Int Urol Nephrol (2008) 40:1133–1142
DOI 10.1007/s11255-008-9464-2

NEPHROLOGY - REVIEW

Vascular access in elderly patients with end-stage renal disease

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Received: 7 June 2008 / Accepted: 18 August 2008 / Published online: 16 September 2008

Abstract During the last few years, the number of elderly patients with end-stage renal disease (ESRD) has been increasing worldwide. Establishment of a viable vascular access is of primary importance in these patients. This review discusses the advantages and disadvantages of the available vascular access modalities [namely arteriovenous (AV) fistulae, AV grafts, and central venous catheters (CVCs)] in elderly ESRD patients. AV fistulae seem to be superior when compared with other vascular access alternatives with respect to patency, morbidity and mortality rates. On the other hand, due to the age-related advanced atherosclerosis in the elderly, higher failure rates for AV fistulae in this age group have been described. Two controversial issues, namely the higher infection and thrombosis rates in elderly ESRD patients, are also discussed. Current evidence suggests that old age should not comprise a drawback when selecting the appropriate vascular access modality (AV fistula, AV graft or CVC) for the performance of hemodialysis. The possible vascular access options in elderly ESRD patients should not be different from younger individuals.

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Keywords Hemodialysis · End-stage renal disease · Vascular access · AV fistula · AV graft

Introduction

The incidence of end-stage renal disease (ESRD) is increasing worldwide. According to the 2007 United States Renal Data System (USRDS) Annual Data Report, more than 106,000 new patients began therapy for ESRD in 2005 (2.0% more than in 2004), while the prevalent dialysis population reached 341,000 (3.3% more than in 2004) [1]. A forecast in the early 2000s projected the number of new patients with ESRD in the United States to increase to 129,200 ± 7,742 by 2010, with accompanying Medicare expenditures of $28.3 ± 1.7 billion [2]. A more recent study predicted that by 2015 there will be 136,166 (range 110,989–164,550) new patients with ESRD in the United States per year [3]. These data clearly underline the importance of the growing epidemic of ESRD with its accompanying socioeconomic consequences. According to the 2007 USRDS Annual Data Report, although the fastest growth in absolute numbers occurs among patients aged 45–64 years, ESRD rates are rising the most quickly among those aged 65 and older [1].

A recent report from the Centers for Disease Control and Prevention showed that in 2005, nearly two-thirds (61.4%) of patients hospitalized with kidney disease were aged ≥65 years, compared with 49.9% in 1980 [4]. An increase of approximately 300% (from 19.3 to 56.2 per 10,000 population occurred among persons aged 65–74 years, and an increase of approximately 350% (from 119.0 to 393.2 per 10,000 population) occurred among persons aged ≥75 years [4]. According to the 2007 USRDS Annual Data Report [1], in 2005 the overall median age of new ESRD patients was 64.6 years. Although the incident rates between 2000 and 2005 have been relatively steady for most age groups, for patients ≥75 years, the rate has grown 10%, from 1,570 to 1,725 per million population [1]. Two similar analyses from Wisconsin [5] and Japan [6] similarly showed that the incidence of ESRD is increasing, particularly among the elderly. In addition, diabetes and hypertension, two conditions affecting the vessels, are more frequent in the elderly than in younger groups.

This article provides a critical overview of the vascular access alternatives in elderly patients with ESRD.

Specific characteristics of the elderly ESRD population

Some studies have supported that the elderly population (>75 years) differs considerably from younger ESRD patients in terms of vascular access choice and outcome [7–10]. In addition, older hemodialysis (HD) patients have specific age-related problems, such as carotid atherosclerosis/carotid artery stiffness [11], congestive heart failure [12], and coronary heart disease [13]. In comparison to younger individuals, elderly patients are more likely to have poor quality (or absent) forearm or leg veins because of prior medical interventions and are more likely to have atheroma or medial calcifications affecting their radial or brachial arteries [14].

Vascular access alternatives in the elderly: AV fistulae versus AV grafts versus permanent central venous catheters

The creation and maintenance of a viable and well-functioning vascular access is the mainstay of delivering adequate HD therapy. In 1966, Brescia et al. introduced the endogenous arteriovenous (AV) fistula [15], which comprised a revolutionary therapeutic modality for the management of renal patients. The AV fistula is still considered to be the optimal vascular access for HD by many international guideline committees, such as the National Kidney Foundation–Kidney Dialysis Outcome and Quality Initiative (NFK–K/DOQI) [16] and the Dialysis Outcomes and Practice Patterns Study (DOPPS) [17] committees.

There are a number of surgical problems with AV fistulae in the elderly. Firstly, elderly patients have more atherosclerotic vessels than younger individuals; as a result, the failure rates are higher in this age group. Indeed, a study evaluating the operative factors associated with early failure of dialysis access showed that the mean time to AV failure was 297, 232, 213, 231, and 178 days for patients aged <20 years, 21–40, 41–60, 61–80 and >80 years, respectively [18]. In addition, vascular calcifications and age-related vascular changes increase the likelihood of early AV graft failure in the elderly.

Native AV fistulae are superior compared with AV grafts and permanent cuffed central venous catheters (CVCs), because of the smaller number of corrective interventions, improved patency, and longer overall survival rates [19–22]. A report of the renal registry of Catalunya, Spain, including 3,073 patients receiving HD, showed that the average duration of a functioning AV fistula was 3.5 years, that of vascular grafts 2 years, and that of CVCs <1 year [23]. Alternatively, tunnelled CVCs are discouraged as permanent vascular access due to their increased risk of luminal thrombosis and infection [24–28], unreliable blood flows [24], risk of central venous stenosis [29, 30], shorter life expectancy after the first cannulation [31], and patient cosmetic concerns [24]. However, in patients that were referred late, "trial dialysis", and a failed AV fistula, both cuffed and non-cuffed CVCs may provide suitable access [32]. In such individuals, the right internal jugular vein is the preferred location for a dialysis CVC [32].

A disadvantage of AV fistulae is that these are not readily utilizable after placement; indeed, early cannulation has been shown to be associated with shorter survival [17, 33]. Although the NKF–K/DOQI committee suggested that the initial use of AV fistulae should be delayed for at least 4 weeks after surgery [16], the DOPPS guideline committee recommended that a 2-week period is sufficient for AV fistula maturation before the first cannulation [17]. The utilization of AV fistulae should be delayed to allow enlargement and "arterialization" of the vein in order to achieve adequate blood flow through the fistula and lower the risk of local hemorrhage at the cannulation site, wall damage, fibrosis, and, eventually, occlusion [17]. Due to advanced age, it should be expected that the elderly require a longer AV fistula maturation time.

A prospective cohort study of incident dialysis patients, the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) study, was initiated in 1995 to investigate the effect of vascular access modality choice on different outcomes of dialysis care [34]. After a median follow-up of 27 months, the use of an AV fistula was associated with a lower mortality rate compared with CVCs (11.7 vs 16.1 per 100 person-years, respectively; $P = 0.008$ by log-rank test) [34]. In an unadjusted Cox proportional hazards regression model, CVC use was associated with a 67% increased mortality risk [hazard ratio (HR) 1.67; 95% confidence interval (CI) 1.14–2.45; P value not mentioned]. After adjustment for age, race, gender, history of peripheral vascular disease, history of cardiovascular disease, presence of diabetes, index of coexistent disease, body mass index, smoking status, education, timing of referral to a nephrologist, and insurance status at initiation of dialysis this risk was only moderately reduced (HR 1.47; 95% CI 1.01–2.17; P value not mentioned) [34]. When individuals ≥65 years of age were considered, the use of a CVC and an AV graft were associated with a 28% (HR 1.28; 95% CI 0.73–2.22; P value not mentioned) and 46% (HR 1.46; 95% CI 0.84–2.54; P value not mentioned) increased mortality risk, respectively, compared with the use of an AV fistula [34]. Three other similar studies also supported the superiority of AV fistulae with respect to morbidity and mortality risk compared with AV grafts and CVCs [35–37]. In the first [35], the relative mortality risk was shown to be higher for diabetic patients with ESRD with an AV graft (relative risk = 1.41, $P < 0.003$) and a CVC (relative risk = 1.54, $P < 0.002$) compared with an AV fistula. In the second study including 784 incident HD patients (245 AV fistulae vs 539 AV grafts), the relative risk of access failure for a patient with an AV fistula was 67% lower at the age of 40 years, 54% lower at the age of 50 years, and 24% lower at the age of 65 years compared with patients of the same age with an AV graft [36]. In the third study including 66,595 incident HD patients ≥67 years, 1-year crude death rates were 24.9, 27.2, 28.1, and 41.5% for patients with simple AV fistulae, autologous vein grafts, synthetic grafts, and CVCs, respectively [37]. Patients with simple AV fistulae had the lowest likelihood of death compared with those with synthetic grafts (HR 1.160; 95% CI 1.084–1.241; $P < 0.0001$) or CVCs (HR 1.696; 95% CI 1.593–1.806; $P < 0.0001$) [37]. From these data [34–37], it can be concluded that in the elderly AV fistulae are associated with better patency and mortality rates and thus comprise a better vascular access option than either AV grafts or CVCs.

Factors affecting AV fistula patency rate

An important issue that arises when creating an AV fistula is the selection of an available outflow vein. In the upper limb, there are normally three potential outflow veins available: the cephalic, the basilic, and the median antecubital vein. The brachial–cephalic, brachial–basilic, and brachial artery-to-median antecubital vein AV fistulae have been studied individually [38–40]. A comparison of the three antecubital vascular access procedures with respect to time to first cannulation, maturation, patency, and complication rates showed that there are no significant differences between these three AV fistula types [41].

Besides the selection of the appropriate outflow vein, other factors affecting AV fistula patency rates include AV fistula thrombosis and infection. The frequency of vascular access thrombosis and infection rates in elderly compared with younger patients is a controversial issue. Didlake et al. found no difference in the frequency of thrombosis, infection, flow rates, or pseudoaneurysm formation between elderly and young patients [42]. In contrast, Dobkin et al. reported a fourfold increase in deaths due to vascular access-related infections [43]. Furthermore, recombinant human erythropoietin (rhEPO)-associated vascular access thrombosis was more common in elderly patients for both native AV fistulae and AV grafts compared with younger patients [44]. Consequently, the therapeutic approach of vascular access thrombosis and/or infection may be different in elderly patients compared with younger ones.

A factor which may affect AV fistula patency rates is the presence of temporary CVCs at the time of HD initiation. A single-center longitudinal cohort study examined vascular access outcomes of all patients with ESRD ($n = 197$) who started HD therapy (defined as any kind of extracorporeal treatment) during a period of 7 years [45]. Of the study group, 117 patients (59.7%) had a temporary CVC at the start of HD therapy, whereas an AV fistula was created in the rest. Among those who began therapy using a temporary CVC, 39 patients (33.3%) had already undergone vascular access surgery, whereas 67 (57.3%) did so during the first month of HD and 11 patients (9.4%) thereafter. Patients who started HD therapy with a CVC used their AV fistula significantly earlier (median maturation time before needling: 23 vs 32 days, respectively; $P = 0.01$) [45]. The need to start dialysis with a temporary CVC was associated with a worse AV fistula survival ($P = 0.03$) [45]. These findings suggest that the insufficient maturation period may be a causal link between CVC utilization and AV fistula failure [45].

Another study from the same group showed that late referral and use of temporary CVCs at HD initiation predicted earlier utilization of the AV fistula, which in turn proved to be a strong independent predictor of shorter primary (the time from AV fistula creation to first failure) and secondary (the time from AV fistula creation to the point it could no longer be used for HD, regardless of the number of revisions required to maintain patency) AV fistula survival [46]. The risk of primary failure was 50% less in AV fistulae that were left to mature for 1–2 months, and was even lower with longer maturation periods, compared with cannulation earlier than 15 days. In addition, the presence of cardiovascular disease (e.g., history of heart failure, coronary artery disease, peripheral arterial disease) independently predicted greater risk for AV fistula failure [46]. Interpretation of these findings leads to two conclusions: (1) that adequate maturation of the AV fistula is essential before its initial utilization, and (2) that strict control of cardiovascular risk factors and appropriate treatment of cardiovascular disease may also have beneficial consequences on AV fistula maturation and survival [46]. These findings may hold particular implications for the elderly, since (1) the time needed for AV fistula maturation is longer, and (2) cardiovascular risk factor management is more complex with advanced age.

Another issue which may be important particularly for elderly HD patients is the AV fistula cannulation technique. A recent modification in the standard “rope-ladder” technique for AV fistula cannulation is the so-called “buttonhole” technique; that is, cannulation of exactly the same AV fistula site [47–49]. A study comparing the two techniques showed that the “buttonhole” technique is an easier cannulation procedure [47]. These results hold considerable implications for patients with limited access cannulation sites or with a difficult-to-cannulate AV fistula [47]. It was suggested that this technique offers important advantages to self-cannulating patients, thus enabling home dialysis and providing a better quality of life [47–49].

AV fistulae in the elderly

The NFK–K/DOQI [16] and DOPPS [17] Guidelines for vascular access recommend that the radial–cephalic autogenous AV fistula should be the first-choice access procedure for patients commencing dialysis.

A number of studies compared AV fistula patency rates in elderly versus non-elderly patients (Table 1). A single-centre, retrospective analysis of 444 AV fistulae supported that age should not be a limiting factor for creation of an AV fistula [50]. The lack of an age-related effect on primary AV fistula patency rates was also verified in other studies [51–54]. Other studies, however, supported worse AV fistula patency rates in patients >65 years compared with younger individuals [55–57]. Increased age has been associated with increased intima-media thickness [58] and lower AV fistula rates [59], both associated with AV fistula failure. Therefore, based on the results of these reports, no definite conclusion could be drawn regarding the effect of age on AV fistula patency rates.

Permanent CVCs in the elderly

Although a permanent vascular access (i.e., an AV fistula or an AV graft) is the best option for dialysis,

Table 1 Studies evaluating the effect of age on AV fistula patency rates

Study (year)	Study design	Outcome
Prischl et al. (1995) [57]	Evaluation of the effect of age on AV fistula patency in 139 patients divided into five age groups: (1) ≤39, (2) 40–49, (3) 50–59, (4) 60–69, and (5) ≥70 years	No significant difference in AV fistula patency rates was demonstrated with either overall comparison ($P = 0.6$) or pairwise comparisons of all groups (e.g., patients ≤39 vs. ≥70 years; $P = 0.97$)
Grapsa et al. (1998) [52]	Comparison of AV fistula patency rates between patients < 60 and ≥ 60 years of age (101 vs 48 patients, respectively)	No significant difference in 5-year AV fistula survival rates between the two groups (45 vs 35% for patients <60 and ≥60 years, respectively; *P* not significant)
Golledge et al. (1999) [53]	Comparison of AV fistula patency rates between patients aged <63 versus >63 years	No difference in 24-month primary (41 vs 59%, respectively; $P = 0.1$) and secondary (61 vs 65%, respectively; $P = 0.1$) AV fistula survival rates in patients <63 years compared with >63 years
Wolowczyk et al. (2000) [51]	Comparison of AV fistula patency rates between patients <70 and >70 years of age (132 vs 74 AV fistulas, respectively)	Age >70 years failed to affect AV fistula survival ($x^2 = 0.002$; $P = 0.969$)
Burt et al. (2001) [54]	Comparison of AV fistula patency rates between patients <60 and ≥60 years of age (26 vs 27 fistulas, respectively)	Compared with patients ≥ 60 years, those aged < 60 years did not show significantly different primary (74% vs 69%, respectively) or secondary (82 vs 70%) 12-month patency rates
		Compared with patients ≥60 years, those aged <60 years did not show significantly different primary (60 vs 53%, respectively) or secondary (62 vs 64%) 24-month patency rates ($P = 0.39$)
Ridao-Cano et al. (2002) [55]	Comparison of AV fistula patency rates between patients <65 and ≥65 years of age	No difference in AV fistula patency rates in patients <65 years compared with ≥ 65 years old
Obialo et al. (2003) [56]	Comparison of AV fistula patency rates between patients <65 and ≥65 years of age (110 vs 57 fistulas, respectively)	No difference in 1-year AV fistula survival rates in patients <65 years compared with ≥65 years old (50 vs 65%, respectively; $P = 0.13$)
Lok et al. (2005) [50]	Comparison of AV fistula patency rates between patients <65 and ≥65 years of age (139 vs 92 patients, respectively)	Compared with patients ≥65 years, those <65 years had similar 1-year (75.1 vs. 79.7%, respectively) and 5-year (64.7 vs 71.4%, respectively) patency rates

this is not always possible in elderly HD patients. As a result, temporary or permanent CVCs are often used in this population [60, 61]. A recent report sought to identify patient characteristics associated with delayed transition from CVC use to a permanent vascular access among ESRD patients [60]. At HD therapy initiation, 71% of the patient cohort used a CVC, 13% an AV fistula, and 16% were dialyzed with an AV graft [60]. Surprisingly, the majority of patients starting dialysis with a CVC failed to transition to a permanent vascular access within 90 days (1,117 of 1,880 patients; 59.4%) [60]. Only one in four patients (25.4%) received an AV graft and 15.2% received an AV fistula [60]. Age >75 years was more than twofold associated with the risk to remain CVC-dependent at 90 days compared with those patients <50 years [odds ratio (OR) 2.14; 95% CI 1.46–3.16; $P < 0.001$] [60]. Possible explanations for this finding include inadequate or late vascular access referral or greater primary access failure [60]. It was suggested that early referral, a close follow-up, and patient education may counteract overutilization of CVCs for HD [61].

Another finding that supports the association between older age and decreased AV fistula use/increased use of CVCs is the presence of unsuitable vasculature with increasing age; vein distensibility may be affected by a greater prevalence of vascular disease among the elderly, which is supported by the greater risk of AV fistula failure found among older HD patients [36, 62, 63].

Temporary or permanent CVCs are coupled with a number of complications when used as a long-term vascular access. These include CVC thrombosis, CVC avulsion and/or rupture, exit site infections, and bacteremias [64–66]. Catheter-related infections are a common and serious complication. Several antibiotics have been tested in clinical trials in an attempt to reduce the incidence of CVC-related infections; among others, these include topical application of povidone–iodine [67] or mupirocin [68, 69] ointments, use of antibiotic or silver-coated CVCs [70–72], various antimicrobial lock solutions [73–77], or application of a topical polysporin triple antibiotic ointment composed of 500 U/g bacitracin, 0.25 mg/g gramicidin, and 10,000 U/g polymyxin B [78]. Although several of these trials have reported positive results, the optimal strategy for long-term prophylaxis for CVC exit site infections and CVC-related bacteremias has not yet been established.

Another issue which has been the subject of extensive debate is the use of heparin versus citrate catheter locks as the optimal solution for the prevention of interdialytic CVC thrombosis. Citrate locking solutions have emerged as an effective and safe alternative to heparin for the prevention of CVC thrombosis [79–82]. A recent study, the Citrate 4% versus Heparin and the Reduction of Thrombosis Study (CHARTS), showed that, due to their cost-effectiveness and more favorable side-effects profile, citrate solutions may even be superior to heparin as indwelling intraluminal locking agents [83]. Verification of these results holds implications for the establishment of the optimal HD catheter locking solution for the prevention of CVC thrombosis.

AV fistula patency rates in the elderly versus younger patients

A recent meta-analysis of 13 studies published during a period of 10 years showed an increased risk of radial–cephalic AV fistula failure in the elderly at 12 months (OR 1.525; $P = 0.001$) and 24 (OR 1.357; $P = 0.019$) [84]. The results of this meta-analysis appear to question the NFK–K/DOQI Guidelines. However, only 10 of the 13 studies specifically compared patency of radial–cephalic AV fistulae of younger compared with elderly patients [84]. In addition, several different definitions of "elderly" were used among the studies included (e.g., ">50 years," ">70 years," etc.) [84].

The results of this meta-analysis were questioned in a study comparing the outcomes of radial–cephalic and brachial–cephalic AV fistulae in the elderly using three different age ranges [85]. This study included 658 elderly (median age 68.5 years; interquartile range 54.4–76.5 years) patients with AV fistulae (361 radial–cephalic and 297 brachial–cephalic AV fistulae) [85]. Of the patient cohort, 564 individuals (or 85.7%) went on to receive HD, while in 45.7% of the study group the AV fistula was never used for dialysis [85]. Age did not have an effect on patency rates: for radial–cephalic AV fistulae the 1- and 2-year primary patency rates were 46.0 and 27.1% for patients <65 years, 47.0 and 36.0% for those aged between 65 and 79 years, and 45.7 and 38.1% for patients ≥80 years, respectively [85]. No significant difference for primary ($P = 0.3508$) or secondary ($P = 0.2761$) patency rates was found among the age groups, and no factors could be identified that were associated with loss of primary or secondary patency of the AV fistula [85]. Similarly, for brachial–cephalic AV fistulae, the 1- and 2-year primary patency rates were 39.30 and 31.0% for patients <65 years, 53.3 and 37.5% for those aged between 65 and 79 years, and 46.3 and 42.6% for patients ≥80 years, respectively. Again, no significant difference for primary ($P = 0.1453$) or secondary ($P = 0.2470$) patency rates was found among the age groups, and no factors could be identified that were associated with loss of primary or secondary patency of the AV fistula [85]. The conclusion reached was that age did not affect usability, primary, or secondary patency of either radial–cephalic or brachial–cephalic AV fistulae [85]. Based on these results, old age should not comprise a drawback for the creation of an AV fistula.

A different opinion was supported in another study [86]. This retrospective review of 494 new vascular access procedures performed in 348 chronic HD patients >65 years (mean 71.5 ± 5.3; range 65–88 years) of age showed that the direct elbow AV fistula (constructed between the brachial artery and a suitable vein) was superior than the radial–cephalic AV fistula (1-year patency rates 91.9 vs 60.2%, respectively; 3-year patency rates 78.0 vs 57.2%, respectively; $P < 0.05$) [86]. Based on these results, the authors suggested that an elbow AV fistula should be preferred in elderly patients over a radial–cephalic one.

AV fistula versus AV graft in the elderly

A recent retrospective analysis using the USRDS Wave II dataset investigated whether old age (>65 years) is associated with inferior patency and survival rates in patients receiving AV fistulae compared with AV grafts [87]. It was demonstrated that old age was not a predictor of lower patency and/or mortality rates in these patients regardless of the presence (OR 1.34; 95% CI 0.92–1.95; $P = 0.123$) or the absence (OR 1.05; 95% CI 0.81–1.36; $P = 0.735$) of diabetes mellitus [87]. Furthermore, HD via an AV fistula was independently associated with a trend toward a significant increase in access patency in elderly non-diabetics (OR 1.478; 95% CI 0.952–2.294; $P = 0.082$), but not in elderly individuals with diabetes (OR 1.486; 95% CI 0.763–2.891; $P = 0.244$) [87]. The authors argued that a larger dataset could uncover a statistically significant benefit to AV fistula use [87].

Conclusions

Individuals >75 years of age constitute a considerable percentage of patients with ESRD. Regarding vascular access in this patient group, AV fistulae show superior results compared with AV grafts and CVCs with respect to both primary and secondary patency rates, as well as to infection and thrombosis. Adequate maturation time of the AV fistula should be pre-planned to ensure optimal primary and secondary patency rates.

Elderly ESRD patients should not be denied renal replacement therapy solely on the grounds of old age. Current evidence suggests that the possible vascular access options and outcome in elderly ESRD patients are not different from younger individuals.

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