Original Articles

Status of research in vascular access for dialysis

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Abstract

Background. Vascular access issues impose a major financial burden to health care and can be associated with increased morbidity and mortality. In this context, strategies, guidelines and available published information become important tools for health-care facilities and workers. While published data form a sound basis of formulating clinical practice guidelines for vascular access (VA), quality of the medical information is critically important. This study investigates the current status of VA publications.

Methods. A PubMed search was performed to capture all articles related to dialysis vascular access published from January 1997 to December 2009. The articles were categorized by publication type, study subject, year of publication and specialty of the authors.

Results. A total of 2260 articles from 60 medical journals were identified. Insignificant publications (letters/communications, n = 125) were excluded from the analysis. Therefore, 2135 articles formed the basis for analysis. Sixteen of the 60 journals routinely published on vascular access and generated 1747 articles [nephrology = 7 (publications = 782); radiology = 4 (publications = 333); surgery = 5 (publications = 486)], while 44/60 journals published scarcely and produced 388 articles over the 13-year period. Overall, 1213 (57%) of the articles were published by the direct involvement of nephrologists [nephrologists alone (n = 564); nephrologists in collaboration with others (n = 649)]. There were 1194 observational studies, 444 case reports/series, 375 review/editorials, 51 basic research, 12 meta-analyses and 59 randomized controlled trials published over the 13-year period. The average impact factor for nephrology, radiology and surgery journals that routinely published on vascular access was 4.425, 3.099 and 2.679, respectively.

Conclusions. Despite an increased rate of scholarly activity in the area of vascular access, there remains a significant challenge ahead due to the lack of randomized controlled trials and research focusing on the biology of vascular access stenosis.

Keywords: arteriovenous fistula; arteriovenous graft; catheters; haemodialysis; vascular access

Introduction

The management of vascular access has always been one of the critically important components in the care of haemodialysis patients. It is for this reason that, since 1997, the National Kidney Foundation (NKF) has published the Dialysis Outcomes Quality Initiative (DOQI) clinical practice guidelines for vascular access with regular updates [1]. These guidelines provide the framework in an attempt to optimize vascular access care of haemodialysis patients. The guidelines use the available data from published literature as well as the opinion of the leaders in the vascular access arena (the work group) when the evidence regarding a particular issue is not available. While the availability and inclusion of published data form a sound basis of formulating guidelines, quality of the medical information is critically important. It is important to note that the optimal study design to evaluate an intervention and outcome questions is a randomized controlled trial (RCT) [2,3]. Indeed, it is the inclusion of quality and quantity of RCTs that lends credibility and greatly impacts the validity of clinical practice guidelines. It is worth mentioning that observational studies have made immense contribution in the field of vascular access.

Vascular access issues impose a major financial burden to health care and can be associated with increased morbidity and mortality. Consequently, strategies to combat these issues must be based on well-conducted studies. This study investigates the current status of research in the field of dialysis vascular access.

Materials and methods

An extensive search was performed to capture all articles related to dialysis vascular access published over a 13-year period [January 1997 (inception of NKF-DOQI) to December 2009]. This was accomplished by performing the search through PubMed (using the terms ‘tunneled haemodialysis catheters for dialysis’, ‘arteriovenous fistula for dialysis’ and ‘arteriovenous graft for dialysis’) and individually probing each edition of 60 separate journal titles in general medicine, nephrology, general and interventional radiology, and general and vascular surgery. Articles were deemed relevant if they directly addressed dialysis vascular access. Therefore, articles on arterial vasculature not directly related to vascular access
were excluded. Once identified, the articles were divided by publication type, study subject, year of publication and specialty of the author/s.

The publication types were divided into the following groups: RCTs, observational, case series and reports, review or editorials, meta-analyses, letters to the editor and related correspondence, and basic science research. Major topics examined by the studies were investigated. The number of citations in each topic was documented. The year of publication was recorded to assess the changes over time in number and type of studies. The specialty of the authors was divided into five main groups as follows: nephrology, radiology, surgery, collaborative (nephrology included), and collaborative (non-nephrology).

### Results

A total of 2260 articles from 60 medical journals were identified. All letters to the editors and related correspondences \( n = 125 \) were excluded. Therefore, a total of 2135 articles from 60 journals were used for analysis. Sixteen of the 60 journals routinely published on vascular access and generated 1747 articles \( \text{nephrology} = 7 \) (publications = 863); \( \text{radiology} = 4 \) (publications = 359); \( \text{surgery} = 5 \) (publications = 525) \( \) (Table 1). On the other hand, 44/60 journals published scarcely and produced 388 articles over the 13-year period (Appendix).

Table 1 shows the distribution of articles among the 16 journals. There were seven nephrology, four radiology and five surgery journals. Over the 13-year period, there were 863, 359 and 525 articles published by these journals, respectively (Table 1). The number of articles published from January 1997 to December 2009 has gradually increased since the inception of NKF-KDOQI since 1997. There has been an increase in number of articles related to arteriovenous fistulae and catheters. However, the greatest increment per year has been observed in the area of arteriovenous fistulae (AVFs). Articles related to this type of access increased from 8 in 1997 to 57 in 2009. Catheter-related articles also increased from 22 in 1997 to 54 in 2009. Table 2 shows the number of articles according to the subject of publication.

The articles published per year by the three specialists (radiologists, surgeons and nephrologists) were also analysed. A major increment was seen in the number of articles published by surgeons and nephrologists. The number of articles for surgeons increased from 8 in 1997 to 43 in 2009. Similarly, the number of articles for nephrologists increased from 20 in 1997 to 42 in 2009. It is important to note that 1213 (57%) of the articles were published by the direct involvement of nephrologists [nephrologists alone \( n = 564 \); nephrologists in collaboration with others \( n = 649 \)]. Collaborative effort resulted in 106 (5%) of the articles where nephrologists were not part of the collaboration.

The 16 specialty journals that routinely published on vascular access are presented in Table 1. The average impact factor for nephrology, radiology and surgery journals was 4.425, 3.099 and 2.679, respectively. A great majority (55.9%) of the 2135 of the published articles were observational studies \( n = 1194 \). There were 444 case reports/series (20.7%) and 375 review/editorials (17.6%) published during the 13-year period. A minor fraction (2.3%) of the 2129 articles was dedicated to basic research on vascular access and meta-analyses \( n = 12 \); 0.56%. Only 2.7% of the

### Table 1. Journal titles, medical specialty, number of articles and randomized studies, and impact factors of the 16 journals that routinely published on vascular access are shown

<table>
<thead>
<tr>
<th>Journal title</th>
<th>Specialty</th>
<th>Number of articles</th>
<th>Number of RCTs</th>
<th>Journal impact factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>J Am Soc Nephrol</td>
<td>Nephrology</td>
<td>69</td>
<td>9</td>
<td>7.505</td>
</tr>
<tr>
<td>Kidney Int</td>
<td>Nephrology</td>
<td>123</td>
<td>11</td>
<td>6.418</td>
</tr>
<tr>
<td>Am J Kidney Dis</td>
<td>Nephrology</td>
<td>161</td>
<td>5</td>
<td>4.822</td>
</tr>
<tr>
<td>Nephrol Dial Transplant</td>
<td>Nephrology</td>
<td>260</td>
<td>3</td>
<td>3.568</td>
</tr>
<tr>
<td>Semin Dial</td>
<td>Nephrology</td>
<td>172</td>
<td>0</td>
<td>2.671</td>
</tr>
<tr>
<td>ASAIO</td>
<td>Nephrology</td>
<td>55</td>
<td>1</td>
<td>1.631</td>
</tr>
<tr>
<td>Radiology</td>
<td>Radiology</td>
<td>52</td>
<td>4</td>
<td>5.990</td>
</tr>
<tr>
<td>J Vase Interv Radiol</td>
<td>Radiology</td>
<td>206</td>
<td>9</td>
<td>2.217</td>
</tr>
<tr>
<td>Cardiovasc Intervent Radiol</td>
<td>Radiology</td>
<td>61</td>
<td>2</td>
<td>1.721</td>
</tr>
<tr>
<td>AJR</td>
<td>Radiology</td>
<td>40</td>
<td>0</td>
<td>2.470</td>
</tr>
<tr>
<td>J Vase Surg</td>
<td>Surgery</td>
<td>145</td>
<td>9</td>
<td>3.770</td>
</tr>
<tr>
<td>Eur J Vasc Endovasc Surg</td>
<td>Surgery</td>
<td>54</td>
<td>1</td>
<td>3.007</td>
</tr>
<tr>
<td>Ann Vasc Surg</td>
<td>Surgery</td>
<td>69</td>
<td>1</td>
<td>1.262</td>
</tr>
<tr>
<td>J Vase Access</td>
<td>Surgery</td>
<td>218</td>
<td>2</td>
<td>Not reported</td>
</tr>
<tr>
<td>Vase Endovasc Surg</td>
<td>Surgery</td>
<td>39</td>
<td>0</td>
<td>Not reported</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>1747</td>
<td>57</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. All topics covered by publications on vascular access from January 1997 to December 2009

- AVG (all topics excluding thrombosis) 192
- Vascular access (epidemiology and comparisons by type of access) 212
- Catheter (all topics) 476
- Access flow 194
- AVF (all topics excluding thrombosis) 397
- Thrombosis 181
- Hand ischaemia syndrome 64
- Endovascular stents 94
- Vessel mapping 51
- PTA technique 66
- Neo-intimal hyperplasia 49
- Central venous stenosis 54
- Anatomy 19
- Imaging techniques 24
- New devices 16
- High output cardiac failure 21
- Interventional nephrology 17
- Physical examination 7
- Total 2135
publications were randomized controlled trials. Topics covered by RCTs are presented in Table 3. Thirty-nine percent (23/59) of the RCTs focused on catheter-related issues, 20% (12/59) reported on arteriovenous graft-related issues and 13% (8/59) examined surveillance concerns.

Discussion

The current study finds that, over the past decade, all three specialists, including radiologists, surgeons and nephrologists, have made contributions to the literature on vascular access. Of these experts, nephrologists alone or in collaboration with other specialties have made the most contributions (Table 1). This was reflected by the fact that 57% of the publications over the 13-year period had direct involvement of nephrologists. The current report documented that a great majority of publications were supported by peer-reviewed, high impact factor nephrology journals. Because vascular access is a major cause of morbidity and mortality, it is encouraging to observe that, along with radiologists and surgeons, nephrologists are also playing a more active role in investigating the etiology and applying the interventions to combat access predicaments.

The present report demonstrates that AVFs and haemodialysis catheters were a major focus of the publication activity. In particular, there has been a surge of AVF articles since 2004. This, in part, might be driven by the ‘Fistula First’ initiative. The Fistula First Breakthrough was developed in 2003 as the National Vascular Access Improvement Initiative to maximize AVF in the USA [4]. Eighteen ESRD Networks led the effort and were successful in increasing fistulae from 32% in 2003 to 53.4% at the end of 2009 [4]. The increment in fistulae has also brought some of the complications associated with fistulae, i.e. early arteriovenous fistula failure and reliance on tunneled catheters. Over 70% of the incident and 22% of the prevalent haemodialysis patients are using tunneled haemodialysis catheters for dialysis therapy [5]. It is then not surprising to find that 22.3% (475/2129) of all vascular access-related publications in the current analysis were related to catheter issues.

The current study also analysed the type of literature published on vascular access [2,6]. A great majority (56%) of publications reviewed by the current report were observational studies. Case series/reports, reviews and editorials formed another major component of the literature on vascular access. Randomized controlled trials made only a minor contribution (2.7%). During the 13-year period, there have been only 59 RCTs related to vascular access. This finding was rather disappointing and consistent with a previous report documenting paucity of RCTs in nephrology. In that publication, Strippoli et al. [7] disclosed that the number of RCTs published in nephrology from 1966 to 2002 (n = 2779) were fewer than all other specialties of internal medicine including haematology and cardiology (n = 27109). In addition, these investigators found that the overall quality of RCTs in the area of nephrology was low. While a randomized controlled trial is considered to be the optimal study design to answer intervention and outcome questions, multiple barriers continue to surround such investigations. An important report by Lok and Moist [2] describes specific challenges in conducting RCTs in relation to vascular access. These investigators emphasize that funding, regulatory burden, carrier disincentives and high research cost continue to serve as major limitations. Strategies to overcome these problems would result in more RTCs and improvement in patient care [2].

It is important to mention that some progress has been recently made in the area of RCTs. The funding by National Institute of Health (NIH) of the dialysis access consortium (DAC) has resulted in two large RCTs [8,9]. One of these evaluated the role of clopidogrel on early fistula failure, and the other one focused on the role of dipyridamole plus aspirin on the patency of arteriovenous grafts. While frequency of early thrombosis was reduced, clopidogrel did not increase the proportion of fistula that became suitable for dialysis [8]. On the other hand, dipyridamole plus aspirin demonstrated a reduction in the risk of stenosis and improvement in unassisted patency [9]. Another multicentre randomized study sponsored by NIH will soon begin to address non-maturing arteriovenous fistulae. In addition to the NIH, industry is another source of support to conduct RCTs. The recent stent graft randomized study is an example of such collaboration [10].

While randomized controlled trials are important, observational studies have made major contributions to the area of vascular access. For instance, the Dialysis Outcomes and Practice Pattern Study (DOPPS) is a prospective cohort study of haemodialysis practices based on the collection of observational longitudinal data in 12 countries including Australia, some European countries, Japan and the USA [11–17]. The study was initiated in 1996 and has provided invaluable information on >38 000 patients. The main purpose of these investigations is to improve patient care and to determine which dialysis practices are associated with the best patient outcomes. Vascular access has been a major focus of DOPPS investigation. Issues studied have included some of the most practical elements of vascular access such as creation of an arteriovenous fistula and its survival, timing of cannulation and access failure, hospitalization as well as impact of access type on mortality, and paying attention to patient’s vasculature when creating an arteriovenous access.

<table>
<thead>
<tr>
<th>Table 3. Topics covered and the number of randomized controlled trials is shown</th>
</tr>
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<tbody>
<tr>
<td>Flow/surveillance</td>
</tr>
<tr>
<td>AVG</td>
</tr>
<tr>
<td>AVF</td>
</tr>
<tr>
<td>Both</td>
</tr>
<tr>
<td>Catheters</td>
</tr>
<tr>
<td>Catheter infection/lock</td>
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<tr>
<td>Catheter design</td>
</tr>
<tr>
<td>Catheter fibrin sheath</td>
</tr>
<tr>
<td>Catheter patency</td>
</tr>
<tr>
<td>Arteriovenous grafts</td>
</tr>
<tr>
<td>AVG patency</td>
</tr>
<tr>
<td>AVG design</td>
</tr>
<tr>
<td>AVG thrombosis</td>
</tr>
<tr>
<td>Arteriovenous fistula patency</td>
</tr>
<tr>
<td>Brachytherapy (in AVG)</td>
</tr>
<tr>
<td>Life site device</td>
</tr>
<tr>
<td>Thoracotomy device (in AVG)</td>
</tr>
<tr>
<td>Endovascular stents</td>
</tr>
<tr>
<td>General vascular access</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>
DOPPS has clarified that major differences regarding the type of vascular access use have existed between Europe and the USA. While the situation has improved somewhat in the USA, DOPPS had demonstrated that AVF was used by 80% of European countries and 24% of US prevalent patients in 2002 [12]. For incident patients, 66% of the patients had AVF in Europe compared with 15% in the USA (AOR = 39, P < 0.0001), and 31% of the patients had catheters in Europe while 60% in the USA dialysed with a catheter. There were 2% grafts in Europe versus 24% in the USA. Unfortunately, the situation has not changed dramatically for AVF placement for incident patients in the USA [5]. In addition, US Renal Data System has emphasized that catheter use has increased to 80% among the patients who are new to dialysis in the USA [5]. Even today, catheter and graft use continue to be greater in the USA than in many European countries [5]. A more recent DOPPS analysis has indicated that, after adjusting for demographics, co-morbid conditions and laboratory values, greater mortality risk was seen for patients using a catheter (relative risk, 1.32; 95% confidence interval, 1.22–1.42; P < 0.001) or graft (relative risk, 1.15; 95% confidence interval, 1.06–1.25; P < 0.001) versus an AVF [17]. Within a facility, every 20% greater case-mix-adjusted catheter use was associated with 20% greater mortality risk (versus facility AVF use, P < 0.001), and every 20% greater facility graft use was associated with 9% greater mortality risk (P < 0.001). Increased facility catheter and graft use were both associated with greater all-cause and infection-related hospitalization. Vascular access practice differences accounted for increased mortality for the USA compared with Europe and Japan [17].

Basic science provides the foundation for understanding dialysis access function and disease process at the cellular level and leads to development of further scientific and clinical questions. Indeed, advances in basic science often underlie scientific and clinical progress in this area [18]. However, there are too few reports and only a handful of centres conducting such research work. The problem is compounded by the fact that, at present, there is a significant lack of interest in dialysis access at the fellowship programme level both in terms of clinical teaching and basic research. Incorporation of vascular access teaching and research into nephrology training programmes would likely produce fruitful results in this area [19–21].

Despite positive signs pointing to an increasing rate of scholarly activity in the area of vascular access, there remains a significant challenge ahead. Due to the lack of RCTs, clinical practice guidelines for vascular access are largely based on observational studies and expert opinion. In this context, a cultural change in the research of vascular access and true collaboration among nephrologists, radiologists, surgeons and basic research scientists is urgently needed.

Acknowledgements. This project was not funded by any grants or funding agencies.

Conflict of interest statement. None declared.

Appendix

Forty-four journals that reported scarcely on vascular access over the 13-year period (388 articles) are presented.

n represents the number of articles published by these journals over the 13-year period.

(1) Cardiology Clinics (n = 3)
(2) Therapeutic Apheresis and Dialysis (n = 9)
(3) Radiographics (n = 7)
(4) Nephron (n = 9)
(5) American Journal of Therapeutics (n = 1)
(6) American Journal of Nephrology (n = 8)
(7) Anesthesia Analgesia (n = 6)
(8) Journal of Clinical Ultrasound (n = 14)
(9) Journal of Ultrasound Medicine (n = 6)
(10) Dialysis and Transplantation (n = 15)
(11) Archives of Surgery (n = 8)
(12) Clinical Imaging (n = 4)
(13) Annals of Anatomy (n = 8)
(14) Journal of Anatomy (n = 6)
(15) Clinical Nephrology (n = 2)
(16) American Journal of Surgery (n = 12)
(17) Nephrology News and Issues (n = 22)
(18) Advances in Renal Replacement Therapy (n = 19)
(19) British Journal of Surgery (n = 11)
(20) International Journal of Artificial Organs (n = 9)
(21) European Journal of Radiology (n = 17)
(22) Seminars in Interventional Radiology (n = 13)
(23) Seminars in Nephrology (n = 18)
(24) Current Opinions in Nephrology and Hypertension (n = 10)
(25) Journal of Interventional Cardiac Electrophysiology (n = 6)
(26) Techniques in Vascular and Interventional Radiology (n = 15)
(27) Journal of Vascular Technology (n = 12)
(28) European Radiology (n = 16)
(29) Journal of Endovascular Surgery (n = 17)
(30) Journal of Endovascular Therapy (n = 6)
(31) Cardiovascular Surgery (n = 16)
(32) Hemodialysis International (n = 3)
(33) Journal of Nephrology (n = 6)
(34) Renal Failure (n = 2)
(35) Blood Purification (n = 11)
(36) British Journal of Surgery (n = 6)
(37) Transplant Proceedings (n = 6)
(38) Nature Reviews Nephrology (n = 6)
(39) NEJM (n = 2)
(40) JAMA (n = 2)
(41) Clinical Trials (n = 2)
(42) BMC Medicine (n = 3)
(43) Advances in Chronic Kidney Diseases (n = 8)
(44) VASA-Journal of Vascular Disease (n = 6)
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PREFABL: predictors of failure of antibiotic locks for the treatment of catheter-related bacteraemia

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Abstract

Background. Antibiotic lock (ABL) solutions can effectively treat catheter-related bacteraemia (CRB) without the need for catheter exchange. This approach does not increase secondary infectious complications. We evaluated the risk factors that contribute to failure when CRB is treated with ABLs and systemic antibiotics in paediatric haemodialysis patients.

Methods. A retrospective chart review of 72 children on haemodialysis between January 2004 and June 2006 was