AV Access Intervention: How the Past Leads to the Future

Bart Dolmatch, MD, FSIR
Disclosure

Speaker name: Bart Dolmatch, MD FSIR

I have the following potential conflicts of interest to report:

☒ 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
ESRD – now what?

Do Nothing

Renal Replacement Therapy (RRT)
- Kidney Transplantation
- Peritoneal Dialysis
- Hemodialysis
Dr. Joseph E. Murray of Peter Bent Brigham Hospital in Boston removed a healthy kidney from 23-year-old Ronald Herrick and implanted it in his identical twin, Richard, who was dying of severe kidney disease.
Dr. Murray received the Nobel Prize for Medicine in 1990.
Incident cases (in thousands)

USRDS Annual Report 2016
Peritoneal Dialysis
1923: Georg Ganter performed the first peritoneal dialysis at the University of Würzburg

Why so sad?

Incident cases (in thousands)

USRDS Annual Report 2016
Hemodialysis (HD): The Heavyweight
Incident cases (in thousands)

USRDS Annual Report 2016
Cycling Blood Efficiently: Vascular Access Options

Venous catheter

AV Graft (AVG)

AV Fistula (AVF)
Quinton-Scribner Shunt 1960’s-1970’s
Arteriovenous Graft (AVG)

Approx. 20% Prevalence in US*

*USRDS Annual Report 2016
Bovine Carotid Artery Heterografts (1970)

THE NATURAL SOLUTION VS. SYNTHETIC

Artegraft – Think of it as a *Fistula in a Bottle*™
EXPANDED POLYTETRAFLUOROETHYLENE (PTFE) SUBCUTANEOUS ARTERIOVENOUS CONDUIT: AN IMPROVED VASCULAR ACCESS FOR CHRONIC HEMODIALYSIS

L. D. Baker, Jr., J. M. Johnson, and D. Goldfarb
Effect of Dipyridamole plus Aspirin on Hemodialysis Graft Patency

Bradley S. Dixon, M.D., Gerald J. Beck, Ph.D., Miguel A. Vazquez, M.D., Arthur Greenberg, M.D., James A. Delmez, M.D., Michael Allon, M.D., Laura M. Dember, M.D., Jonathan Himmelfarb, M.D., Jennifer J. Gassman, Ph.D., Tom Greene, Ph.D., Milena K. Radeva, M.S., Ingemar J. Davidson, M.D., T. Alp Ikizler, M.D., Gregory L. Braden, M.D., Andrew Z. Fenves, M.D., James S. Kaufman, M.D., James R. Cotton, Jr., M.D., Kevin J. Martin, M.D., James W. McNeil, M.D., Asif Rahman, M.D., Jeffery H. Lawson, M.D., Ph.D., James F. Whiting, M.D., Bo Hu, Ph.D., Catherine M. Meyers, M.D., John W. Kusek, Ph.D., and Harold I. Feldman, M.D., for the DAC Study Group*
13 Centers (US)
649 New AV Grafts
1:1 Randomized Placebo:ASA-Dipyridamol
Prospective Study of Patency
Stenosis at Venous End of Graft is the Primary Failure Mode
3-12 months

Initial AVG VAS

8mm PTA

Post PTA

3 mo post-PTA

3 months
The Cutting Edge Trial

94 AVG venous anastomotic PTAs
Prospective 6-month clinical follow-up

Target Lesion 6-mo. 1º Patency 46.9 %
Access Circuit 6-mo. 1º Patency 40.9 %

AV Graft Covered Stents: The “FLAIR”
FLAIR® - Device Details

Self-expanding
Two layers ePTFE
  Carbon impregnated
  Fully encapsulated
Flared & straight configurations
Pivotal Trial: Summary

Improved 6 month TAPP & ACPP when used for venous anastomotic stenosis in patent PTFE grafts

...then the RENOVA PMA Study

Access Circuit Primary Patency
Arterial Anastomosis to SVC / Right Atrial Junction

<table>
<thead>
<tr>
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<th>Pivotal Study 6 months</th>
<th>RENOVA Study 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTA</td>
<td>19.8%</td>
<td>24.1%</td>
</tr>
<tr>
<td>Stent Graft</td>
<td>38.0%</td>
<td></td>
</tr>
<tr>
<td>Percent (%)</td>
<td></td>
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</table>

$P < 0.008$ $P = 0.005$
Pre-Treatment 6mm AVG

Post-Treatment

21 month (no intervention)
Pre-Treatment 7mm graft

10 months

35 month (no intervention)
The GORE® VIABAHN® demonstrated statistical superiority over PTA at the treatment site. Kaplan-Meier estimates ($p = 0.008$).
The VIABAHN demonstrated greater circuit primary patency.

Kaplan-Meier estimates (p=0.035)
The VIABAHN group demonstrated fewer circuit interventions over 24 months.
The GORE® VIABAHN® Endoprosthesis reduced costs by ~$2000 per patient over 24 months

<table>
<thead>
<tr>
<th></th>
<th>VIABAHN n=131</th>
<th>PTA n=138</th>
<th>Difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Procedure Costs</td>
<td>$7,820</td>
<td>$3,440</td>
<td>($4,380)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Repeat Intervention Costs at 24-Months</td>
<td>$16,585</td>
<td>$23,022</td>
<td>$6,436</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Note: Only 26 VIABAHN patients and 28 PTA patients had secondary lesions at initial procedure. All costs are reported in constant 2012 dollars and costs in year 2 are discounted at 3%. All repeat procedure costs account for patients that were lost to follow-up by using an inverse probability weighting adjustment (Bang and Tsiatis (2000), Glick et al. (2007)).
Arteriovenous Fistulae (60-65%) (Plural of Fistula is Fistulae – NOT Fistulas!)
Brescia

Appell

Cimino

(the surgeon!)
The AV Fistula: Our 50 year old “Gold Standard”

“First” AV Fistula, 1966

AV Fistula in 2016
Mean time from referral to surgery was 5 months.

Problem #2: AVF Failure to Mature (FTM)

Mean time from access surgery to access use was 6 months.

Effect of Clopidogrel on Early Failure of Arteriovenous Fistulas for Hemodialysis
A Randomized Controlled Trial

9 Centers (US)
877 New AV Fistulae
1:1 Randomized Placebo:Clopidogrel
“Maturity” if successful cannulation
8 of 12 successive times within 4 months

### Table: Suitability failure (all patients)

<table>
<thead>
<tr>
<th>No. (%) of Patients</th>
<th>Clopidogrel (n = 385)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Placebo (n = 373)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suitability failure (all patients)</td>
<td>238 (61.8)</td>
<td>222 (59.5)</td>
</tr>
</tbody>
</table>

**60% Immaturity Rate**
Medicare claims and CROWNWeb, 2014-2015

**Early AVF Failure Rates**

<table>
<thead>
<tr>
<th>Total AV fistula placements</th>
<th>Percentage of failed placements</th>
<th>Number of days between AV fistula placement and first use</th>
</tr>
</thead>
<tbody>
<tr>
<td>31,720</td>
<td>33.8%</td>
<td>Average: 114, Median: 78, 25th percentile: 171, 75th percentile: 171</td>
</tr>
</tbody>
</table>

34% 4.5 months
AVF Failure to Mature (FTM)

- Prior vein abuse (PICC, IV)
- Pre-op vascular mapping
- Surgical Decision
- Surgical Skill
- Flow Dynamics
- Patient’s Anatomy
- Patient’s Physiology
- Comorbid Factors:
  - CAD
  - PAD
  - Age
  - Race
  - ...and more
Surgical manipulation of the vein is associated with fistula failure\(^1,2\)

2. Roy-Chaudhury et al. JASN 2006;17:1112-27
Two Non-surgical AVF Technologies (Not yet Available in the U.S.)

TVA everlinQ endoAVF System

- RF Electrode
- Magnetic Catheter Coupling
- Ceramic Backstop
- RF Generator

Avenu Medical Ellipsys®: Thermal Resistance Anastomosis Device (tRAD)

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.

DISCLAIMER: The Ellipsys® Vascular Access System is an investigational device and is limited by federal law to investigational use and is not for sale in the United States.
endoAVF

Arterialized Veins

Cephalic Vein

Basilic Vein

endoAVF
Non-surgical AVF Creation: Will it Improve Care?
AVF stenosis: What beyond PTA?
Drug Coated Balloons (DCB’s)
1° Endpoint: Treatment Site Primary Patency

Figure 5. Kaplan-Meier analysis of TLPP through 12 months
2° Endpoint: Access Circuit Primary Patency

Table 12. Kaplan Meier Analysis, ACPP through 12 months

<table>
<thead>
<tr>
<th>Description</th>
<th>LTX DCB (N=141)</th>
<th>Standard PTA (N=144)</th>
<th>Difference % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Events, n (%)</td>
<td>79 (56.0%)</td>
<td>95 (66.0%)</td>
<td></td>
</tr>
<tr>
<td>Number Censored, n (%)</td>
<td>62 (44.0%)</td>
<td>49 (34.0%)</td>
<td></td>
</tr>
<tr>
<td>Discontinued Early</td>
<td>23 (16.3%)</td>
<td>11 (7.6%)</td>
<td></td>
</tr>
<tr>
<td>No Event</td>
<td>39 (27.7%)</td>
<td>38 (26.6%)</td>
<td></td>
</tr>
<tr>
<td>Time to Event (days, median)</td>
<td>229.0</td>
<td>210.0</td>
<td>19.0</td>
</tr>
<tr>
<td>6 Month (180 Day) Event Free Rate</td>
<td>62.2%</td>
<td>58.1%</td>
<td>4.2% (-7.5%, 15.9%)</td>
</tr>
<tr>
<td>9 Month (270 Day) Event Free Rate</td>
<td>46.5%</td>
<td>42.5%</td>
<td>4.0% (-8.1%, 16.0%)</td>
</tr>
<tr>
<td>12 Month (365 Day) Event Free Rate</td>
<td>36.8%</td>
<td>30.8%</td>
<td>6.1% (-5.6, 17.7)</td>
</tr>
</tbody>
</table>

95% CI of the rate and rate difference at each time point were calculated based on normal approximation using Greenwood formula variance estimators without adjustment for multiplicity.
The past leads to...the current and future status of hemodialysis access

Current Status

Manage AV Access failure with PTA, stent-grafts, DCB

Future Status

Create useable and durable AV access, reduce intervention rates

GOAL: Improve outcomes for ESRD patients who require hemodialysis
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