Should a fistula first policy be revisited in elderly haemodialysis patients?

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ABSTRACT

Life-sustaining haemodialysis requires a durable vascular access (VA) to the circulatory system. The ideal permanent VA must provide longevity for use with minimal complication rate and supply sufficient blood flow to deliver the prescribed dialysis dosage. Arteriovenous fistulas (AVFs) have been endorsed by many professional societies as the VA of choice. However, the high prevalence of comorbidities, particularly diabetes mellitus, peripheral vascular disease and arterial hypertension in elderly people, usually make VA creation more difficult in the elderly. Many of these patients may have an insufficient vasculature for AVF maturation. Furthermore, many AVFs created prior to the initiation of haemodialysis may never be used due to the competing risk of death before dialysis is required. As such, an arteriovenous graft and, in some cases, a central venous catheter, become a valid alternative form of VA. Consequently, there are multiple decision points that require careful reflection before an AVF is placed in the elderly. The traditional metrics of access patency, failure and infection are now being seen in a broader context that includes procedure burden, quality of life, patient preferences, morbidity, mortality and cost. This article of the European Dialysis (EUDIAL) Working Group of ERA-EDTA critically reviews the current evidence on VA in elderly haemodialysis patients and concludes that a pragmatic patient-centred approach is mandatory, thus considering the possibility that the AVF first approach should not be an absolute.

Keywords: arteriovenous fistula, arteriovenous graft, central venous catheter, elderly, haemodialysis, vascular access

INTRODUCTION

The successful creation and maintenance of haemodialysis vascular access (VA) remains of profound importance in patients reliant on regular dialysis. The 2015 Annual Report of the ERA-EDTA registry reported that 42% of the total prevalent European renal replacement therapy patients were aged ≥65 years, the mean age being 60.8 years, ranging from 48.6 years in Ukraine to 66.8 years in Portugal [1]. The majority (85%) started renal replacement therapy with haemodialysis. Overall, patients aged 65–74 and >75 years now represent 23 and 19%, respectively, of the total prevalent European renal replacement therapy population [2]. Furthermore, according to this report, 52% of patients commencing renal replacement therapy were aged ≥65 years, the mean age being 63.1 years, ranging from 48.1 years in Albania to 70.6 years in the Dutch-speaking part of Belgium [1]. The Annual Data Report 2014 of the United States Renal Data System noted that the mean age at the start of renal replacement therapy was 62.3 years for men and 63.4 years for women, with the highest incident rates of treated end-stage kidney disease now in the 70- to 79-year-old age group with a peak of 1543 per million population [3].

Life-sustaining haemodialysis requires a durable VA to the circulatory system. The ideal permanent VA must provide longevity of use with minimal complication rate and supply sufficient blood flow to deliver the prescribed dialysis dosage [4]. While evidence from randomized controlled trials is lacking, there is a broad consensus that the VA type not only contributes to patient morbidity, but also contributes independently to pa-
The native arteriovenous fistula (AVF) is considered the optimum access to initiate patients on haemodialysis because of its longer survival and lower complication rate as compared with other forms of VA, such as synthetic arteriovenous grafts (AVGs) and central venous catheters (CVCs) [11]. Large studies have shown a graded mortality risk from both cardiovascular and infectious diseases depending on access type, with the highest risk associated with CVCs, followed by AVGs, and the least with AVFs [5–10].

AVFs are recommended by many national and international clinical guidelines as the VA of choice for haemodialysis patients [12–15]. However, there is concern as to whether general guidelines equally apply to the elderly population [16], and suggestions have been made on how to modify the recommendations for VA choice in these patients [17]. Specific recommendations of national and international guidelines as far as the VA choice in the elderly patients is concerned are not numerous [14, 15]. Most of them underline the concurrent comorbidities and the poor quality of upper extremity vessels as the main reasons for high early AVF failure rates in this population. In this context, the elderly patients may benefit from the use of AVGs. Early cannulation arteriovenous grafts (eAVGs) might avoid the use of CVCs with their inherent high risk of infection, particularly when urgent haemodialysis treatment is necessary and AVF creation/maturation is problematic [14, 15]. Of note, regular monitoring after VA placement is mandatory and high-risk patients such as the elderly and diabetic patients should be evaluated carefully [14]. The reduced life expectancy and high cardiovascular risk that contraindicate AVF placement are indications for CVC use [15].

The population on haemodialysis throughout the world is ageing. This article of the European Dialysis (EUDIAL) Working Group of ERA-EDTA critically reviews the current evidence on VA in elderly patients with haemodialysis. Actually, encouraging research, communicating knowledge, teaching and contributing to education in the field of haemodialysis are the main aims of the EUDIAL Working Group of ERA-EDTA.

**VA STRATEGIES IN THE ELDERLY PATIENT**

There is currently no general consensus as to the best VA option for elderly patients, and the debate continues. Elderly patients with end-stage kidney disease have high prevalence of comorbidities, disability, cognitive function and frailty, all of which have been shown to have prognostic significance [18]. In addition, quality of life has shown to be poor in this population [19]. Many patients may prioritize quality of life over life expectancy, making the choice of VA in this population more complex. Furthermore, they often face complex ethical, psychosocial, financial and transportation issues [20]. The creation and use of a VA in elderly patients requires the complex integration of the patient, biological and surgical factors as the VA type might be a key factor influencing survival [21–24]. In reality, VA planning in the elderly is different from that in younger patients, and the ‘fistula first’ policy may not always be the preferred approach for older patients because of their reduced life expectancy and conflicting results after surgery [25].

Another critical issue is the optimal timing of VA creation: it remains challenging, above all for elderly patients. A recent study demonstrated that among the 3418 elderly chronic kidney disease patients undergoing pre-dialysis VA creation, 67.4% started dialysis, 15.1% died and 17.5% survived without requiring dialysis by the end of the 2-year follow-up [26]. As far as the issue of pre-emptive AVF creation in the elderly is concerned, Hod et al. explored the relationship between when an AVF was placed before the start of haemodialysis and its subsequent use at dialysis initiation in a retrospective cohort of 17 511 patients from the US Renal Data System [27]. Overall, 54.9% of subjects initiated dialysis using an AVF; after stratification by time of AVF creation before haemodialysis initiation, the odds ratio for successful AVF use improved steadily for up to 6–9 months. The cumulative number of access procedures per patient also rose steadily the longer the AVF was placed before dialysis initiation and levelled off after 6–9 months. In other words, placing an AVF for >6–9 months pre-dialysis in the elderly may not associate with a better AVF success rate [27].

It has been shown that age affects outcomes in chronic kidney disease [28]. Generally, older patients lose renal function at lower rates than younger ones, have a lower rate of events of progression to end-stage kidney disease and a have shorter survival due to competing risks of mortality [29]. Actually, elderly patients may be more likely to die before benefitting from an AVF [26]. Furthermore, they may be more likely to experience primary AVF failure with a higher incidence of CVC use at haemodialysis initiation, which was associated with increased morbidity and mortality [30, 31]. Patients aged >65 years have been reported to have an AVF failure rate double than that of younger patients [32]. Unfortunately, unsuccessful AVF placement results in a high incidence of temporary CVC use at the start of haemodialysis treatment, resulting in significant risks and complications from CVC use including bacteraemia and thrombosis [33], despite a significant lower rate of bloodstream infections in older patients compared with younger patients [34]. Actually, one study showed that initiation of haemodialysis with a CVC was higher in an AVF group than an AVG group in the elderly [35].

Colour Doppler ultrasound plays a key role in planning VA construction by providing useful data on the pre-operative morphological and functional characteristics of the vessels used for AVF construction [36]. Vessel mapping has been highly encouraged and current international guidelines support the routine use of colour Doppler ultrasound before AVF surgery [12, 13]. It is important to keep in mind that, the smaller the arterial and vein diameters, the higher the risk for immediate AVF non-function. There is a ‘grey-zone’ interval in arterial and vein diameters for the creation of a viable radio-cephalic AVF: 1.6–1.9 mm for the artery and 2.0–2.4 mm for the vein [37]. Pre-operative ultrasound findings may have an impact on the patency rate of VA, and although the patency rate is significantly lower in patients aged ≥75 years, a better patency rate can be obtained when the arterial diameter is ≥2.0 mm or greater [38]. Another study focusing on the AVF construction in patients >80 years enrolled only patients who had received...
WHAT VA IN THE ELDERLY PATIENT?

Advantages and disadvantages of an AVF

Many studies clearly demonstrate a high rate of ‘technical feasibility’ of AVF construction in elderly patients [25, 40–42] and age alone should not disqualify octo- and nonagenarians from AVF surgery [39, 43]. However, several authors have highlighted the problem of early AVF failure, which may range from 20 to 60% [44]. The high primary failure rate and need for multiple procedures to maintain patency may impact negatively on quality of life in the elderly patient [45, 46]. In skilled hands, endovascular treatment of AVF complications appears to be a valuable approach, even in nonagenarians, in view of its low invasiveness, low complication rate and relatively good long-term patency rate [47]. Furthermore, an analysis from the US Renal Data System data between 2005 and 2007 on the apparent survival advantage of AVFs, after adjustment for health status, suggests that AVF should still be the VA of choice for elderly patients initiating haemodialysis [48]. The benefits of an AVF over an AVG only become evident when the use or the expected use of the AVF is >18 months, suggesting that patients with a life expectancy of <18 months do not experience the benefit of the longer patency expected from AVF placement [49]. An observational study comparing clinical outcomes in patients aged >67 years, starting haemodialysis with a CVC and subsequently having an AVF or AVG placed, showed that, despite extended CVC dependence, patients undergoing AVF placement within 6 months had fewer hospitalizations due to infections and a lower likelihood of death than those receiving an AVG [50]. A recent decision analysis on the VA choice in incident haemodialysis patients suggested that an AVF attempt strategy is superior to AVG and CVC access, in terms of reduced mortality and lower cost, for the majority of patients. However, on the contrary, in women with diabetes and elderly men with diabetes the outcomes become similar, regardless of access type. As such, the advantages of an AVF attempt strategy significantly decline in older patients, particularly for women with diabetes [51].

A scoring system has been proposed to predict the likelihood of AVF failure to mature, dependent on the individual patient’s clinical profile, including factors such as age (>65 years), coronary artery disease, peripheral vascular disease and race [32]. It must be said, however, that the same risk prediction model was not found to be discriminative in a cohort of European patients [52]. A recent cohort study on the factors predicting failure of the ‘fistula first’ policy in the elderly demonstrated that there is an association of older age, female gender, black race, diabetes, cardiac failure, shorter pre-end-stage kidney disease and nephrology care with pre-dialysis AVF failure, suggesting that the rate of AVF failure increases by 1% for every year for the age group >67 years [35]. Whether a distal AVF has the same risk of failure as a more proximal one in the elderly patients may be relevant in the decision-making process. A recent meta-analysis reported a significant higher rate of radial-cephalic AVF failure in the elderly compared with younger patients, with a pooled effect in favour of the elbow AVF [51]. The elbow AVF created at the origin of the radial artery is an efficient primary choice for elderly patients, and has been reported to have a higher survival compared with wrist and snuff-box AVFs [40, 53]. In this regard, the bend of the elbow area is of great strategic interest for VA surgery. Reasons for this interest are the presence of arteries of adequate size that are less affected by atherosclerotic processes, of a venous network connecting the forearm and the arm and of a patent perforating vein at the elbow. The perforating vein AVF may be preferred in elderly patients affected by diabetes mellitus and arterial hypertension [54]. Thus, in elderly patients, conservation of proximal access sites might be of minor importance due to their limited life expectancy, and a more liberal use of proximal access types may be justified [55]. However, especially in the elderly, a VA conundrum exists, as the distal VA is more likely to result in slower access blood flow rate and a higher incidence of early failure, although microsurgery techniques may allow the creation of distal AVFs in elderly patients aged >70 years with an acceptable failure risk [56]; on the other hand, the more proximal VA is more likely to result in very high access blood flow rate, increasing the risk of steal syndrome and high output heart failure [57]. In this regard, it is imperative to recall the cardiac ‘toxicity’ of the peripheral arteriovenous access [58]. The functional bypass of a significant fraction of cardiac output resulting from the creation of an arteriovenous access occurs throughout the whole day and not just during the dialysis treatment. This cardiac shunting may be in the range of 20–30% of the cardiac output, but may reach 50% in the case of upper arm AVFs [59]. This becomes an increasing burden for the ageing heart where cardiac output systematically decreases with increasing age [60], thus increasing the relative access blood flow rate to cardiac output ratio for a given access blood flow rate. Another point is the systematic reduction in treatment efficiency of haemodialysis sessions caused by the functional bypass of ‘cardiopulmonary recirculation’ [61]. This reduction would be expected to increase with decreasing cardiac output. Interestingly, these limitations are absent with CVCs, but they are present with AVGs.

Advantages and disadvantages of an AVG

Data on AVG in the elderly are conflicting. Some studies advocate the use of AVF rather than AVG and provide evidence that, in elderly patients, autogenous VA may have a patency rate similar to those of younger patients [39]. In contrast, other data support the opposite strategy of ‘AVG first’ in octogenarians and report a higher risk of death before the start of dialysis with AVF than with AVG [62]. In patients aged ≥67 years, only 50.7% of those with AVF placement initiated dialysis using their AVG, and 43.4% started with a CVC; in contrast, among those patients that received an AVG as first access only 25.4% started dialysis with a CVC; in other words, patients who receive an
AVG are less likely to need a CVC at their first haemodialysis treatment compared with those who received an AVF [62]. In a retrospective cohort study addressing the early failure of dialysis access in the elderly, it was noted that AVF creation was associated with a lower mortality rate than AVG in the first 12 months after formation. However, the incidence of repeat AVF/AVG creation and CVC placement was substantially higher in the first 12 months after AVF creation compared with AVG [63]. Finally, a very recent paper by Lee et al. reported that in elderly haemodialysis patients initiating dialysis with a CVC and later having an AVF or AVG placed, there were trade-offs with AVF or AVG placement [64]: AVGs resulted in shorter CVC dependence and less frequent interventions to make the VA (AVG) functional, but required more interventions to maintain patency after maturation, compared with AVFs. On the other hand, AVFs were less likely to have successful use after creation, and more likely to require interventions to make them functional. Furthermore, they were associated with longer CVC dependence, but required fewer interventions to maintain patency after successful use and experienced fewer abandonment in the first year after successful use, compared with AVGs [64].

Although AVGs require more procedures to ‘maintain’ patency, AVFs require more procedures to ‘establish’ patency, with the result that the overall patency may not differ substantially between the two forms of permanent access [65]. Of note, in a low-income population with high rates of hypertension, obesity, diabetes and tobacco use, the primary patency rates of AVF and AVG stratified by age, ≤60 and >60 years, revealed a benefit for AVF in those aged ≤60 years. The outcomes did not differ between AVF and AVG in those aged >60 years [66].

The AVG is a valid alternative form of VA when no suitable anatomy for AVF creation and rapid renal progression are present, allowing consideration of VA at a later date [67]; in such cases, the use of an ecAVG might be suitable as a CVC sparing strategy, because of the high risk of non-maturing autologous AVF [23], even though the mortality benefit of AVG over CVC may not apply in the oldest (>89 years) age group [22]. A recent randomized controlled trial of new and established haemodialysis patients who required immediate arteriovenous access demonstrated superiority of ecAVGs over tunnelled CVCs in terms of bacteraemia and mortality, while proving cost neutral at 6 months [68]. Within that cost envelope re-intervention made up the largest proportion of costs in the ecAVG arm while infection-related costs made up the largest proportion in the tunnelled CVC arm [68]. Furthermore, variations in outcomes of VA by race or ethnicity in the elderly, have been reported. The decreased risk of early failure after AVG versus AVF creation is greater for blacks compared with whites [69]. Finally, as already discussed for AVF, the creation of an AVG may increase the risk of vascular steal and high-output heart failure, resulting in ischaemia to the hand and complications ranging from frank gangrene to motor and sensory neuropathies and ischaemic pain. In addition, brachial AVFs or AVGs increase the degree of cardiac shunting, and in elderly patients with cardiac compromise, this may lead to exertional dyspnoea, particularly in those with significant aortic valve disease [38].

### Advantages and disadvantages of a CVC

In the context of an intent-to-defer haemodialysis treatment strategy, a tunnelled CVC could be the best choice, because no maturation time is required and with the lower risk of CVC-related bloodstream infections reported in elderly patients [34]. The CVC does not systematically increase cardiac work load and provides the highest extracorporeal clearance for a given extracorporeal blood flow in absence of CVC recirculation [70, 71]. Furthermore, a tunnelled CVC may be the best VA in end-of-life situations regardless of age. In addition, the person’s preference for the type of VA varies with age, as elderly patients are more likely to prefer CVC access to AVF, as they are concerned by bleeding and bruising complications more so than younger patients [72]. Most importantly, strict protocols for nursing care and optimal CVC management should be implemented in every centre [73]. For a correct/objective decision-making process in this area, a randomized feasibility trial comparing CVCs with AVFs in the elderly patient starting haemodialysis has been proposed [74].

In a recent study the CVC prevalence and conversion to AVF/AVG (non-CVC), and their effects on outcomes during the first year of haemodialysis in a multinational cohort of almost 15 000 elderly patient (≥70 years) were studied [75]. In these incident haemodialysis patients, survival was significantly worse when using a CVC at all times. In Europe, the conversion frequency from CVC to non-CVC was higher in the younger fraction. Conversion from non-CVC to CVC was associated with worsened outcomes only in the older fraction. The results of this study corroborate the need for early preparation in the elderly haemodialysis population [75].

Some recent papers discussed whether CVC really causes increased mortality. Brown et al. showed that patient factors are likely affecting AVF placement and may explain at least two-thirds of mortality benefit seen in patients with an AVF [76]. Patients initiating with an AVF had a lower mortality; furthermore, patients initiating with a CVC after failed AVF placement had lower mortality than patients initiating with a CVC alone [76]. In addition, Quinn et al. showed that the excess mortality in patients dialysing with a CVC may not be due to the access-related complications from the CVC, but may be the result of residual confounding, unmeasured comorbidity, or treatment selection bias [77]. With these data suggesting some mortality risk of CVC possibly attributable to patient factors when compared with AVF/AVG, it is conceivable that a CVC could be a first option in a subgroup with a very limited prognosis, depending on patient preferences (Figure 1). Further research is required to explore this option.

Table 1 summarizes the advantages and disadvantages of the different types of VA in the elderly patient.

### A Patient-Centred Approach

There are no randomized controlled trials answering the question of what is the optimal VA for the elderly patient. It is well recognized from observational studies that the superiority of AVFs has important limitations and confounders, and a randomized controlled trial comparing mortality with the different
access strategies is very difficult to undertake. The risk of bias in studies comparing clinical outcomes by haemodialysis access type is substantial, especially when elderly people are included [78].

A patient-centred approach is mandatory in the elderly (Figure 1). VA outcomes in haemodialysis are critically important for both patients and clinicians, but frequently are neither patient-relevant nor consistently reported in randomized trials. A Standardized Outcomes in Nephrology-Hemodialysis consensus workshop identified VA as one out of the four core outcome domains in haemodialysis. Proposed outcome measures for function included ‘uninterrupted use of

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**Table 1. Advantages and disadvantages of the different types of VA in the elderly patient**

<table>
<thead>
<tr>
<th>VA type</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
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<tbody>
<tr>
<td>Pre-emptive AVF</td>
<td>No age limit for this procedure with adequate vessels</td>
<td>Competing risk of death before haemodialysis start</td>
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<tr>
<td></td>
<td>Lower infection rates compared with CVC and AVG</td>
<td>More AVFs created than used</td>
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<td></td>
<td></td>
<td>More likely to start dialysis with a CVC or AVG</td>
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<tr>
<td>AVF after start of dialysis</td>
<td>Surgery as needed</td>
<td>Need of additional access procedures</td>
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<tr>
<td></td>
<td>No age limit for this procedure with adequate vessels</td>
<td>Higher rates of failure to mature compared with AVG</td>
</tr>
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<td></td>
<td>Most functioning AVFs will be used</td>
<td>Potential steal syndrome</td>
</tr>
<tr>
<td>AVG</td>
<td>Short waiting time between the operation and utilization (days–weeks)</td>
<td>Increased right-sided cardiac pressures</td>
</tr>
<tr>
<td></td>
<td>Lower infection rates than CVC</td>
<td>Increased cardiac output</td>
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<tr>
<td></td>
<td></td>
<td>Left ventricular hypertrophy</td>
</tr>
<tr>
<td>CVC</td>
<td>Quick and easy procedure</td>
<td>Higher cost</td>
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<tr>
<td></td>
<td>No needle punctures</td>
<td>Needs accurate maintenance with interventional procedures</td>
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<tr>
<td></td>
<td>Higher patient preference</td>
<td>Higher infection rates than AVF</td>
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<tr>
<td></td>
<td>No maturation time</td>
<td>Potential steal syndrome</td>
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<td></td>
<td>No cardiac load</td>
<td>Increased right-sided cardiac pressures</td>
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<td>Increased cardiac output</td>
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<td></td>
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<td>Left ventricular hypertrophy</td>
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**FIGURE 1:** Patient-centred VA assessment in the elderly. ‘Age >90 years’ in the third box derives from references [22] and [62], reporting no benefit associated with AVF placement in this population. CKD, chronic kidney disease.
the access without the need for interventions’ and ‘ability to receive prescribed dialysis’, but not ‘access blood flow’, which was deemed too expensive and unreliable [79]. These are the critical priorities for the patient. In this context, VA planning and its placement in the elderly patient with end-stage kidney disease requires integrating patient’s values and preferences. All the VA options should be weighed on an individual basis and reassessed longitudinally. Besides comorbidity burden, functional status, all the considerations for achieving the right VA for the individual patient and the patient-reported view on quality of life should be always taken into account [80]. On the other hand, the optimal access type and timing of access creation are also influenced by factors external to the patient, such as surgical experience and processes of care [81] (Figure 2).

A pragmatic approach to the ideal VA conundrum in the elderly is mandatory. The main factors to be considered include: the quality of life of the patient, life expectancy, comorbidity and potential complications from each type of VA. While a ‘fistula first’ approach has been advocated within the context of the Fistula First Initiative, individualization (‘patient first’) is more important for the elderly patient. For example, whereas an AVF would be considered the most appropriate access in the elderly patient with minimal comorbidities, managed in a predialysis clinic with an expected dialysis start in >6 months, an AVF would not be appropriate for the patient with severe aortic stenosis. Additional factors, such as the dialysis modality chosen (haemodialysis versus online haemodiafiltration), the therapeutic targets, any residual kidney function, the ability to use wider bore needles or any needles at all (e.g. in patients with dementia, needle phobia or bleeding diathesis), the ability to anticoagulate the circuit and the patient, its haemodynamic stability and other concomitant treatments (e.g. cytotoxic drugs), very often come into play when considering the most appropriate access choice for this population. Even so, timing of AVF creation must be considered in view of the lack of evidence for early initiation of dialysis [82]. In another situation, an AVG could also be considered appropriate in the elderly patient with multiple comorbidities and a life expectancy of <1–2 years. Finally, although a CVC is the least preferred option, it could be an appropriate option for the patient with multiple comorbidities and a minimal life expectancy, or a severely demented patient with a risk of needle dislodgement. We emphasize, however,
that all these decisions are dependent on access to care, time to surgical creation, expertise of the surgeon and surgical outcomes, facility practice patterns, availability of procedures to assist with maturation and, last but not least, the rates of complications including catheter-related bacteraemia (Figure 2).

KEY MESSAGES

No randomized controlled trials have been published answering the question of the optimal VA option for the elderly patient. Furthermore, current clinical guidelines do not have specific recommendations for the elderly patient.

The EUDIAL Working Group believes that, in order to achieve the best clinical practice, the nephrologist should strive to obtain the most appropriate VA for each patient based on local expertise, patient comorbidities, physical examination, ultrasound mapping and surgical anatomy, regardless of age. Surgical strategies aimed at minimizing VA complications, such as the higher AVF failure rate, increased risk of steal syndrome and congestive heart failure, are necessary for elderly patients.

Current evidence suggests that AVF should still be the first choice VA for the majority of elderly individuals starting haemodialysis. AVG placement might be an appropriate option in the elderly patients with no useable forearm veins, in those with a limited life expectancy, those who are rapidly progressing and may not have time to wait for AVF maturation, and in certain subgroups, such as older patients, particularly women with diabetes mellitus. The aim is to avoid the CVCs with their inherent high infection risk. However, a CVC may be the best VA in some clinical conditions and end-of-life situations and may even convey cardiac as well as efficiency benefits, regardless of age. In conclusion, a pragmatic patient-centred approach is mandatory, thus considering the possibility that the ‘AVF first’ approach should not be an absolute.

CONFLICT OF INTEREST STATEMENT

None declared.

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