.2	NR	NR	Mortality, Infection, patency, maturation failure	(21)
Jhee et al, 2019	South Korea	Retrospective	4,026	>65	AVG=74.3 AVF=73	AVG=52.2 AVF=58.4	AVG=21.9 AVF=22.3	AVG=41.1 AVF=40.3	AVG=52.4	AVG=13.8 AVF=14	AVG=2.5 AVF=2.8	NR	Overall survival	(25)
Lee et al, 2019	USA	Retrospective	14,370	65-74	AVG=65 AVF=60	AVG=87.5 AVF=54.4	NR	NR	NR	NR	NR	NR	Overall survival, access free survival	(23)
Murea et al, 2020	USA	RCT	44	>65	AVG=72.8 AVF=78.9	AVG=52.2 AVF=71.4	AVG=30.9 AVF=25.5	AVG=65.2 AVF=76.2	AVG=87 AVF=90.5	AVG=13 AVF=9.5	AVG=26.1 AVF=23.8	215 days	Mortality	(17)
Robinson et al, 2021	USA	RCT	29	>65	AVG=77.5 AVF=75.4	AVG=56 AVF=78	AVG=30.3 AVF=27.6	AVG=56 AVF=67	AVG=82 AVF=89	AVG=11 AVF=22	AVG=22 AVF=22	321 days	Mortality, infection, maturation failure	(18)
Saleh et al, 2017	USA	Retrospective	10,030	70-80	AVG=70.7 AVF=70.2	AVG=91 AVF=96	NR	AVG=67 AVF=66	NR	AVG=26 AVF=24	AVG=26 AVF=25	NR	Overall survival	(20)
Woo et al, 2015	USA	Retrospective	16,464	>66	AVG=78 AVF=77.1	AVG=55.6 AVF=40.6	NR	AVG=77.5 AVF=73.2	AVG=99.1 AVF=99	AVG=82.9 AVF=79.8	AVG=15.8 AVF=15	1 year	Mortality	(19)
Xue et al, 2003	USA	Retrospective	25,226	>67	AVG=74.9 AVF=74.6	AVG=57 AVF=62.2	NR	AVG=39.2 AVF=37.8	NR	NR	NR	1 year	Mortality	(24)

BMI, body mass index; DM, diabetes Mellitus; HTN, hypertension; CAD, coronary artery disease; NR, not reported; RCT, randomized controlled trial; USA, United States of America.

Table II. Quality assessment for observational studies amongst the included studies (n=10).

Study no.	First author, year	Representativeness	Sample size justification	Non-response	Ascertainment of exposure	Control for confounding	Assessment of outcome	Statistical tests	Overall Quality	(Refs.)
1	Arhuidese et al, 2019	0 star	0 star	0 star	1 star	1 star	1 star	1 star	Poor	(9)
2	Bae et al, 2018	0 star	1 star	1 star	1 star	1 star	1 star	1 star	Poor	(10)
3	Choi et al, 2020	0 star	0 star	1 star	0 star	0 star	1 star	1 star	Poor	(11)
4	Cui et al, 2016	0 star	1 star	0 star	0 star	0 star	1 star	0 star	Poor	(22)
5	Jadlowiec et al, 2016	0 star	0 star	0 star	1 star	1 star	1 star	1 star	Satisfactory	(21)
6	Jhee et al, 2019	0 star	0 star	0 star	1 star	2 stars	1 star	1 star	Satisfactory	(25)
7	Lee et al, 2019	0 star	1 star	1 star	1 star	0 star	1 star	0 star	Poor	(23)
8	Saleh et al, 2017	0 star	0 star	1 star	1 star	0 star	1 star	1 star	Poor	(20)
9	Woo et al, 2015	0 star	0 star	0 star	0 star	0 star	1 star	1 star	Poor	(19)
10	Xue et al, 2003	0 star	0 star	0 star	0 star	0 star	1 star	0 star	Poor	(24)

Then, seven studies (9,10,17-19,21,24) compared the mortalities in elderly patients that received AVG and AVF for haemodialysis access. The pooled OR was 1.23 (95% CI, 1.09-1.40; I^2=75.1%), further confirming that elderly patients receiving AVG access for haemodialysis had significantly higher rate of mortality when compared with patients with AVF (Fig. 3).

Access survival. Next, two studies (11,23) compared the access survival in AVG and AVF groups of elderly patients. The pooled HR of 1.60 (95% CI, 1.54-1.66; I^2=0%) indicated that AVG was associated with significantly worse access survival compared with AVF in elderly haemodialysis patients (Fig. 4).

Two additional studies (9,21) have reported the difference in primary patency rate (intervention-free access survival) in terms of count outcomes between the two groups of patients. The pooled OR was 1.81 (95% CI, 0.73-4.49; I^2=79.2%), not indicating any significant difference in terms of primary patency rate between AVG and AVF groups (Fig. 5).

Maturation failure. There were four studies (10,11,18,21) that reported the difference in maturation failure between AVG and AVF groups of elderly haemodialysis patients. The pooled OR was 0.33 (95% CI, 0.12-0.91; I^2=70.4%) indicating that patients undergoing AVG had significantly lower risk of maturation failure when compared with patients undergoing AVF (Fig. 6).

Infection. Finally, three studies (9,18,21) reported the difference in infection rate in terms of count outcomes between AVG and AVF groups of elderly patients. The pooled OR was 9.74 (95% CI, 2.60-36.49; I^2=52.4%) indicating that there is 9-fold higher risk of infection in patients who received AVG haemodialysis access compared with patients with AVF (Fig. 7).

Additional analysis. Sensitivity analysis was performed to check the small study effects by removing each of the studies one-by-one for all outcomes. No significant variation in the effect size (magnitude and direction) was detected by the sensitivity analysis. This indicated a lack of single study effect on the overall estimate for any of the outcomes.

Discussion

The current recommended guidelines for vascular access do not provide any specific age-based recommendations for the preferred placement of AVF over the AVG (3). Elderly patients undergoing haemodialysis present unique challenges, such as diminished vein and elasticity, high prevalence of atherosclerosis, increased risk of infection and comorbidities, for the establishment and usage of the vascular access (4). The present systematic review assessed the risk of survival outcomes associated with AVG and AVF access for haemodialysis among elderly patients.

The present study investigated 12 studies that fulfilled the eligibility criteria. The majority of these studies were conducted in the USA followed by South Korea and China. Almost all the studies [except for Murea et al (17) and Robinson et al (18)] were retrospective, and the majority of them were of poorer quality with a high risk of bias. It was revealed that AVG was

Table III. Quality assessment for RCTs amongst the included studies (n=2).

Study no.	First author, year	Randomization process	Deviation from intended intervention	Missing outcome data	Measurement of outcome	Selection of reported result	Overall risk of bias	(Refs.)
1	Murea *et al*, 2020	Low risk	Low risk	Some concerns	High risk	High risk	High risk	(17)
2	Robinson *et al*, 2021	Low risk	Low risk	Low risk	Some concerns	Low risk	Some concerns	(18)
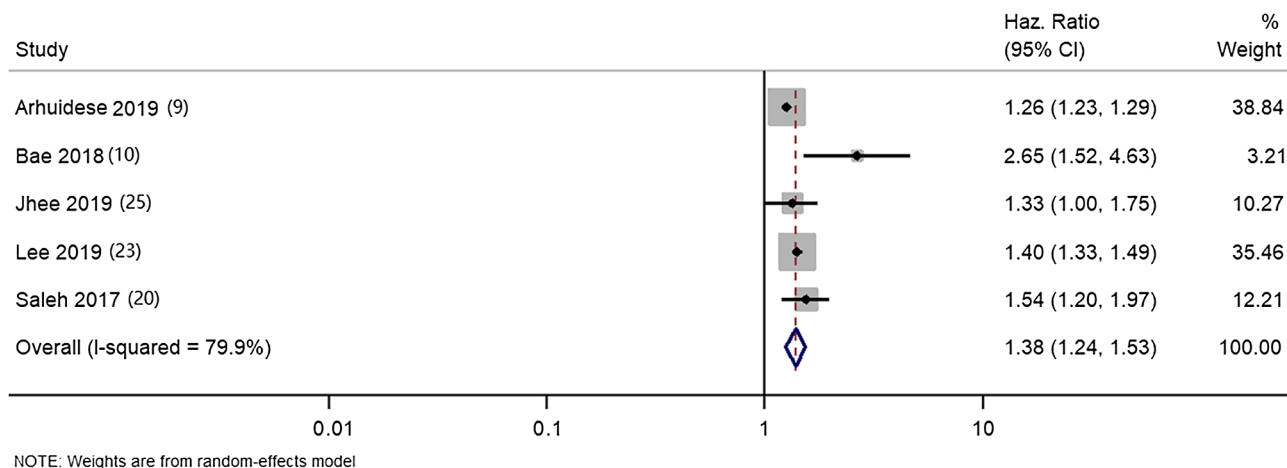
Figure 2. Forest plot showing the difference in overall survival between arteriovenous graft and arteriovenous fistula for elderly haemodialysis patients. CI, confidence interval.
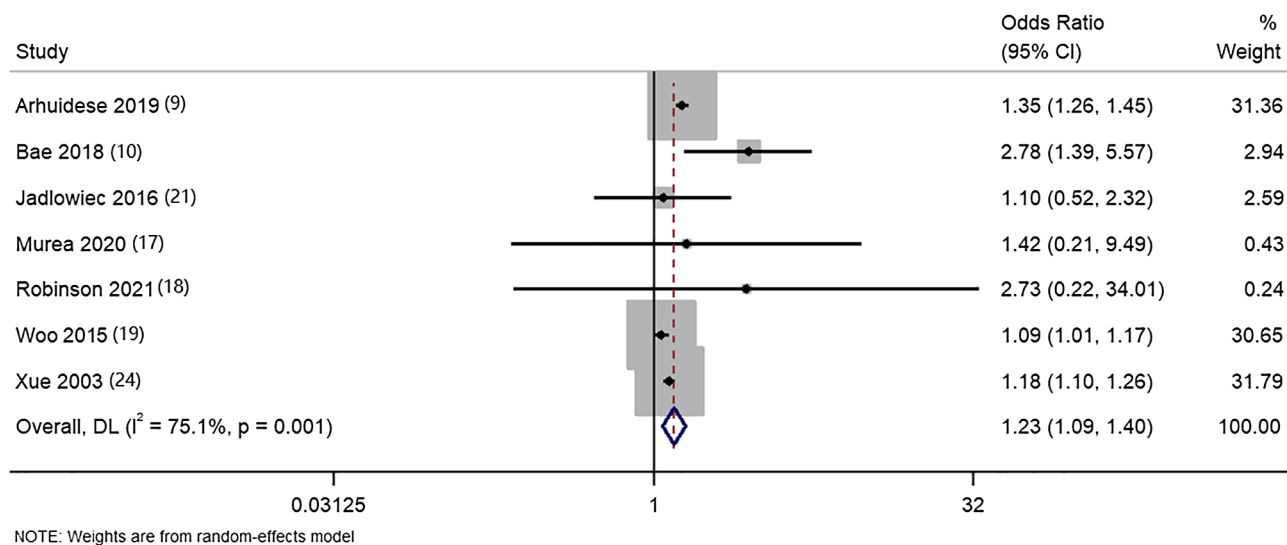
Figure 3. Forest plot showing the difference in mortality rate between arteriovenous graft and arteriovenous fistula for elderly haemodialysis patients. CI, confidence interval.

associated with significantly higher risk of mortality, lower access survival and higher rate of infection. At the same time, AVG access in these patients correlated with significantly lower risk of maturation failure. Though subgroup analysis was not possible due to limited number of studies for each outcome, there was some variation in the individual study estimates based on the age cut-off, with higher magnitude of association in higher-age group of patients. Sensitivity analysis did not reveal significant effect of any single study on the magnitude or direction of association.
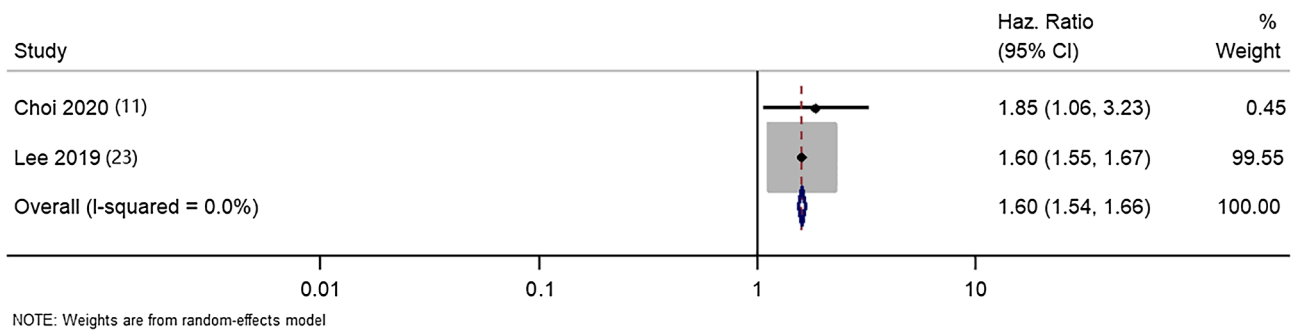
Figure 4. Forest plot showing the difference in access survival between arteriovenous graft and arteriovenous fistula for elderly haemodialysis patients. CI, confidence interval.
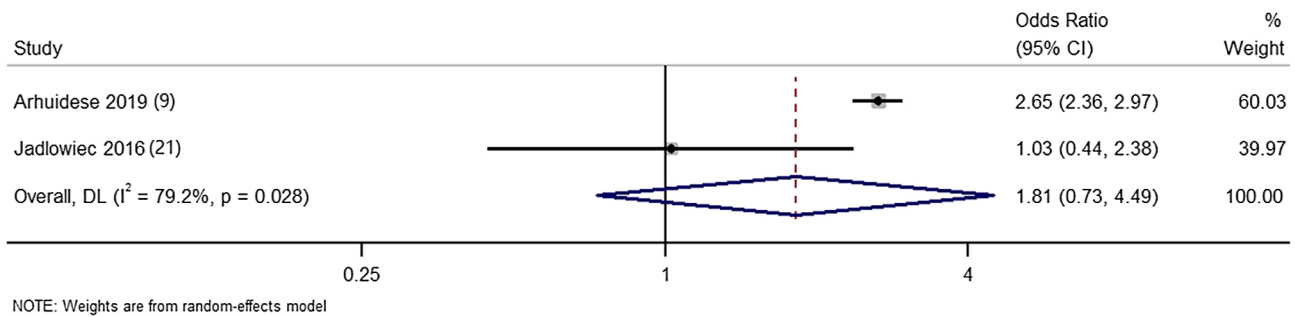

Figure 5. Forest plot showing the difference in primary patency rate between arteriovenous graft and arteriovenous fistula for elderly haemodialysis patients. CI, confidence interval.
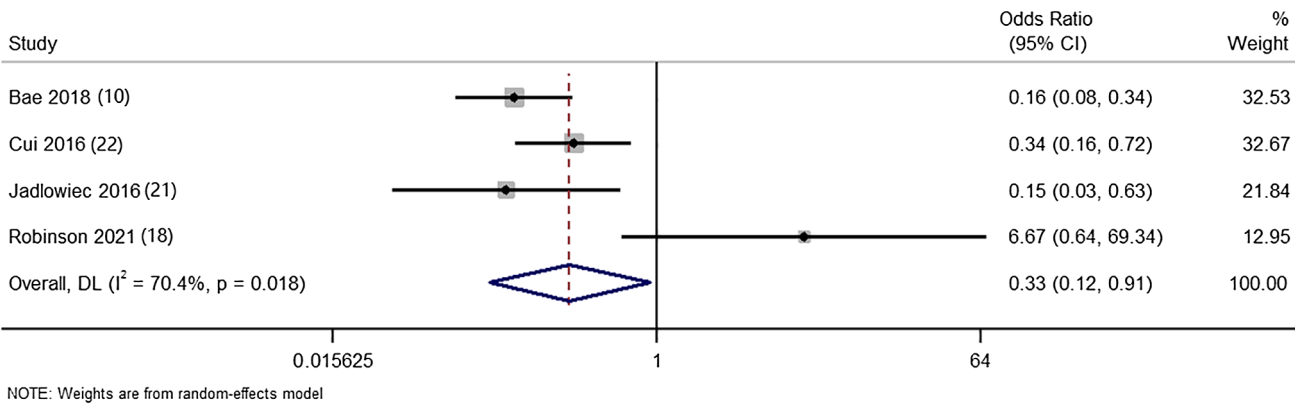

Figure 6. Forest plot showing the difference in maturation failure between arteriovenous graft and arteriovenous fistula for elderly haemodialysis patients. CI, confidence interval.

These results were further confirmed by using adjusted HR for the pooling of effect size. The crude estimates are prone for confounding as they are not adjusted for any important risk factors. The use of adjusted HR takes into account these relevant confounding factors, and thus provides more reliable estimate of the differences between the two vascular access methods in elderly patients. While there are no existing reviews to compare the observations of the present study in an elderly age group, the current results were in agreement with the reviews that focused on adult patients and compared AVG and AVF for haemodialysis access (26-28). A possible explanation for the observed differences in the outcomes between these two haemodialysis access types may be due to a higher rate of infections as a result of the colonization of the foreign materials within the vascular space by skin microorganisms. This may lead to poor overall survival and access survival in patients undergoing AVG for haemodialysis access (26).

The increased mortality rate associated with AVG when compared with AVF in the elderly population cannot be solely attributed to the choice of vascular access. It is important to consider that the selection between AVG and AVF is typically dictated by patient-specific factors such as vascular health, comorbidities, and the overall clinical profile of the patient (4). This introduces an inherent selection bias that may lead to worse outcomes in patients approved for AVG.
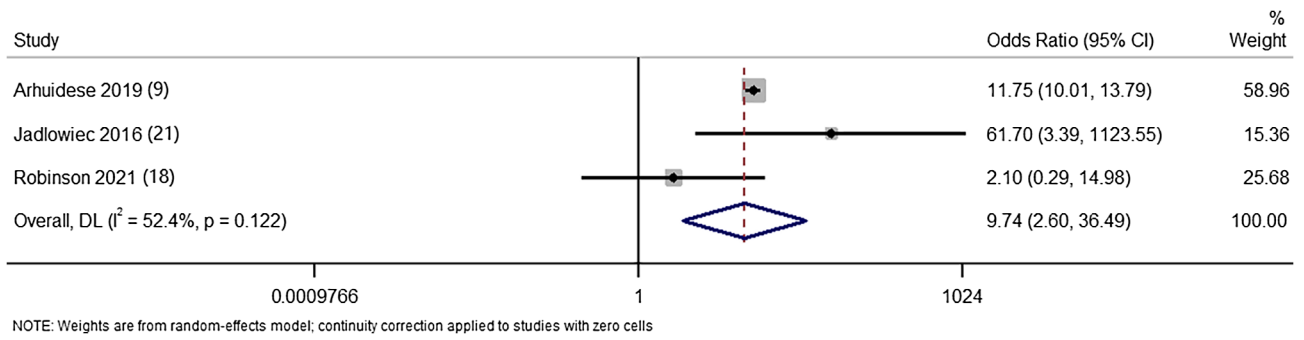
Figure 7. Forest plot showing the difference in infection rate between arteriovenous graft and arteriovenous fistula for elderly haemodialysis patients. CI, confidence interval.

An important finding of the present study is the higher rate of infection in patients with AVG. However, the present analysis did not distinguish between infections at the access site and systemic events, nor was the severity of these infections graded. Future studies should consider investigating these aspects in more detail, as the type and severity of infection could influence the decision-making process regarding the choice of access type.

AVFs have a significantly higher risk of the maturation failure, often requiring various intercurrent guidelines strongly recommend AVF as a first-line and optimal vascular access method for haemodialysis. There is insufficient information available for evaluating the qualities of this methods (29). Since AVF is associated with higher maturation failure and frequently requires repetitive interventions, its indiscriminate use might result in the ineffective usage of the services and resources (29).

The major strength of the present review was the rigorous methodology and comprehensive literature search that adds to the limited evidence available on the comparison these two methods of vascular access. The present study did not detect any significant changes in the effect size, as indicated by the sensitivity analysis. This further enhanced the credibility of these results. However, there are some limitations in the current study. Substantial between-study variability was found for most of the outcomes. The majority of the studies were of poorer quality and limited heterogeneity. This might affect the external validity (generalisability) of the findings. In addition, publication bias was unable to be assessed due to the small number of studies, which further limits the credibility of the evidence. The retrospective nature of the included studies made it challenging to establish the causal association. Hence, longitudinal evidence is required for the identification of reliable effect size. This will allow making evidence-based recommendations for deciding on the appropriate vascular access type for elderly haemodialysis patients at the hospital setting. Finally, the results of the present review may not be credible as nine out of the 12 studies had high-risk of bias. Given these limitations, it is crucial to stress that the present results should not be interpreted as definitive evidence for the decision-making in the clinical setting. The small number and the retrospective design of most of the included studies, and other potential biases restrict us from deriving firm evidence-based recommendations from this meta-analysis.

Nevertheless, the present study had certain important implications for the healthcare professionals treating elderly haemodialysis patients. A stronger association of survival outcomes was revealed with AVG compared with AVF in elderly patients. However, the maturation failure was higher with AVF and limited evidence was available in terms of RCTs. The potential confounding effect of infections on survival analyses was also notable. Although the meta-analysis showed a worse survival rate with AVG, whether this was influenced by the increased rate of infections in this group was not specifically investigated. Thus, the impact of infections on survival outcomes remains unclear. In the future, more rigorous statistical methods may be necessary to control for such confounding factors and accurately determine the individual effects of AVG and AVF on survival rates in the elderly.

While the current analysis revealed a stronger association of survival outcomes with AVG compared with AVF in elderly patients, a higher maturation failure rate was observed with AVF. The limited availability of RCTs evidence restricted the current study from deriving firm evidence-based recommendations from the results. However, importantly, the KDOQI guidelines recommend basing the decision on vascular access not only on the age of the patient or access type but to follow a comprehensive, individualized life plan that takes into consideration the history of the patient, comorbidities, vascular health, life expectancy and future needs. These guidelines should be considered when deciding on the appropriate access type for each elderly haemodialysis patient.

read and approved the final manuscript. JL, HL, ZX, QL and HS confirm the authenticity of all the raw data.

Ethical approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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