Shifting the paradigm for dialysis access: The latest everlinQ endoAVF clinical experience and technology evolution

Dr. Tobias Steinke
(Düsseldorf, DE)
Disclosure

Speaker name: Dr. Tobias Steinke

I have the following potential conflicts of interest to report:

- [X] Consulting
- [ ] Employment in industry
- [ ] Stockholder of a healthcare company
- [ ] Owner of a healthcare company
- [ ] Other(s)

- [ ] I do not have any potential conflict of interest
AV Fistula: “Gold Standard of AV-Access”

Limited innovation in 50 years
## Limitations of Current AV Fistulas

### Clinical Outcomes

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary failure rate</td>
<td>20-60%</td>
</tr>
<tr>
<td>Mean maturation time</td>
<td>4-9 months</td>
</tr>
<tr>
<td>Average re-interventions</td>
<td>2-3</td>
</tr>
<tr>
<td>Occlusions (thrombosis)</td>
<td>17-25%</td>
</tr>
</tbody>
</table>

### Clinical Challenges

- Availability of AVF anatomic sites
- Patient acceptance of surgery
- Surgical consistency
- Cost of interventions & complications

---

**Need for innovation to improve AVF outcomes**

Increasing arteriovenous fistulas in hemodialysis patients: problems and solutions.

Allon M, Robbin ML.

<table>
<thead>
<tr>
<th>Citation</th>
<th>N accesses</th>
<th>Primary failures %</th>
<th>Primary (unassisted) survival at 1 year %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fistula</td>
<td>Graft</td>
<td>Fistula</td>
</tr>
<tr>
<td>Bonalumi, 1982 [63]</td>
<td>177</td>
<td>10</td>
<td>83</td>
</tr>
<tr>
<td>Reilly, 1982 [64]</td>
<td>150</td>
<td>11</td>
<td>80</td>
</tr>
<tr>
<td>Palder, 1985 [65]</td>
<td>154</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Winsett, 1985 [66]</td>
<td>273</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Kherlakian, 1986 [21]</td>
<td>100</td>
<td>12</td>
<td>71</td>
</tr>
<tr>
<td>Churchill, 1992 [67]</td>
<td>227</td>
<td>4</td>
<td>90</td>
</tr>
<tr>
<td>Coburn, 1994 [20]</td>
<td>59</td>
<td>31</td>
<td>84</td>
</tr>
<tr>
<td>Rocco, 1996 [23]</td>
<td>48</td>
<td>26</td>
<td>83</td>
</tr>
<tr>
<td>Wong, 1996 [48]</td>
<td>60</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Miller, 1997 [34]</td>
<td>75</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Hodges, 1997 [68]</td>
<td>87</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>Silva, 1998 [51]</td>
<td>108</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Hakaim, 1998 [38]</td>
<td>58</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Golledge, 1999 [69]</td>
<td>107</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Miller, 1999 [25]</td>
<td>101</td>
<td>53</td>
<td></td>
</tr>
<tr>
<td>Konner, 2000 [70]</td>
<td>347</td>
<td>2</td>
<td>77</td>
</tr>
<tr>
<td>Ascher, 2000 [52]</td>
<td>99</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Murphy, 2000 [71]</td>
<td>74</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Renavur, 2000 [72]</td>
<td>137</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Wolowczyk, 2000 [45]</td>
<td>208</td>
<td>20</td>
<td>65</td>
</tr>
<tr>
<td>Gibson, 2001 [35]</td>
<td>130</td>
<td>23</td>
<td>56</td>
</tr>
<tr>
<td>Allon, 2001 [13]</td>
<td>139</td>
<td>46</td>
<td>42</td>
</tr>
<tr>
<td>Oliver, 2001 [12]</td>
<td>115</td>
<td>26</td>
<td>65</td>
</tr>
<tr>
<td>Sedlacek, 2001 [43]</td>
<td>140</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Dixon, 2002 [26]</td>
<td>205</td>
<td>30</td>
<td>53</td>
</tr>
<tr>
<td>Pisoni, 2002 [18]</td>
<td>177</td>
<td>23</td>
<td>68</td>
</tr>
</tbody>
</table>

Primary failure is defined as thrombosis or failure to mature adequately for dialysis, while primary survival is time from access placement to initial intervention.
Hemodialysis Arteriovenous Fistula Patency Revisited: Results of a Prospective, Multicenter Initiative

Henricus J.T. Huijbregts,† Michiel L. Bots,‡ Cees H.A. Wittens,§ Yvonne C. Schrama,‖ Frans L. Moll,† Peter J. Blankestijn,* and on behalf of the CIMINO study group

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>35</td>
<td>53</td>
<td>27</td>
<td>13</td>
<td>22</td>
<td>37</td>
<td>10</td>
<td>34</td>
<td>21</td>
<td>11</td>
<td>22</td>
<td>285</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>69</td>
<td>59</td>
<td>63</td>
<td>69</td>
<td>59</td>
<td>68</td>
<td>50</td>
<td>77</td>
<td>57</td>
<td>82</td>
<td>59</td>
<td>65</td>
</tr>
<tr>
<td>Age ≥65 yr (%)</td>
<td>51</td>
<td>55</td>
<td>59</td>
<td>54</td>
<td>54</td>
<td>73</td>
<td>62</td>
<td>50</td>
<td>56</td>
<td>52</td>
<td>27</td>
<td>41</td>
</tr>
<tr>
<td>CAD (%)</td>
<td>33</td>
<td>23</td>
<td>15</td>
<td>31</td>
<td>14</td>
<td>22</td>
<td>20</td>
<td>19</td>
<td>29</td>
<td>33</td>
<td>18</td>
<td>25</td>
</tr>
<tr>
<td>PVD (%)</td>
<td>6</td>
<td>8</td>
<td>7</td>
<td>23</td>
<td>9</td>
<td>3</td>
<td>30</td>
<td>9</td>
<td>10</td>
<td>18</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>20</td>
<td>43</td>
<td>44</td>
<td>46</td>
<td>36</td>
<td>27</td>
<td>50</td>
<td>21</td>
<td>33</td>
<td>9</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>BMI ≥30 kg/m² (%)</td>
<td>3</td>
<td>17</td>
<td>8</td>
<td>0</td>
<td>19</td>
<td>11</td>
<td>20</td>
<td>24</td>
<td>15</td>
<td>0</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>RRT before cannulation (%)</td>
<td>69</td>
<td>74</td>
<td>82</td>
<td>69</td>
<td>59</td>
<td>51</td>
<td>80</td>
<td>85</td>
<td>76</td>
<td>91</td>
<td>73</td>
<td>72</td>
</tr>
<tr>
<td>Forearm AVF (%)</td>
<td>66</td>
<td>42</td>
<td>33</td>
<td>85</td>
<td>46</td>
<td>76</td>
<td>62</td>
<td>62</td>
<td>62</td>
<td>36</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Preoperative duplex (%)</td>
<td>54</td>
<td>96</td>
<td>93</td>
<td>0</td>
<td>73</td>
<td>30</td>
<td>50</td>
<td>65</td>
<td>62</td>
<td>82</td>
<td>23</td>
<td>62</td>
</tr>
<tr>
<td>AVF surveillance (%)</td>
<td>20</td>
<td>43</td>
<td>63</td>
<td>15</td>
<td>45</td>
<td>22</td>
<td>40</td>
<td>47</td>
<td>86</td>
<td>20</td>
<td>94</td>
<td>42</td>
</tr>
<tr>
<td>Primary failure rate (%) (11)</td>
<td>24</td>
<td>38</td>
<td>50</td>
<td>43</td>
<td>39</td>
<td>8</td>
<td>24</td>
<td>46</td>
<td>35</td>
<td>32</td>
<td>33</td>
<td>33</td>
</tr>
<tr>
<td>PFP loss (%)</td>
<td>37</td>
<td>28</td>
<td>48</td>
<td>69</td>
<td>32</td>
<td>14</td>
<td>20</td>
<td>27</td>
<td>29</td>
<td>27</td>
<td>23</td>
<td>31</td>
</tr>
<tr>
<td>Secondary failure rate (%)</td>
<td>17</td>
<td>6</td>
<td>7</td>
<td>39</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>9</td>
<td>0</td>
<td>9</td>
<td>23</td>
<td>10</td>
</tr>
</tbody>
</table>

*CAD, coronary artery disease; PVD, peripheral vascular disease; PFP, primary functional patency.
TVA everlinQ endoAVF System

AV fistula created without open surgery to minimize vessel trauma for high fistula usability with low interventions

DISCLAIMER: The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.

1. TVA Medical data on file. GLP Animal Studies.
Endovascular AV Fistula

Potential Advantages

Endovascular AVF creation¹
- Consistent hemodynamic anastomosis¹
- Minimal vessel trauma, torque or tension¹

Clinical improvements²,³
- Low failure rates
- Few interventions
- Low complication rate

Improved delivery of care
- Additional anatomic option for patients
- Reproducible outcomes²,³

Mature cephalic fistula

No surgical scar or tissue trauma at site of anastomosis

¹ TVA Medical data on file. GLP Animal Studies.
³ TVA Medical data on file. NEAT Study Results at 3 months.

DISCLAIMER: The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.
Next Evolution: The everlinQ™ 4 endoAVF System

Image of everlinQ™ 4 endoAVF System under fluoro

4Fr RX catheters
RF Electrode
Magnetic Coupling
Ceramic Backstop
Venous Catheter
Arterial Catheter
RF Generator

Image of everlinQ™ 4 endoAVF System under fluoro
Next Evolution:
The everlinQ™ 4 endoAVF System

4 Fr System

- Enables additional creation sites for an endovascular fistula
- Enables wrist access or upper arm access
- Facilitates access site hemostasis

endoAVF Creation Sites

Access Site

Access Sites

<24 hours post-procedure

DISCLAIMER: The everlinQ™ 4 endoAVF System is not currently cleared for use or available for sale in any market.
endoAVF Procedure

Courtesy of Dr. med. Arne Schwindt, St. Franziskus-Hospital Münster, Germany

Arterial Catheter Advanced to AVF Site

DISCLAIMER: The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.
Histology and Gross Anatomy Shows Minimal Vessel Trauma of the endoAVF

- Well-healed endoAVF tract with organized, mature fibrous remodeling
- Lining of endoAVF tract well covered in endothelial cells

DISCLAIMER: Sheep model. These case images are shared for informational purposes only. The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.

TVA Medical Data on file. RR0055 GLP Animal Study.
Clinical Evidence
Multiple Studies Support the endoAVF

FLEX Study
Feasibility and safety of using the everlinQ endoAVF system

Design
• Single-center, multi-operator, prospective study
• 33 patients, 4 sequential cohorts

Key Outcomes
• 97% Technical success
• 96% Maturation
• 96% Patency @ 6 mo

Completed in 2014

NEAT Study
Safety and efficacy of using the everlinQ endoAVF system

Design
• Multicenter, prospective in Canada, Australia and New Zealand
• 60 patients, single arm
• 1, 3, 6, & 12 month follow-up

Completed in 2016

EASE Study
Safety and efficacy of using the everlinQ 4 (4Fr)

Design
• Single center prospective study
• 32 patients
• 3 - 6 month follow-up

Ongoing

Expanded Population
EU Post-Market Study
“Real world” multi-center study designed to continue building clinical evidence with everlinQ endoAVF

Design
• Multicenter, prospective study
• ~120 patients, single arm
• 1, 3, 6, & 12 month follow-up
• Includes radiocephalic AVF candidates

Study initiated in 2016

Pilot Study

ENDSMER Study
Feasibility and safety of using the everlinQ endoAVF system

Key Outcomes
• 97% Technical success
• 96% Maturation
• 96% Patency @ 6 mo

Completed in 2016

DISCLAIMER: The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.

Clinical Experience: FLEX Study

<table>
<thead>
<tr>
<th>Clinical Endpoint</th>
<th>FLEX Study Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVF maturation time</td>
<td>58 days</td>
</tr>
<tr>
<td>Interventions/patient-year</td>
<td>0.15**</td>
</tr>
<tr>
<td>Thrombosis</td>
<td>4% (1/26)</td>
</tr>
<tr>
<td>Stenosis</td>
<td>0%</td>
</tr>
<tr>
<td>Access infection/patient-year</td>
<td>0%</td>
</tr>
<tr>
<td>Serious device-related adverse events</td>
<td>3% (1/33)*</td>
</tr>
</tbody>
</table>

+ 1 patient developed venous hypertension at 37 days from a central vein stenosis. Patient received balloon angioplasty. EndoAVF occluded at 106 days.

* 1 patient developed pseudoaneurysm during procedure due to arm motion from neuromuscular stimulation. Pseudoaneurysm was resolved with thrombin injection. A procedure modification to limit arm motion mitigated this risk in subsequent cases.

** Interventions for Groups C & D (coil embolization performed at index procedure). 1 intervention in 14 patients, median follow-up time 177 days. Rate reported per patient-year.


DISCLAIMER: The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.
Clinical Experience: NEAT Study

Study Overview

- Multicenter, prospective design
  - Canada, Australia, New Zealand
- 80 patients, single arm
- 3, 6, & 12 month follow-up
- Study endpoints:
  - Fistula Usability
  - Patency
  - Safety
- Study completed August 2016

Patient Demographics

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender male</td>
<td>65.0%</td>
</tr>
<tr>
<td>Age (years)</td>
<td>59.9 ± 13.6</td>
</tr>
<tr>
<td>BMI</td>
<td>28.0 ± 6.1</td>
</tr>
<tr>
<td>BMI &gt; 25</td>
<td>64.4%</td>
</tr>
<tr>
<td>Caucasian</td>
<td>60.0%</td>
</tr>
<tr>
<td>Predialysis at enrollment</td>
<td>56.7%</td>
</tr>
<tr>
<td>Previous AVF</td>
<td>31.7%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>65.0%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>91.7%</td>
</tr>
<tr>
<td>CAD</td>
<td>21.7%</td>
</tr>
<tr>
<td>Prior renal transplant</td>
<td>13.3%</td>
</tr>
<tr>
<td>Prior PD</td>
<td>30.0%</td>
</tr>
<tr>
<td>Central venous catheter use at enrollment</td>
<td>41.7%</td>
</tr>
</tbody>
</table>

+ n=60

DISCLAIMER: The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.
NEAT Results: Primary Outcomes

- **98% success at creating endoAVF**
  - 1 procedure was unsuccessful; use of braided introducer sheath caused inadequate RF energy to be delivered
  - 8.3% (5/60) of patients experienced a serious procedure- or device-related adverse event*
  - 0% procedure-related infections

- **91% of endoAVF matured**

- **10.5% thrombosis at 12 months**

---

DISCLAIMER: The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.
Primary Patency: Time from successful endoAVF creation to the first intervention designed to address thrombosis or stenosis, assist in maturation or cannulation of endoAVF, or endoAVF abandonment.

Secondary Patency: Time from creation to the abandonment of endoAVF (censor patients with renal transplant)

DISCLAIMER: The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.
NEAT: AVF Post-Creation Procedures

~6X fewer post-creation procedures with endoAVF (US data)

DISCLAIMER: The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.

* Surgical AVF control group is a propensity-score matched cohort
(endoAVF) Clinical Study
The everlinQ novel endo vascular Arterio Venous Fistula

**Study Overview**
- Multicenter, prospective design
  - Germany, Netherlands, United Kingdom
- 120 patients, single arm
- 0-7 days and 1, 3, 6, & 12 month follow-up
- Key selection criteria:
  - Hemodialysis/pre-hemodialysis ESRD stage 4 or 5
  - Target vein/artery ≥2 mm dia
  - Patent radial and ulnar arteries
  - Presence of a perforator vein
  - Target cannulation vein >2.5 mm
  - Not NYHA class III or IV

**Outcome Measures**
- Cumulative functional patency rates
- Primary patency
- Primary assisted patency
- Secondary patency
- Procedure success
- Time to endovascular fistula maturation via time to first cannulation or established duplex ultrasound criteria (fistula usability)
- Duration of central venous catheter exposures
- Adverse events associated with access creation and maintenance
- Intervention rate
EU endoAVF Experience to date

• Approximately 250 endoAVF cases performed with the everlinQ endoAVF system globally

~70 cases completed at 16 sites in Germany, Netherlands and UK

• Real world outcomes are consistent with clinical study results from the FLEX and NEAT studies
Initial Experience - Germany

Clinical Outcome and Complications

<table>
<thead>
<tr>
<th>Condition</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious Periinterventional Complications</td>
<td>0% (0/16)</td>
</tr>
<tr>
<td>Time to Maturation in Days (Median, min.-max.)</td>
<td>56 (10 - 137)</td>
</tr>
</tbody>
</table>

Interventions

- 2 endoAVFs required revisions for low flow
  - 1 successfully receiving dialysis via the vein matured by endoAVF, sparing CVC placement
  - Other patient is still pre-dialysis
  - In hindsight, both endoAVFs may have been rescued endovascularly#
- 1 pre-planned elevation was performed (initiated dialysis on day 86)

*1 Patient lost to follow-up and 1 patient is still pre-dialysis with a patent endoAVF

DISCLAIMER: The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.
Next Evolution: EASE Study everlinQ™ 4 endoAVF System

Initial outcomes show high technical success, no access site complications, high maturation at 30 days

- 100% (32/32) successful endoAVF creation
- 1/32 endoAVF stented due to wire perforation that occurred at beginning of procedure
- 81% (22/27) reached maturation by 30d f/u
  - 18 have been cannulated by 30d f/u
Conclusions

• Experience with the everlinQ endoAVF System has shown:
  – The everlinQ endoAVF System can reliably create AV fistulas without open surgery
  – The endoAVF can be used successfully for dialysis delivery with minimal interventions required
  – The endoAVF has high patency at 12 months

• The 4Fr system, everlinQ 4, will enable wrist access, additional creation sites, and facilitate hemostasis more easy

• Initial outcomes with the 4Fr system show high technical success, no access site complications and high maturation at 30 days

• Initial real world experience is consistent with clinical study outcomes

• The endoAVF is a paradigm shift for dialysis access

DISCLAIMER: The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.
THANK YOU
endoAVF Procedure

The system consists of: 2 Catheters and a RF Generator.

DISCLAIMER: The everlinQ endoAVF System has been issued European CE Mark and Health Canada Medical Device License for the creation of an arteriovenous fistula for hemodialysis. The everlinQ™ endoAVF System is not available for sale in the United States and is under FDA review.
Shifting the paradigm for dialysis access: The latest everlinQ endoAVF clinical experience and technology evolution

Dr. Tobias Steinke
(Düsseldorf, DE)