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REVIEW

A Review on the Hemodialysis Reliable Outflow (HeRO) Graft for Haemodialysis Vascular Access

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WHAT THIS PAPER ADDS

Our systematic review assesses outcomes of the Hemodialysis Reliable Outflow (HeRO) graft and discusses its usage in complex haemodialysis patients with central venous stenosis. There have been various single centre studies published, but this manuscript offers to combine the whole literature to date on its outcomes in terms of patency, dialysis access associated steal syndrome, interventions, and bacteraemia. This will allow clinicians to accurately understand the whole literature on the HeRO graft.

Objectives: With improved dialysis survival there are increasing numbers of patients who have exhausted definitive access options due to central venous stenosis and are maintaining dialysis on a central venous catheter. The Hemodialysis Reliable Outflow (HeRO) allows an alternative by providing a definitive access solution. The aim of this study is to systematically review the published outcomes of the HeRO graft and discuss the role in complex haemodialysis patients.

Methods: Electronic databases were searched for studies assessing the use of the HeRO graft for dialysis in accordance with PRISMA published up to December 31 2014. The primary outcomes for this study were 1-year primary and secondary patency rates. Secondary outcomes were rates of dialysis access associated steal syndrome, HeRO-related bacteraemia rates and rates of interventions.

Results: Following strict inclusion/exclusion criteria, eight studies including 409 patients were included in our review. Primary and secondary pooled patency rates in this complex cohort of dialysis patients were found to be 21.9% (9.6–37.2%) and 59.4% (39.4–78%). The rate of dialysis access associated steal syndrome was low at 6.3% (1–14.7%) as was the range of HeRO-related bacteraemia (0.13–0.7 events per 1000 days).

Conclusions: This literature review shows that the HeRO graft is an acceptable option for complex dialysis patients who are catheter dependent. Owing to device availability, published data are predominantly North American and further longer-term studies in other populations may be necessary. In this challenging patient group, randomized controlled trials are required to allow comparisons with alternative access options.

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INTRODUCTION

A critical factor in the survival of renal dialysis patients is the surgical creation of definitive vascular access (VA). Arteriovenous fistulas (AVFs) are the preferred choice due to their superior long-term outcomes[1] and have been promoted by guidelines, for example the fistula first initiative in the United States.[2] With improved survival of dialysis patients most clinicians will encounter a subgroup of complex patients who may have had repeated failed AVFs or arteriovenous grafts (AVGs) and exhausted all upper arm

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options and be catheter dependent, with the increased risks of associated bloodstream infections, central venous stenosis, and mortality.

Over the last few years, an alternative to central catheters for these complex patients has been proposed with the Hemodialysis Reliable Outflow (HeRO) graft (Cryolife Inc company; Eden Prairie, MN, USA). Comprising two elements, a graft and venous outflow component, the graft is anastomosed to the ipsilateral brachial artery and tunnelled subcutaneously. The venous outflow component is placed percutaneously into the right atrium through the subclavian or internal jugular vein and superior vena cava. This component is tunnelled subcutaneously towards the graft. Therefore, it bypasses central stenosis, primarily in the brachial, cephalic, and subclavian veins by positioning the tip of the outflow component beyond it in the right atrium. The two elements are subsequently attached to each other subcutaneously through a purpose designed titanium connector. This then provides a definitive access with continuity from the artery through to the right atrium. None of the catheter is exposed therefore reducing the risk of infection (Fig. 1). The FDA approved the HeRO graft in 2008 and there are reports of its usage from North American studies; however, it has only recently been introduced in Europe. The aim and purpose of this review was to systematically assess the published outcomes of the HeRO graft and discuss its usage in complex haemodialysis patients.

METHODS

Search methodology for identification of relevant studies

Searches of Pubmed Central, Medline, Embase, and the Cochrane Library were performed using the following specific search terms: HeRO graft, HeRO access, HeRO catheter, and Hemodialysis Reliable Outflow graft to identify articles in English language published prior to December 31 2014, dealing primarily with the use of the HeRO graft for dialysis. In addition, the references cited in selected articles were reviewed for any further relevant available studies. All studies of vascular access creation using the HeRO graft were eligible for inclusion.

We included randomized trials and observational studies. Exclusion criteria were published abstracts, case reports, review articles, editorials without original data, and non-English language publications. Articles that assessed the grafts in non-vascular access procedures were excluded. The systematic review was performed in accordance with PRISMA.[3] Therefore, all included studies were assessed for inclusion on the basis of their topic, type of study, method, number of patients included and availability of their original results.

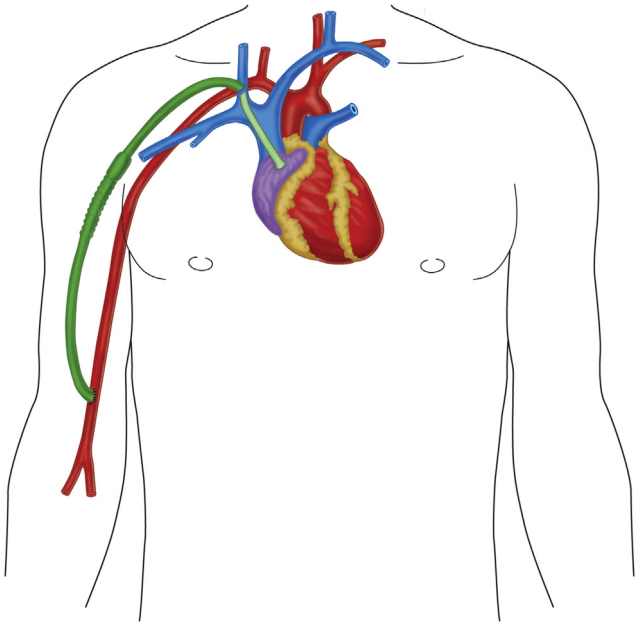

Figure 1. Illustration of HeRO graft anastomosed to the brachial artery and inserted via right internal jugular vein into right atrium.

Primary and secondary outcomes

All studies that met the set criteria were thoroughly reviewed and assessed for methodological quality. The two reviewers (J.A. and N.I.) independently extracted data using a standardized table. This was done in duplicate to increase accuracy. If there was any difference in the extracted data, we resolved it by consensus. Data extracted included primary and secondary outcome as well as year of publication, number of patients included, and duration of follow-up. The primary outcomes for this study were 1-year primary and secondary patency rates. Secondary outcomes were rates of early failure, dialysis access associated steal syndrome, graft infection, HeRO-related bacteraemia rates, and rates of re-interventions.

Statistical analysis

Characteristics and results of each included study were compiled into a tabulated form. The inverse of the Freeman—Tukey Double Arcsine transformation[9] was applied to the primary and secondary patency rates, which were then pooled using random effects (DerSimonian and Laird) models.[4] Weighed pooled rates were calculated with confidence intervals.

RESULTS

Ninety-eight articles and abstracts were identified using our search strategy. After screening the contents of the abstract, 24 full text articles underwent assessment for eligibility and quality inspection of methodology (Fig. 2). Following the assessment, eight articles were found to be eligible for the review (Table 1).

As all studies were based in the United States, it is important to look at the demographics of the patients (Table 2) as these may be different from other countries. The vast majority of patients were African American and diabetic. There was no significant difference in the number of male and female patients. It is important to notice that only three papers specified the mean number of previous

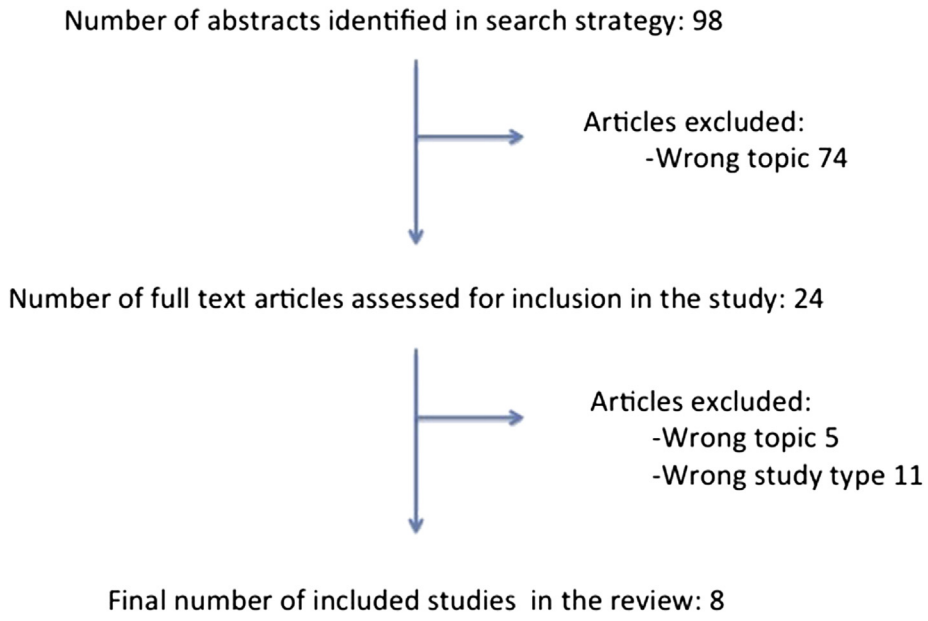

Figure 2. Flowsheet of results of search strategy with inclusion and exclusions following searches and screening.

Table 1. Summary of included studies and methodologies.

First author (reference)	Study type	Number of centres	Selection bias	Information bias	Attrition bias	Disclosures	Follow-up (months)
Katzman[5]	Prospective	Multi-centre	None Patients had no remaining upper limb options	None Clear definitions	None No patient lost to follow up	Industry funded	8.6
Gage[6]	Retrospective	Multi-centre	None. Patients had moderate to severe central venous stenosis/ occlusion	None. Clear definitions	Not every patient had complete outcome data	Industry funded	12.8
Steerman[7]	Retrospective	Single centre	None Patients had no remaining upper limb options	None Clear definitions	None No patient lost to follow up	None	13.9
Kokkosis[8]	Retrospective	Multi-centre	None. Patients had central venous occlusive disease	None. Clear definitions	None. No patient lost to follow up	None	9.1
Wallace[9]	Retrospective	Single centre	None Patients had no remaining upper limb options	Definitions of outcomes not present	None No patient lost to follow up	None	7
Nassar[10]	Prospective	Multi-centre	Patients with possible standard upper limb options could receive HeRO	None. Clear definitions	Study terminated early which could be an important factor in their results	Industry funded	18.5
Kudlaty[11]	Retrospective	Single centre	Patients without central venous occlusive disease received HeRO which is likely to mean that they would have standard upper limb options	None. Clear definitions	1 patient lost to follow up	None	15
Torrent[12]	Retrospective	Single centre	Not clear if patients had exhausted standard upper limb options	None. Clear definitions	None. No patient lost to follow-up	None	12.7

Table 2. Summary table for demographic of patients of included studies.

First author (reference)	Number of HeRO	Age	African American (%)	Male sex (%)	Diabetes (%)	Previous central catheter use (%)	Mean number of previous accesses	BMI
Katzman[5]	38	62.7	37	50	68	100	5.4	29
Gage[6]	164	55.9	78	49	46	NS	NS	NS
Steerman[7]	60	58.2	88	49	61	100	3.1	32
Kokkosis[8]	12	52	73	92	46	NS	NS	NS
Wallace[9]	21	54.8	58	47	53	NS	2	NS
Nassar[10]	52	62.9	46	46	65	NS	NS	28.9
Kudlaty[11]	20	57.1	91	45	60	NS	NS	29.2
Torrent[12]	41	55	88	34	55	NS	NS	NS

NS = not specified.

accesses prior to HeRO placement, and these ranged between 2 and 5.3.

A total of 409 HeRO grafts from eight different studies (Table 3) have been reported so far in the literature. Mean 1-year primary and secondary patency rates were calculated to be 21.9% (9.6—37.2%) and 59.4% (39.4—78%) respectively. The pooled rate of steal syndrome from the six papers that reported its incidence was 6.3% (1—14.7%). and device related bacteraemia (per 1,000 days) ranged between 0.13 and 0.7 in the six studies that reported it. The rate of interventions required to maintain HeRO patency ranged between 1.5 and three procedures per year.

DISCUSSION

In most dialysis programmes there will be patients who have exhausted definitive access options due to central venous stenosis and are maintaining dialysis on a central venous catheter. A recent technological advance in vascular access is the introduction of the HeRO device, which incorporates a standard dialysis graft with a 6-mm central venous outflow component that is radiologically placed into the right atrium. The two components of the device are joined subcutaneously to create a graft from the brachial artery that flows directly into the right atrium via the venous outflow section bypassing any central stenosis and is entirely subcutaneous with no external component as is the case with a tunnelled catheter. Although this venous outflow segment is often described as a "line" it is more realistic in considering it a full-length central stent from upper limb to right atrium. When considered as such, the rationale for use of a HeRO versus multiple central venous balloon venoplasty and stenting or for recalcitrant stenosis, the HeRO may be a useful and cost-effective alternative to multiple stents.

The HeRO graft has shown promise with 1-year primary and secondary patency rates of 21.9% (9.6—37.2%) and 59.4% (39.4—78%) respectively. Although these results are poor compared with a native AVF or AVG, in the general dialysis population, the cohort of patients having a HeRO placed are highly selected complex patients who have had multiple failed AVFs or AVGs.

Alternative options include lower limbs arteriovenous grafts (LLAVGs) that were found to have similar patency rates in the two studies that compared them with HeRO. Kudlaty et al.[11] found that both access options are adequate and have similar results. The study was not randomized and the selection criteria for the procedures were unclear, with a higher rate of diabetes and peripheral vascular disease in the HeRO group. Despite comparable patencies the infection rate in the LLAVG was 29%, which

Table 3. Summary table of HeRO outcomes of included studies.

Reference	Number of HeRO	Early failure rate (%)	Primary Patency rate (%)	Secondary Patency rate (%)	Dialysis access associated steal syndrome (%)	HeRO graft infection (%)	HeRO related bacteraemia per 1000 days	Rate of intervention per year	Mean time with HeRO (d/patient)
Katzman[5]	38	2.6	38.9[a]	72.2[a]	2.6	2.6	0.7	2.5	276
Gage[6]	164	NS	48.8	90.8	1.4	NS	0.14	1.5	NS
Steerman[7]	60	NS	15	57	1.7	22	0.61	2.2	NS
Kokkosis[8]	12	8.3	9.1	45.5	NS	25	NS	1.5	NS
Wallace[9]	21	14	11	32	22.2	NS	0.5	3	186
Nassar[10]	52	3.8	34.8	67.6	3.8	3.8	0.13	2.2	238
Kudlaty[11]	20	30	29	53.5	4.8	10	0.53	1.7	238
Torrent[12]	41	NS	8.4	53.7	NS	NS	NS	2.8	380
Weighed Pooled rate % (95% CI)		9.2 (1.9—19.9)	21.9[b] (9.6—37.2)	59.4[b] (39.4—78.0)	6.3 (1—14.7)	10.1 (2.5—21)			

NS = not specified.

[a] 8.6 months rates.

[b] Pooled rate excluding Katzman et al paper.

was almost twice that of the HeRO rate. Steerman et al.[7] describe similar rates of patency with no difference in infection between LLAVG and HeRO; however, selection bias with respect to BMI is stated. Those patients with higher body mass index in the HeRO group would be much higher risk of graft infection which may explain the differences in the studies.

If both approaches are equivalent in terms of outcome, the cost of the device must also be considered. Although the HeRO is initially more expensive, a health economic study revealed that the HeRO was the least costly dialysis access with an average 1-year cost of $6521 compared with LLAVG ($9,567).[13] These assumptions may be challenged as they are based on data from other studies but they do serve to guide on the costings of the two approaches.

Despite the HeRO graft being anastomosed to a proximal artery, the evidence of dialysis access associated steal syndrome secondary to it is low at 6.3% (1—14.7%). This figure is lower than that reported for proximal AVF.[14] An explanation may be that HeRO devices tend to be used in patients with previous access and arterial accommodation is likely to have occurred with previous fistulas and grafts. In addition the HeRO is a long device with a 5 mm internal diameter outflow which is more likely to limit flow be less prone to steal than larger conduits. Despite, this Wallace et al.[9] did show a high rate of steal syndrome in their cohort of patients (22%). This can be explained by their small number of patients ($n = 4$) who all had severe pre-existing arterial disease and required graft removal.

A concern with the volume of artificial material is infection. This analysis summarizes the HeRO-procedure-related bacteraemia rate per 1,000 days, which ranged between 0.13 and 0.7; this is lower than the reported incidence of catheter-related bacteraemia, which ranges between 0.6 and 6.5 episodes per 1,000 days.[15,16] This would suggest an important benefit of the HeRO graft over dialysis catheters, although many studies report lower line-related bacteraemia than that seen in these studies.

HeRO grafts while allowing definitive access in challenging patents do require surveillance as further endovascular interventions are common, ranging from 1.5 to three procedures per year according to the current literature. The details of interventional procedures are not highlighted in all publications but Gebhard et al.[17] describe interventions in their series of 25 patients with HeRO dysfunction. The majority of cases were treated with routine management as would be applied to a thrombosed graft. Of interest, stenoses requiring treatment were identified in 71% of procedures. Intervention for infection is the same as for prosthetic grafts. The outflow segment can be easily withdrawn and removed if required.

The current literature does have some limitation as all studies were North American and based on a specific population. In addition some studies had low number of patients and some publication bias may occur in the published studies as they represent experts and enthusiasts' series and therefore may not reflect international variations in practice.

CONCLUSION

The HeRO graft is an alternative access option for complex dialysis patients who are catheter dependent. The current literature confirms that the number of bacteraemia episodes is significantly lower with the HeRO device than catheters. The primary patency while low can produce acceptable secondary patency rates following interventions. The number of interventions required to maintain the HeRO are similar to other series of secondary access particularly in this especially complex population.[5] Further international studies are necessary to report the experience of the HeRO graft in non-US populations and multicentre randomized controlled trials to compare the graft with catheters or alternative access procedures in such complex access problems.

CONFLICT OF INTEREST

N.I. and R.G.J. have received honoraria for teaching and training from Cryolife.

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