The vascular access in the elderly: a position statement of the Vascular Access Working Group of the Italian Society of Nephrology

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Abstract

The incident hemodialysis (HD) population is aging, and the elderly group is the one with the most rapid increase. In this context it is important to define the factors associated with outcomes in the elderly patients. The high prevalence of comorbidities, particularly diabetes mellitus, peripheral vascular disease and congestive heart failure, usually make vascular access (VA) creation more difficult. Furthermore, many of these patients may have an insufficient vasculature for fistula maturation. Finally, many fistulas may never be used due to the competing risk of death before dialysis initiation. In these cases, an arteriovenous graft and in some cases a central venous catheter become a valid alternative form of VA. Nephrologists need to know what is the most appropriate VA option in these patients. The

aim of this position statement is to critically review the current evidence on VA in the elderly HD patients. To this purpose the relevant clinical studies and recent guidelines on VA are reviewed and commented. Experts of the Vascular Access Working Group of the Italian Society of Nephrology prepared this position statement in order to discuss the main advantages and potential drawbacks of the different VA modalities in the elderly patients.

Key words: vascular access, elderly, arteriovenous fistula, arteriovenous graft, central venous catheter.

Introduction

Peoples aged over 65 years are increasing worldwide, and it is predicted that over the next few decades the number of peoples over 65 years will increase by a factor of three (1). It is estimated that almost half of 65-74 year-old peoples have a five or greater chronic health conditions, and this may reach 70% once individuals are aged over 85 years (1). As nephrologists, we are facing increasing numbers of elderly patients affected by chronic kidney disease (CKD) and a high prevalence of comorbidities such as diabetes mellitus, peripheral vascular disease, hypertension and congestive heart failure. Between 1982 and 2000, the greatest growth in incident hemodialysis (HD) patients older than 65 years has been reported (2). The 2012 Annual Report of the European Renal Association - European Dialysis and Transplant Association (ERA-EDTA) Registry shows that pa-

tients aged 65-74 years represent 22% of the total prevalent renal replacement therapy population, and those aged > 75 years represent 20% (3). The clinical practical guidelines for the evaluation and management of CKD recently published by the Kidney Disease Initiative Global Outcomes (KDIGO) provide only minimal recommendations targeted for the elderly (4); in addition, renal replacement therapy in the elderly patients raises several critical issues such as life expectancy, quality of life, and other moral, ethical, financial, social, and legal issues (5). Arteriovenous fistulas (AVFs) are recommended by many national clinical guidelines as the vascular access (VA) of choice in HD patients; however, concerns exist regarding the issue of whether general guidelines could also apply to elderly population (6), and suggestions are made how to modify the recommendations for VA choice in these patients (7). In fact, the VA planning in the elderly is different from that in younger patients, and the Fistula First Initiative may not be the preferred approach for older patients because of their reduced life expectancy and conflicting results after surgery (8). Although AVF may be superior to arteriovenous graft (AVG) and central venous catheter (CVC) in all age groups, including the elderly, many of these patients have a heavy burden of comorbidities and insufficient vasculature for fistula maturation, resulting in a reduced rate of AVF patency (9). Patients over 65 years have a fistula failure rate two times higher than the younger population (10); furthermore, many fistulas will never be used due to the competing risk of death before dialysis initiation in this group (11). Unsuccessful fistula placement results in high incidence of CVC use

at start of HD treatment, with significant risks and complications from catheter such as bacteremia and thrombosis (12). However, bloodstream infections in older patients may be significantly less than in younger patients (13). Data about the AVG in the elderly are conflicting. Some studies advocate the use of AVF rather than AVG and provide evidence that in the elderlies autogenous VA may have a patency rate similar to that of younger patients (14). Differently, other data support the competing strategy of AVG first in octogenarians and show a higher chance of dying before the start of dialysis with an AVF over an AVG (15). Patient survival is strongly influenced by important factors, such as nutritional status, predialysis nephrology care, cardiovascular disease, and most importantly the VA. Nephrologists should strive for the most appropriate VA if an hope of prolongation of an enjoyable life span exists. The aim of this position statement is to critically review the current evidence on HD VA in the elderly patients. Experts of the Vascular Access Working Group of the Italian Society of Nephrology prepared this position statement in order to discuss the main advantages and the potential drawbacks of the different VA modalities in the elderly patients.

Timely VA placement in the elderly

A predialysis formalized pathway and timely placement of VA are considered the good clinical practice in the VA care. Timely preparation and education for dialysis are crucial, as these are associated with a number of benefits, including elective dialysis start with access in place, reduction in hospitalizations, higher prevalence of pa-

tients choosing a home-based dialysis modality, and in those starting with HD a reduced prevalence of CVC (16). Older patients loose renal function at slower rates than youngers, have lower rate of events of progression to end-stage renal disease (ESRD), and have shorter survival (5). The elderly patients may be more likely to die before benefiting from an AVF and to experience primary fistula failure with a high incidence of CVC use at the HD initiation, which is associated with increased morbidity and mortality (17,18). A study population has shown that placing an AVF > 9 months before HD start did not improve the success rate but was associated with an increased number of interventional procedures: from 0.64 procedures/patient for AVFs created 6-9 months predialysis to 0.72 procedures/patient for AVFs created > 12 months predialysis. In summary, placing an AVF > 6-9 months predialysis in the elderly is not associated with a better success rate (19). However, the VA teams tend to construct AVFs earlier rather than later before HD initiation, although it must be recognized that the time between the moment the patient was referred to a nephrologist and the start of dialysis was 3.5 weeks for individuals >75 years *vs.* 20.5 weeks for those < 75 years (17). This would be even better, because some authors suggest that the elderly patients with CKD should be referred later to reduce the risk of creating an AVF that is never used (20). In this regard the AVG becomes a valid alternative form of VA, if no suitable anatomy for AVF creation and slow renal progression are present (21); in these cases, the use of early stick graft might be suitable, because of the high risk of non-maturing autologous AVF in these patients (22), even though

mortality benefit of AVG over CVC may not apply in older (>89 years) age groups (9). Life expectancy as well as quality of life are important aspects for most patients considering dialysis, and recent data suggest that, if dialysis is adequately prepared for in advance, it is safe to delay its initiation until the development of signs and symptoms of uremia (23). In a context of an intent-to-defer strategy for dialysis initiation a tunneled CVC could be the best choice, because no maturation time is required. Some authors have supported generalized use of CVC in older patients (24) and, due to the lower risk of catheter-related bloodstream infections in elderly patients, tunneled CVC may represent a suitable dialysis access option in the setting of non-maturing AVF or poorly functioning synthetic grafts (13). However, strict protocols for nursing care and proper catheter management should be implemented in every center (25).

VA in elderly patients: recent findings

There is currently no general consensus as to the best dialysis VA for elderly patients with ESRD, and debate continues. The elderlies need specific health care requirement, as they are at increased risk of comorbidities that may result in frailty, reduced physical and cognitive function; furthermore, they often face complex psychosocial, financial, and transportation issues (26). The creation and use of a VA in elderly patients require the complex integration of patient, biological and surgical factors because the VA type might be a key factor influencing their survival (9,2,22,27). The advantages and disad-

vantages of each form of access may vary depending on the timing of the access placement relative to the dialysis initiation (12) The summary of the recommendations and suggestions from recently published studies on VA in the elderlies are reported in Table 1. Many studies clearly demonstrate a high rate of technical feasibility of fistula construction in the elderlies (28,29,9,30) and age alone should not disqualify patients older than 80 years from access surgery (14,31). Nevertheless, it has been shown that in patients 67 year-old or older, only 50.7% of those with AVF placement initiated dialysis using the AVF, and 43.4% started with a CVC; by contrast, among patients that received a graft as first access only 25,4% started dialysis with a CVC; in other words, the patients who receive a graft are less likely to require a catheter at initiation compared with those who receive a fistula (15). In a retrospective cohort study on the early failure of dialysis access in the elderly, it has been shown that AVF is associated with a lower mortality rate than AVG in the first 12 months after creation. However, the incidence of repeat AVF/AVG creation and CVC placement is substantially higher in the first 12 moths after AVF creation compared with AVG (32). Although grafts require more procedures to maintain patency, fistulas require more procedures to establish patency, with the result that overall patency may not differ substantially between the two forms of permanent access (33). Due to the high primary failure rate and need for multiple procedures to maintain patency with a poor patient quality of life, the eligibility in elderly patients should be carefully determined (34,35). However, in skill hands the endovascular treatment of AVF

complications appears to be a valuable approach even in nonagenarian in view of low invasiveness, low complication rate, and relatively good long-term patency rate (36). Furthermore, a recent analysis from USRDS data between 2005-2007 on the apparent survival advantage of AVFs, after adjustment for health status, suggests that AVF should still be the VA of choice for elderly individuals beginning HD, until more definitive findings eliminating selection bias become available (37). The benefits of an AVF over an AVG only become evident when the use or expected use of the AVF is >18 months, suggesting that patients with a life expectancy of less than 18 months do not experience the benefit of the longer patency expected from AVF placement (38). A recent decision analysis on the VA choice in incident HD patients provided evidence that the AVF attempt strategy is superior to AVG and CVC with regard to mortality and cost for the majority of patient characteristic combinations; on the contrary, in women with diabetes and elderly men with diabetes has similar outcomes, regardless of access type. The advantages of an AVF attempt strategy significantly diminish among older patients, in particular in women with diabetes (39). In fact, in a survey of European experts exploring barriers to the fistula-first concept, less than a third of the respondents believed that the majority of nephrologists in their country would consider AVF creation in a 75-year-old woman with comorbidities (40). The VA-related outcomes may be optimized by considering individual patient characteristics and a patient based approach is recommended (41).

Surgical strategy in elderly patients

Several authors have highlighted the problem of early failure, which may span from 20 to 60% (42). A scoring system has been derived with the ability to predict the likelihood of failure to mature dependent on the patient clinical profile including factors such as age (> 65 years), coronary artery disease, peripheral vascular disease and race (10); however, the elderly patients have a higher fistula failure rate (43), and the combination of age and diabetes impairs fistula outcome with significantly higher failure rates, up to 42% (44). A recent cohort study on the factors predicting failure of AV "fistula first" policy in elderly, demonstrates that there is an association of the older age, female gender, black race, diabetes, cardiac failure, shorter pre-ESRD nephrology care and predialysis AVF failure (45). The aging incident ESRD population might require different strategies in order to minimize risk of failure and number of surgical procedures. A recent meta-analysis showed a significant higher rate of radial-cephalic AVF failure in the elderly compared with the younger, with a pooled effect in favor of the elbow fistula (43). The elbow fistula created at the origin of the radial artery is an efficient primary choice in elderly patients, and has a higher survival compared to wrist and snuff-box AVFs (28,46). In this regard, the bend of the elbow area is of great strategic interest for VA surgery. Arteries of adequate size and less affected by atherosclerotic processes, the venous network connecting the forearm and the arm and presence of a patent perforating vein of the elbow allow the surgeon great flexibility

in the type of AVF to construct. The perforating vein fistula may be preferred in elderly patients with diabetes and hypertension (47). Thus, in elderly patients conservation of proximal access sites might be of minimal importance due to their limited life expectancy, and a more liberal use of proximal access types may be justified (43). However, especially in the elderly, a VA conundrum does exist, as the distal VA more likely results in lower access blood flow and high incidence of early failure, although it has been demonstrated that the use of microsurgery enabled the creation of distal AVFs in elderlies > 70 years with acceptable risk of failure (48); by contrast, the proximal VA more likely results in very high access blood flow, increasing the risk of steal syndrome and congestive heart failure.

Conclusions

It is well known that observational studies that established the superiority of fistulas have important limitations and a randomized study comparing mortality with different access strategies is very difficult to plan. The risk of biases in studies comparing clinical outcomes by HD access type is substantial (49), especially when elderly peoples are included. To provide a best VA option in elderly people a semantic paradigm shift has been recently suggested: it should address comorbidity as the main subject line, and then age becomes one of the many covariants, instead of an independent risk factor for mortality (50). Age should not be a limiting factor when determining candidacy for AVF creation (51).

In conclusion, because of heterogeneity in life expectancy, health status, health priorities, and illness experiences, no approach to VA can be expected to meet the needs of all older adults with advanced kidney disease. In this context, our opinion is that a multidisciplinary team should review elderly patients starting on dialysis, aiming to identify the most appropriate VA. In these circumstances, we believe that dialysis VA selection in the elderly should be guided by patient's preference and surgeon experience, based on comprehensive, balanced and unbiased informations, including their relative advantages and disadvantages (Table 2), adopting an individualized approach that tries to achieve the best outcomes regardless of age.

Key messages

1) Renal replacement therapy in the elderly raises several issues.
2) The VA planning in the elderly is different from that in younger patients: elderlies could be referred later to reduce the risk of creating an AVF that is never used.
3) The elderly with limited life expectancy may be less likely to benefit from an AVF first approach.
4) The patient's preference for the type of VA should be taken into account.
5) We advice to adopt an individualized approach, regardless of age.

Final suggestions

- The Working Group acknowledges that randomized clinical trials, eliminating selection biases, are needed for more definitive findings. Current evidence suggests that AVF should still be the VA of choice for elderly individuals beginning HD.
- No specific recommendations targeted for the elderly are provided in the recent published guidelines.
- The Working Group believes that in order to achieve good clinical practice the nephrologist should strive to get the best VA for each patient based on the team's knowledge and skill set, comorbidities, physical examination, ultrasound mapping and surgical anatomy, regardless of age.
- The Working Group suggests that surgical strategies aiming to minimize the VA complications, such as the high fistula failure rate, steal syndrome and cardiac failure, are necessary in the elderly patients.
- The Working Group suggests that in elderly comorbid patients with no useable veins, the AVG placement might be the best option in order to avoid the CVCs with their inherent high infection risk.
- The Working Group believes that a catheter may be the best VA and a better option in end-of-life situations regardless of age.

Ethical Responsabilities of Authors

The manuscript has not been submitted to other journals.

The results presented in this paper have not been published previously in whole or part.

Consent to submit has been received from all co-authors.

Authors whose names appear on the submission have contributed sufficiently to the scientific work and therefore share collective responsibility and accountability for the results.

The research do not involve human participants or animals.

Informed consent is not request.

Compliance of potential conflicts of interest

The Authors have no conflict of interest.

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Table 1. Summary of the recommendations and suggestions from studies on vascular access in the elderly

Author Journal Location	**Study Design**	**Patients' characteristics**	**Intervention Comparator**	**Outcomes**	**Results**	**Notes**
Azevedo Sem Dial 2015 France	Retrospective over prospectively collected data	Nonagenarian = 38 pts, mean age 93.9 years	Only AVF, mostly radiocephalic (=30)	PPR and SPR after endovascular treatment of upper limb AVF (stenosis or throm-	PPR =60% and 43% at 1 and 2 years SPR = 95% and 92% at 1 and 2 years	Endovascular treatment is a valuable approach in nonagenarian patients

				bosis)		
Bonforte JVA 2000 Italy	Retrospective	198 patients > 65 years	Toledo-Pereira, snuffbox, wrist AVF	Primary survival	Best outcome from proximal radial AVF (Toledo-Pereira) in spite of comorbidities	Toledo-Pereira AVF suggested as first access option in elderly
Borzumati JVA 2013 Italy	Retrospective	78 pts Mean age 82,5 years		Survival and complication rate for distal, mid arm, proximal AVF	Overall survival 76% and 71% at 12 and 24 months for AVF	Choose as distal AVF as possible in elderly. AVF is gold standard in elderly as younger

						pts
Chang Sem Dial 2011 USA	Re-stro-spec-tive USRDS Wave II	764pts > 65 years	AVF vs AVG. Dia-betics vs non diabet-ics	Mortality and in-terven-tion re-ferral	No mor-tality dif-ferences AVF vs AVG, for interven-tion refer-ral for di-abetics and non diabetics	Potential benefits derived from AVF com-pared with AVG and CVC may not apply univer-sally.
Cloude anos Ann Vasc Surg 2015 USA	Retro-spec-tive	31 pts, mean age 82 y	32 AVF	PPR, SPR at 1 and 2 years	PPR= 51% and 38% at 1 and 2 years SPR = 75% at 1 and 2	Doubts on ad-vantages of AVF in elderly

					years High level of reinter-vention to mantain patency, high use of CVC. Poor survival	
De Leur Vasc Endovsc Surg 2013 Neth-er-lands	Retro-spec-tive	107 AVF in 90 pts, aged 75years or older	65 RCF vs 42 BCF	PPR and SPR, QOL	PPR for RCF at 1 and 2 years = 31%, 22% SPR for RCF 1 and 2 years 58%, 50% PPR for BCF at 1 and 2 years =	Signifi-cant benefit in creating proximal access QOL high despite a high mor-tality rate

					52% and 41% SPR for BCF at 1 and 2 years = 70% and 57%	
DeSilva JASN 2013 USA	Prospective Cohort study	115,425 Incident HD patients Age: 76.9±6.4 yrs Gender:52.9 % male	Fistula Graft Catheter	Mortality	HR:1.77 CVC vs AVF (p<0.001) HR:1.05 Graft vs Fistula (p=0.06)	Fistula was not superior to graft
Hicks J Vasc Surg 2015 USA	Retrospective	507791 pts on USRDS 2006-2010	Age group	Mortality	AVF is superior to AVG and CVC regardless of the	Mortality benefit of AVG over CVC may not apply

					patient's age, in-cluding in octoge-narians. groups	in older (>89 years) age groups
Hod JASN 2014 USA	Retro-spec-tive	17511 pts Mean Age 76.1 years at the initia-tion HD	AVF suc-cess group (suc-cess) vs AVG+ CVC group (fail-ure)	AVF success initiation of HD using theAVF initially placed, regard-less of the func-tionality and du-rability	Placing an AVF.6–9 months predialy-sis in the elderly may not associate with a better AVF suc-cess rate	Succes rate AVF use in-crease as time between creation and HD initiation in-creased(but not > 9 months)

Lazarides J Vasc Surg 2007 Greece	Meta analysis	Ten studies: 1171 non elderly and 670 elderly Only 5 studies with PPR and SPR Elderly > 65 y	Patency rate distal vs proximal AVF or graft	Distal AV: elderly vs non elderly Distal access in elderly vs proximal or graft	More risk of failure in distal access in elderly Significant benefit n creating proximal access	A more liberal use of proximal access types may be justified
Murea CJASN 2014 USA	Retrospective 2005-2007	464 pts with tCVC 374 non elderly (18–74 years) and 90 elderly (≥75	Risk of CVC infection in age group	Rate of catheter-related blood-stream infection (tCVC)	Hazard ratio = 0.33 for catheter-related blood-stream infection in the elderly	Lower risk of catheter-related blood-stream infection in elderly than younger pts

		years) patients				
Nadeau-Fredette He-modial Int 2013 Cana-dian	Retro-spec-tive 2005-2008	55 pts > 80 years vs 57 pts 50-60	AVF and AVG	Primary Failure Primary and second-ary pa-tency	PF older 40% vs 17% younger PPR simi-lar Second-ary pa-tency shorter in elderly (p=0.005)	Need of a careful selection and evalua-tion in el-derly pri-or to re-ferral. Patient based approach reccmme nded
Olsha J. Vasc Surg 2015	Retro-spec-tive study 2005-2009	146 ac-cess in134 in-cident and prevalent HD pa-	128 AVF 18 AVG Forear m, upper	Patency rate non-matura-tion rate	PPR 39%, 33%, and 23% at 12, 24, and 36 mo.	Age alone should not dis-qualify patients older

Israel		tients Age: 85±2.9 years Gender: 66% male	arm AVF, AVG		SPR 92%, 83%, and 77% at 12, 24, and 36 mo No difference between the different types of accesses	than 80 years from access surgery
Swindlehurst J. Vasc Surg 2011 UK	Retrospectively on prospectively collected data (6	246 pts > 65 years (Group A) 89 pts < 65 years (Group B)	AVF and AVG	PP, APP, SP, ACPR, death with functioning conduit, mean	Patency rates for different types of conduits were similar between the two group Failure to	AVF in elderly possible with high patency rate, short hospital stay and low revi-

	years) First AV attempt			conduit survival, failure to mature	mature > elderly AVG higher cumulative patency in group A	sion rate
Vachharajani CJASN 2011 USA	Retrospective	37 Incident HD patients Age:83.4±3.4yrs Gender: 64% male	Facility HD Home HD	Day HD before death Facility vs home	52±14 vs 386±90 days ($p<0.05$)	Functional status and life expectancy should be assessed
Weale J. Vasc Surg 2008 UK	Retrospective	658 pts Median age 68.5 y	RCAVF BCAVF in age group (< 65,	Usability, primary, secondary patency	Age did no affect usability, primary or secondary patency of	High failure rate Disagreement with Lazarides

			66-79, >80 y)		either RCAVFs or BCAVFs	study
Weyde Blood Purif 2006 Poland	Retrospective 1998-2004	131 consecutive HD patients. Age 79.1 ± 3.6 yrs Gender: 50% male	Only AVF considered (92% forearm)	Successful surgery Primary and secondary AVF patency. Patient survival	Successful AVF: 107/131 patients (82%) PPR: 70% at 6 mo, 59% at 12 mo SPR: 92% at 6 mo, 84% at 12 mo Patients survival : 94% at 6 mo, 88% at 12 mo, 66% at 3	Possible selection bias. Good patients and AVF survival.

					yrs, 45% at 5 yrs	
Zhang Hemodial Int 2014 Canada	Retrospective Registry	39.721pts incidents 27% 65-74 y 26% 75-85 y 5% >85 y	AV access (AVF and graft) Catheters	Mortality by vascular access and age category	Lower adjusted mortality compared with catheter use in each age category	Understand patient preference, complications, and resurce use

AVF= arteriovenous fistula; AVG=arteriovenous graft; CVC=central venous catheter; PPR=primary patency rate; SPR=secondary patency rate; RCF=radiocephalic fistula; BCF=brachiocephalic fistula; QOL=quality of life; PP=primary patency; APP=assisted primary patency; SP=secondary patency; ACPR=assisted cumulative patency rate; PF=primary failure

Table 2. VA advantages and disadvantages in the elderly

	Advantages	Disadvantages
Pre-emptive AVF	• No age limit for this procedure with adequate vessels • Lower infection rates compared to CVC and AVG • Better survival (?) • Patients can shower	• Competing risk of death before HD start • Higher rates of failure to mature compared to AVG • More AVFs created than used (increased morbidity and costs)
AVF after dialysis start	• Surgery as needed • Most functioning AVF will be used • Advantages of pre-emptive AVF are maintained, but CVC is needed	• Start of dialysis with a CVC • Higher AVF dysfunction and infection rates compared to pre-emptive AVF • Higher rates of failure to mature compared to AVG • With low mean survival, actual AVF utilization may

		be short
AVG	• Short timing from procedure to use (days to weeks) • Lower infection rates compared to CVC	• Higher cost • Needs accurate maintenance with interventional procedures
CVC	• Quick and easy procedure • No needle punctures • Higher patient preference	• Increased infection rates, carrying higher morbidity and mortality