VASCULAR ACCESS/ THE VIEW OF THE NEPHROLOGIST

R Vanholder,
University Hospital,
Gent, Belgium
European best practice guidelines on haemodialysis

Endorsed by the European Renal Association–European Dialysis and Transplant Association (ERA–EDTA).

Supported by an unrestricted educational grant from Fresenius Medical Care.
EBPG

- Preparation and preservation
- Upper extremity AVF preferred
- Interventional radiology vs surgery cfr center experience
- For venous outlow stenosis AVF: interventional radiology
- Monitoring by flow assessment
- Pre-emptive intervention on stenosis
- CVC last resort
TOPICS

- Access flow as predictor of thrombosis
- Preventive antiaggregation / anticoagulation
- Various novel aspects
- Central vein catheter infections
ACCESS FLOW AS A PREDICTOR OF THROMBOSIS
Guideline 5.1. Prior to any cannulation, autogenous arteriovenous fistulae and grafts should be assessed by physical examination (Evidence level IV).

Guideline 5.2. Objective monitoring of access function should be performed at a regular base by measuring access flow (Evidence level II).
EFFECT MONITORING ON THROMBOSIS

- Phase I: no screening
- Phase II: screening VP
- Phase III: screening flow

MacCarley et al, KI, 60: 1164-1172; 2001
IN-DEPTH CLINICAL REVIEW

Effect of online haemodialysis vascular access flow evaluation and pre-emptive intervention on the frequency of access thrombosis

Edwin Wijnen, Frank M. van der Sande, Jan H. M. Tordoir, Jeroen P. Kooman and Karel M. L. Leunissen
Abstract

Introduction. Guidelines advocate surveillance of vascular access to reduce incidences of thrombosis. However, the value of online vascular access flow monitoring is still under debate.

Methods. Through a systematic literature search, the effect of online access flow surveillance combined with pre-emptive intervention on thrombosis frequency is reviewed.

Results. Due to methodological differences, adequate comparison of the individual study results is not possible. Moreover, the methodological quality of most of the included studies is not suitable for an adequate statistical analysis of the results.

Conclusion. Until now, there is no conclusive evidence that online access flow evaluation has a significant effect on the rate of thrombosis. Future large-scale studies with adequate study design, adequate surveillance and intervention protocols and, possibly, better pre-emptive intervention alternative(s) are necessary.
Abstract

Introduction. Guidelines advocate surveillance of vascular access to reduce incidences of thrombosis. However, the value of online vascular access flow monitoring is still under debate.

Methods. Through a systematic literature search, the effect of online access flow surveillance combined with pre-emptive intervention on thrombosis frequency is reviewed.

Results. Due to methodological differences, adequate comparison of the individual study results is not possible. Moreover, the methodological quality of most of the included studies is not suitable for an adequate statistical analysis of the results.

Conclusion. Until now, there is no conclusive evidence that online access flow evaluation has a significant effect on the rate of thrombosis. Future large-scale studies with adequate study design, adequate surveillance and intervention protocols and, possibly, better pre-emptive intervention alternative(s) are necessary.
**Abstract**

**Introduction.** Guidelines advocate surveillance of vascular access to reduce incidences of thrombosis. However, the value of online vascular access flow monitoring remains uncertain.

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective</td>
<td>1/8</td>
</tr>
<tr>
<td>Historic control</td>
<td>2/8</td>
</tr>
<tr>
<td>Observational</td>
<td>5/8</td>
</tr>
<tr>
<td>Sequential</td>
<td>2/8</td>
</tr>
<tr>
<td>RCT</td>
<td>2/8 (in one no difference)</td>
</tr>
</tbody>
</table>

*studies with adequate study design, adequate surveillance and intervention protocols and, possibly, better pre-emptive intervention alternative(s) are necessary.*

Wijnen et al, NDTPlus, 1: 279-284; 2008
THROMBOSIS WITH ACCESS BLOOD FLOW SURVEILLANCE VS. STANDARD CARE

Standard care could consist of either venous pressure monitoring or no access surveillance.

Abbreviations: RR, relative risk; CI, confidence interval; F, fistula; VP, venous pressure; G, graft; DU, Doppler ultrasound; UD, ultrasound dilution.

© 2008 Universitair Ziekenhuis Gent

Tonelli et al, AJKD, 51: 630-640; 2008
ACCESS LOSS WITH ACCESS BLOOD FLOW SURVEILLANCE VS. STANDARD CARE

Standard care could consist of either venous pressure monitoring or no access surveillance.

Abbreviations: RR, relative risk; CI, confidence interval; DU, Doppler ultrasound; UD, ultrasound dilution

Tonelli et al, AJKD, 51: 630-640; 2008
CONCLUSIONS

- Low quality of many studies
- More studies are needed
- For grafts, there is no controlled data favoring use of flow measurements
- For AVF: data are contradictory; may be useful to prevent thrombosis, but no differences in outcome
- Practical question: what to do with frequent dramatic but non-consistent ups and downs?
PREVENTIVE ANTIAGGREGATION / ANTICOAGULATION
EBPG 2007
CLOPIDOGREL AND EARLY FAILURE OF AVF (US MULTICENTER TRIAL)

Effect of Clopidogrel on Early Failure of Arteriovenous

Table 2. Fistula Thrombosis

<table>
<thead>
<tr>
<th></th>
<th>No. (%) of Patients</th>
<th>Relative Risk (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Clopidogrel (n = 435)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Placebo (n = 431)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Thrombosis at 6 wk (all patients)</td>
<td>53 (12.2)</td>
<td>84 (19.5)</td>
</tr>
<tr>
<td>By location</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forearm fistula</td>
<td>31 (12.9)</td>
<td>60 (24.7)</td>
</tr>
<tr>
<td>Upper arm fistula</td>
<td>22 (11.3)</td>
<td>24 (12.8)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Six of the 441 patients randomized to clopidogrel and 5 of the 436 patients randomized to placebo were not included because patency was not evaluated.

<sup>b</sup>Relative risks were stratified for fistula location and center.

<sup>c</sup>The 95% confidence interval reported is the repeated confidence interval adjusted for interim monitoring. The repeated P value adjusted for interim monitoring is .018.
Context  The arteriovenous fistula is the preferred type of vascular access for hemodialysis because of lower thrombosis and infection rates and lower health care expenditures compared with synthetic grafts or central venous catheters. Early failure of fistulas due to thrombosis or inadequate maturation is a barrier to increasing the prevalence of fistulas among patients treated with hemodialysis. Small, inconclusive trials have suggested that antiplatelet agents may reduce thrombosis of new fistulas.

Objective  To determine whether clopidogrel reduces early failure of hemodialysis fistulas.

Design, Setting, and Participants  Randomized, double-blind, placebo-controlled trial conducted at 9 US centers composed of academic and community nephrology practices in 2003-2007. Eight hundred seventy-seven participants with end-stage renal disease or advanced chronic kidney disease were followed up until 150 to 180 days after fistula creation or 30 days after initiation of dialysis, whichever occurred later.

Intervention  Participants were randomly assigned to receive clopidogrel (300-mg loading dose followed by daily dose of 75 mg; n = 441) or placebo (n = 436) for 6 weeks starting within 1 day after fistula creation.

Main Outcome Measures  The primary outcome was fistula thrombosis, determined by physical examination at 6 weeks. The secondary outcome was failure of the fistula to become suitable for dialysis. Suitability was defined as use of the fistula at a dialysis machine blood pump rate of 300 mL/min or more during 8 of 12 dialysis sessions.

Results  Enrollment was stopped after 877 participants were randomized based on a stopping rule for intervention efficacy. Fistula thrombosis occurred in 53 (12.2%) participants assigned to clopidogrel compared with 84 (19.5%) participants assigned to placebo (relative risk, 0.63; 95% confidence interval, 0.46-0.97; P = .018). Failure to attain suitability for dialysis did not differ between the clopidogrel and placebo groups (61.8% vs 59.5%, respectively; relative risk, 1.05; 95% confidence interval, 0.94-1.17; P = .40).

Conclusion  Clopidogrel reduces the frequency of early thrombosis of new arteriovenous fistulas but does not increase the proportion of fistulas that become suitable for dialysis.
COCHRANE REVIEW: INCREASING PATENCY OF AVF AND AVG

Medical adjuvant treatment to increase patency of arteriovenous fistulae and grafts (Review)

Osborn G, Escotet X, Da Silva A

3 RCT’s
Aspirin > placebo

3 RCT’s
Ticlopidine > placebo

1 trial
Dipyridamole ± aspirin > placebo

1 trial
Fish oil > placebo

1 trial
Warfarin inefficient; prematurely stopped for bleeding

1 trial
Sulfinpyrazone > placebo

1 trial
Clopidogrel > placebo
Figure 1. Primary unassisted patency is prolonged in patients on aspirin at baseline. Cumulative incidence of loss of primary unassisted graft patency for baseline aspirin users (dashed line) and nonusers (solid line). The median patency in the baseline aspirin users and nonusers was 5.8 (95% CI, 4.8 to 7.4) and 4.1 months (95% CI, 3.5 to 5.3; P = 0.13), respectively.
Randomized Controlled Trial of Clopidogrel plus Aspirin to Prevent Hemodialysis Access Graft Thrombosis


BLEEDING AS A COUNTERBALANCE

Kaufman et al, JASN, 14: 2313-2321; 2003
CONCLUSIONS

- For short-term outcome, ticlopidine has no proven advantage in AVF (US)
- Several studies show an advantage for antiaggregants for maintaining patency; mostly, these are small studies with debatable quality
- Coumarin has little benefit
- Bleeding complications seriously blur the picture
- Many patients receive these drugs for other reasons
VARIOUS NOVEL ASPECTS
### Life-table analysis:

- by patency as intention to treat (n=218): log rank test 6.309, p=0.012
- by AVF use for haemodialysis (n=183): log rank test 6.144, p=0.013

*Figure 3. Assisted primary AVF survival for clinical and ultrasound groups.*
PREOPERATIVE VASCULAR ULTRASOUND

Life-table analysis:
by patency as intention to treat (n=218): log rank test 6.309, p=0.012
by AVF use for haemodialysis (n=183): log rank test 6.144, p=0.013

Figure 3. Assisted primary AVF survival for clinical and ultrasound groups.
DAILY HEMODIALYSIS

Adverse Events during the 12-Month Follow-up Period of the Study.*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Conventional Hemodialysis (N = 120)</th>
<th>Frequent Hemodialysis (N = 125)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of events</td>
<td>no. of patients with event</td>
<td>no. of events</td>
<td>no. of patients with event</td>
</tr>
<tr>
<td>Death</td>
<td>9</td>
<td>5</td>
<td>58</td>
<td>—</td>
</tr>
<tr>
<td>All hospitalizations</td>
<td>114</td>
<td>47</td>
<td>109</td>
<td>58</td>
</tr>
<tr>
<td>Unrelated to vascular access</td>
<td>90</td>
<td>44</td>
<td>79</td>
<td>47</td>
</tr>
<tr>
<td>Related to vascular access</td>
<td>24</td>
<td>14</td>
<td>30</td>
<td>20</td>
</tr>
<tr>
<td>Cardiovascular-related</td>
<td>15</td>
<td>12</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>Infection related</td>
<td>27</td>
<td>20</td>
<td>27</td>
<td>23</td>
</tr>
<tr>
<td>All interventions related to vascular access</td>
<td>65</td>
<td>29</td>
<td>95</td>
<td>47</td>
</tr>
<tr>
<td>Correction of access failure</td>
<td>23</td>
<td>15</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>Other procedures</td>
<td>42</td>
<td>21</td>
<td>76</td>
<td>38</td>
</tr>
<tr>
<td>Episodes of hypertension†</td>
<td>470</td>
<td>87</td>
<td>724</td>
<td>99</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potassium &lt;3.0 mmol/liter</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Potassium &lt;3.5 mmol/liter</td>
<td>6</td>
<td>5</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>Hypophosphatemia§</td>
<td>9</td>
<td>7</td>
<td>15</td>
<td>9</td>
</tr>
</tbody>
</table>

*The hazard ratios and P values for rates of events (including multiple events per patient) between the frequent-hemodialysis group and the conventional-hemodialysis group were calculated with the use of the Andersen–Gill model, except where otherwise noted.
†The percentage of dialysis treatments with recorded hypotensive episodes, defined as the need for a lower ultrafiltration rate, reduced blood flow, or saline administration to ameliorate hypotension, was 10.9% in the frequent-hemodialysis group and 13.6% in the conventional-hemodialysis group (P = 0.04 with the use of generalized estimating equations).
‡The P values for the comparison of the number of patients with at least one event of hypokalemia or hypophosphatemia were calculated with the use of Fisher’s exact test.
§Hypophosphatemia was defined as a phosphorus concentration of less than 2.17 mg per deciliter (0.7 mmol per liter).
**DAILY HEMODIALYSIS**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Conventional Hemodialysis (N = 120)</th>
<th>Frequent Hemodialysis (N = 125)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of events</td>
<td>no. of patients with event</td>
<td>no. of events</td>
<td>no. of patients with event</td>
</tr>
<tr>
<td>All interventions related to vascular access</td>
<td>65</td>
<td>29</td>
<td>95</td>
<td>47</td>
</tr>
<tr>
<td>Correction of access failure</td>
<td>23</td>
<td>15</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>Other procedures</td>
<td>42</td>
<td>21</td>
<td>76</td>
<td>38</td>
</tr>
</tbody>
</table>

*Adverse Events during the 12-Month Follow-up Period of the Study.*
DAILY HEMODIALYSIS

Benefits

- Less hazard for composite endpoint: death or increase in left ventricular mass
- Less hazard for composite endpoint: death or decrease in physical health score

Chertow et al, NEJM, 363: 2287-2300; 2010
Figure 1 Time to first septic permanent access event in conventional hemodialysis vs. nocturnal hemodialysis (NHD)/rope ladder and NHD/buttonhole cannulation groups (univariable analysis).

Van Eps, Hemodial Int, 14: 451-463; 2010
ERBP POSITION STATEMENT on CATHETER RELATED BLOOD STREAM INFECTIONS (CRBSI)

R Vanholder,
University Hospital,
Gent, Belgium
Special Feature

Diagnosis, prevention and treatment of haemodialysis catheter-related bloodstream infections (CRBSI): a position statement of European Renal Best Practice (ERBP)

Raymond Vanholder¹, Bernard Canaud², Richard Fluck³, Michel Jadoul⁴, Laura Labriola⁴, A. Marti-Monros⁵, J. Tordoir⁶ and W. Van Biesen¹

¹Nephrology Section, Department of Internal Medicine, University Hospital, Gent, Belgium, ²Nephrology, Dialysis and Intensive Care Unit, Lapeyronie University Hospital, Montpellier, France, ³Department of Renal Medicine, Royal Derby Hospital, Derby, UK, ⁴Nephrology, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium, ⁵Nephrology Department, Consorcio Hospital General Universitario, Valencia, Spain and ⁶Vascular Surgery, Department of Surgery, Maastricht University Medical Center, Maastricht, the Netherlands

Correspondence and offprint requests to: Raymond Vanholder; E-mail: raymond.vanholder@ugent.be
Editorial Comment

Catheter-related blood stream infections (CRBSI): a European view

Raymond Vanholder¹, Bernard Canaud², Richard Fluck³, Michel Jadoul⁴, Laura Labriola⁴, Anna Marti-Monros⁵, Jan Tordoir⁵ and Wim Van Biesen¹

¹Nephrology Section, Department of Internal Medicine, University Hospital, Gent, Belgium, ²Nephrology, Dialysis and Intensive Care Unit, LaPeyronie University Hospital, Montpellier, France, ³Department of Renal Medicine, Royal Derby Hospital, Derby, UK, ⁴Nephrology, Cliniques Universitaires Saint-Luc, Université Catholique de Louvain, Brussels, Belgium, ⁵Nephrology Department, Consorcio Hospital General Universitario, Valencia, Spain and ⁶Vascular Surgery, Department of Surgery, Maastricht University Medical Center, Maastricht, The Netherlands

Correspondence and offprint requests to: Raymond Vanholder; E-mail: raymond.vanholder@ugent.be

© 2008 Universitair Ziekenhuis Gent
TUNNELED VS. NON-TUNNELED CATHETERS

A.1.1: The use of non-tunneled catheters, except in Acute Kidney Injury (AKI), is esteemed undesirable. In chronic maintenance haemodialysis patients, it is recommended to remove temporary catheters as soon as possible, even without or with only minor complications, and to have them replaced preferentially by an arterio-venous fistula, or if that is impossible, an arterio-venous graft (AVG), or, if that is impossible, a tunneled central vein catheter (CVC).

A.1.2: If haemodialysis catheters are required either due to need or because patients refuse an AVF, the occurrence of a catheter related complication should be a trigger to reevaluate options for alternative access, such as AVF.
ACCESS USE AND HOSPITALIZATION RISK FOR CATHETER INFECTION

Pisoni et al, AJKD, 53: 475-491; 2009
NON-INFECTED ACCESS CATHETERS AND INFLAMMATION

C-reactive protein (CRP) levels (mg per 100 ml) decrease significantly in incident maintenance hemodialysis patients who initially dialyze with a non-infected catheter but with a fistula at 6 months \((P<0.0001)\). By contrast, no change in CRP is observed in incident maintenance hemodialysis patients who initiated dialysis with a catheter and remained with a catheter at 6 months \((P=0.17)\). CRP concentrations are shown as median (interquartile range) in the boxes.
(a) Trends in vascular access use (arteriovenous fistula, catheter or graft) at study entry in DOPPS I, II and III (1996–2007) among prevalent patient cross-sections in Japan, Italy, Germany, France and Spain.

(b) Trends in vascular access use (arteriovenous fistula, catheter or graft) at study entry in DOPPS I, II and III (1996–2007) among prevalent patient cross-sections in Australia and New Zealand (ANZ) the UK, Belgium, Sweden, Canada and the United States.
PREVENTIVE ANTIMICROBIAL LOCKS

- **B.3.1:** The preventive use of antimicrobial locks is advocated to reduce the rate of CRBSI.

- **B.3.2:** In view of the potential risks of spillover of the locking solution, associated risks (arrhythmias, toxicity, allergic reactions, development of resistance to antibiotics) should be balanced with the benefits in terms of prevention of infection. Citrate locks have for the time being most extensively been studied. The 4% solution seems to offer at present the best benefit/risk ratio.

- **B.3.3:** Antimicrobial lock solutions should not replace hygienic standards with regard to catheter care and handling.
META-ANALYSIS

Preventing haemodialysis catheter-related bacteraemia with an antimicrobial lock solution: a meta-analysis of prospective randomized trials

Laura Labriola, Ralph Crott, and Michel Jadoul

HEPARIN PROMOTES AND CITRATE COUNTERACTS BIOFILM FORMATION

The effect of other anticoagulants on S. aureus biofilm formation (A-D)

Gentamicin and citrate together strongly inhibit biofilm formation

Shanks et al, NDT, 21: 2247-2255; 2006
CAVE: LOSS OF SUBSTANCE OUT OF CATHETER

FDA WARNING AGAINST CITRATE AT HIGH CONCENTRATIONS

FDA Issues Urgent Warning On TriCitasol Dialysis Catheter Anticoagulant

WASHINGTON, DC -- April 17, 2000 -- The Food and Drug Administration is issuing an urgent warning to all hospital pharmacies and hemodialysis units that triCitasol, an unapproved product that has been used to keep bloodlines open, may cause death when infused into patients. TriCitasol is marketed in individual, sterile, 30ml glass vials, distributed both individually and in hemodialysis kits.

FDA has learned that a patient died of cardiac arrest shortly after triCitasol, a 46.7 percent concentration of sodium citrate anticoagulant, was injected full strength into a hemodialysis permanent blood access catheter that had just been implanted. Rapid or excessive infusion of citrate solutions can cause fatal heart rhythm disruption, seizures or bleeding due to loss of blood calcium.

Other incidents that may involve triCitasol in the hemodialysis setting are under FDA review.

TriCitasol is manufactured by Cytosol Laboratories, Braintree, Ma, and is distributed by Medcomp, Harleysville, Pa., and previously by Citra Anticoagulants, Inc. Both Cytosol Labs and Medcomp are voluntarily recalling triCitasol for use with blood access catheters.

FDA is urging hospital pharmacies and hemodialysis units across the U.S. to stop using the product. Alternative 4 percent solutions of citrate are available for use in these and most other medical settings.

Because there is a need for this product in some procedures to prepare white cells for transfusion, FDA is working with the company to see that the product currently remains available for this use, which involves dilution.

In an April 9, 2000 letter to its customers, Medcomp announced a recall of its kits (or trays) containing triCitasol and the Medcomp
FDA WARNING AGAINST CITRATE AT HIGH CONCENTRATIONS

FDA Issues Urgent Warning On TriCitrasol Dialysis Catheter Anticoagulant

WASHINGTON, DC -- April 17, 2000 -- The Food and Drug Administration is issuing an urgent warning to all hospital pharmacies and hemodialysis units that triCitrasol, an unapproved product that has been used to keep blood lines open, may cause death when infused into patients. TriCitrasol is marketed in individual, sterile, 30ml glass vials, distributed both individually and in hemodialysis kits.

FDA has learned that a patient died of cardiac arrest shortly after triCitrasol, a 46.7 percent concentration of sodium citrate anticoagulant, was injected full strength into a hemodialysis permanent blood access catheter that had just been implanted. Rapid or excessive infusion of citrate solutions can cause fatal heart

http://www.pslgroup.com/dg/1CD1AE.htm
Locking Solutions for Hemodialysis Catheters; Heparin and Citrate—A Position Paper by ASDIN

John E. Moran, Stephen R. Ash, and the Clinical Practice Committee*

ABSTRACT

There is wide variation in the use of solutions to “lock” or fill tunneled central venous catheters for dialysis. Some centers use undiluted heparin concentrations ranging from 1000 to 10,000 U/ml and other centers place from 1000 to 10,000 U per humen. Based on available evidence, it appears that heparin 1000 U/ml, or 4% sodium citrate are suitable choices for lock solution to maintain patency of tunneled central venous catheters for dialysis. Risks from systemic anticoagulation are lower with heparin 1000 U/ml and 4% sodium citrate, compared with higher concentrations of heparin (5000 and 10,000 U/ml). The need for use of tissue plasminogen activator for maintaining catheter patency is increased by using heparin lock at 1000 U/ml, vs. higher concentrations. Higher concentrations of heparin lock should be reserved for patients who have evidence of catheter occlusion or thrombosis when heparin is used at 1000 U/ml. Similar choices for lock solution are sensible for acute hemodialysis catheters. When heparin is used for catheter lock, the injected volume should not exceed the internal volume of the catheter.
EXIT SITE OINTMENTS

B.5.1: Application of antibiotic ointment at the exit site should be considered after catheter placement until the insertion site has healed, but should be discontinued after healing.

B.5.2: With long term exit site and nasal antibiotic ointment applications, especially of mupirocin, development of resistance should be taken into account as an effect counterbalancing the potential benefit of infectious complications.
EXIT SITE ANTIBIOTIC APPLICATION – CRBSI FREQUENCY

0.001 0.01 0.1 1 10 100 1000
Favours ESAs Favours control

Levin 1991: -1.4028 (0.6454)
Johnson 2002: -2.8941 (1.4770)
Lok 2003: -1.4187 (0.5087)
Subtotal (95% CI):
Test for heterogeneity: \( \chi^2 = 0.94, df = 2 \) \( P = 0.63 \), \( I^2 = 0\%
Test for overall effect: \( Z = 3.92 \) \( P < 0.0001 \)

Exit-site infections

Rabindranath et al, NDT, 24: 3763-3774; 2009
MUPIROCIN RESISTANCE

Figure 1. Selection of mupirocin resistance. Changes in coagulase-negative staphylococci of skin flora over time. (■), Susceptible; (◼), low resistance; (□), high resistance.
ANTIBIOTIC LOCKS

D.2.1: When catheter salvage is attempted, the combination of an antibiotic lock and systemic antibiotic therapy should be applied.

D.2.2: Salvage of the catheter in case of *S. aureus* infection should only be considered when catheter removal and replacement are expected to be problematic.

D.2.3: Urokinase and other thrombolytic locks are not recommended. The use of heparin locks alone in case of CRBSI is discouraged.
RESULTS OF AB LOCK IN STAPH A


*Ivan D. Maya, MD, Donna Carlton, RN, Erin Estrada, RN, and Michael Allon, MD*

**Background:** Dialysis catheter–related bacteremia is often treated successfully by instilling an antibiotic-heparin solution into the catheter lumen (an antibiotic lock) in conjunction with systemic antibiotic therapy without removal of the catheter. The efficacy of this therapy is uncertain in *Staphylococcus aureus* bacteremia.

**Design:** Quality improvement report.

**Setting & Participants:** 113 catheter-dependent hemodialysis outpatients with *S. aureus* catheter-related bacteremia treated with a standardized antibiotic lock protocol. Data for all patients with catheter-related bacteremia are recorded in a prospective database.

**Quality Improvement Plan:** In conjunction with systemic antibiotic therapy (vancomycin for methicillin-resistant *S. aureus* or cefazolin for methicillin-sensitive *S. aureus*), an antibiotic lock was instilled into each catheter lumen after each dialysis session for 3 weeks.

**Measures:** Treatment failure is defined as persistent fever after 48 hours of antibiotic therapy or recurrent *S. aureus* bacteremia within 90 days. Clinical cure is defined as resolution of fever and no recurrence of bacteremia. Major infection-related complications within 6 months were documented.

**Results:** The catheter could not be salvaged in 67 patients (59%) because of persistent fever in 40 patients and recurrent bacteremia in 27 patients. *A clinical cure was achieved in 46 patients (41%).* A serious complication of catheter-related bacteremia occurred in 9.7% of all patients (11 of 113 patients). Serious complications were observed in 25% of patients (10 of 40 patients) with persistent fever, but only 1.4% of all other patients (1 of 73 patients; *P* < 0.0001).

**Limitations:** This was a single-center study. Serum antibiotic levels were not measured.

**Conclusions:** Routine antibiotic lock therapy is not appropriate for patients with *S. aureus* catheter-related bacteremia. Serious complications occur primarily in patients with persistent fever.


**INDEX WORDS:** Arteriovenous access; dialysis catheter; infection; antibiotic.
MOST IMPORTANT MESSAGES

- Central vein catheters as access are discouraged
- If unavoidable they should be tunneled (in CKD)
- Antimicrobial locks are advocated but should not replace hygienic standards
- Track records should be kept of infections and their cause
- Advantages and disadvantages of catheter removal and replacement for infection should be outweighed
- Antibiotics allowing administration pre-dialysis only should be preferred
Back-ups
CONCLUSIONS

- Antimicrobial locks improve several outcome parameters of CVC
- These are further improved by the addition of antibiotics
- Antibiotics as well as other solutions may gradually leak out of CVC
EBPG BECAME ERBP

European best practice quo vadis? From European best practice guidelines (EBPG) to European renal best practice (ERBP)


Anaemia management in patients with chronic kidney disease: a position statement by the Anaemia Working Group of European Renal Best Practice (ERBP)

F. Locatelli, A. Covic, K.-U. Eckardt, A. Wiecek, R. Vanholder, and on behalf of the ERA-EDTA ERBP Advisory Board


Endorsement of the Kidney Disease Improving Global Outcomes (KDIGO) hepatitis C guidelines: a European Renal Best Practice (ERBP) position statement

A. Covic, D. Abramowicz, A. Bruchfeld, G. Leroux-Roels, D. Samuel, W. van Biesen, C. Zoccali, F. Zoulim, and R. Vanholder on behalf of the ERA-EDTA ERBP Advisory Board

COMPARISON OF CENTERS WITH DIFFERENT POLITICS

Unadjusted thrombosis-free survival. The graph shows the unadjusted thrombosis-free survival as of enrollment, according to the Kaplan–Meier analysis. Thrombosis-free survival was significantly better in Flow (open circles, continuous line) than in Control (closed triangles, dashed line). Note that the survival axis is truncated at 50%.

Tessitore et al, NDT, 23: 3578-3584; 2008
RCT: MONTHLY FLOW SURVEILLANCE IN GRAFTS

Q PREDICTING THROMBOSIS

AUC | 95% CI  | SENS | SPEC
---|---|---|---
Q | 0.698 | 0.677 - 0.719 | 53% | 79%

ΔQ PREDICTING THROMBOSIS

TIME INTERVAL OF CHANGE IN FLOW

- 1 MONTH
- 2 MONTHS
- 3 MONTHS

AUC | 95% CI  | SENS | SPEC
---|---|---|---
1 MONTH | 0.645 | 0.620 - 0.670 | 58% | 67%
2 MONTHS | 0.713 | 0.687 - 0.739 | 58% | 75%
3 MONTHS | 0.660 | 0.630 - 0.689 | 56% | 74%

Ram et al, AJKD, 52: 930-938; 2008
FOR WHICH POINTS A (NEW) STATEMENT COULD BE MADE

- No systematized literature review
- No evidence rating team
- No data extraction tables
## EFFECTS OF DRUG THERAPY

<table>
<thead>
<tr>
<th></th>
<th>GF-PP</th>
<th>GF-SP</th>
<th>FF-PP</th>
<th>FF-SP</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEi</td>
<td>1.02</td>
<td>1.16</td>
<td>0.77</td>
<td>0.56</td>
</tr>
<tr>
<td>CCBs</td>
<td>0.86</td>
<td>0.88</td>
<td>1.14</td>
<td>1.16</td>
</tr>
<tr>
<td>Asp</td>
<td>0.84</td>
<td>0.70</td>
<td>0.89</td>
<td>1.15</td>
</tr>
<tr>
<td>A-plat</td>
<td>1.00</td>
<td>1.10</td>
<td>1.06</td>
<td>0.73</td>
</tr>
<tr>
<td>Warf</td>
<td>1.33</td>
<td>1.22</td>
<td>0.95</td>
<td>1.12</td>
</tr>
</tbody>
</table>

GF: Garft Failure; FF: Fistula Failure; PP: Primary Patency; SP: Secondary Patency; Asp: Aspirin; A-plat: anti-platelet agents; Warf: Warfarin; Red: statistically significant

Saran et al, AJKD, 40: 1255-1263; 2002
Regression of Left Ventricular Hypertrophy After Arteriovenous Fistula Closure in Renal Transplant Recipients: A Long-Term Follow-Up

Philippe Unger, Sonia Velez-Roa, K. Martin Wissing, Anh Dung Hoang and Philippe van de Borne

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients</th>
<th>Early post-AVF closure</th>
<th>Late post-AVF closure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVDDI (mm/m²)</td>
<td>29.5 ± 3.4</td>
<td>26.9 ± 2.9*</td>
<td>26.2 ± 3.2*</td>
</tr>
<tr>
<td>LVESDI (mm/m²)</td>
<td>18.1 ± 3.2</td>
<td>16.6 ± 3.4*</td>
<td>16.0 ± 3.5*</td>
</tr>
<tr>
<td>IVS (mm)</td>
<td>12.4 ± 3.0</td>
<td>12.8 ± 3.1</td>
<td>12.2 ± 2.1</td>
</tr>
<tr>
<td>PW (mm)</td>
<td>11.2 ± 1.7</td>
<td>11.6 ± 1.7</td>
<td>11.4 ± 1.7</td>
</tr>
<tr>
<td>RWT (%)</td>
<td>46.9 ± 10.6</td>
<td>52.7 ± 10.2*</td>
<td>51.7 ± 7.6*</td>
</tr>
<tr>
<td>Median</td>
<td>44.1</td>
<td>50.1</td>
<td>49.7</td>
</tr>
<tr>
<td>LVMI (g/m²)</td>
<td>139 ± 44</td>
<td>127 ± 45*</td>
<td>117 ± 40*†</td>
</tr>
<tr>
<td>Median</td>
<td>135</td>
<td>110</td>
<td>107</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>45.2 ± 6.0</td>
<td>42.0 ± 5.7*</td>
<td>42.2 ± 5.8*</td>
</tr>
<tr>
<td>RVEDD (mm)</td>
<td>30.1 ± 4.6</td>
<td>30.2 ± 4.1</td>
<td>27.8 ± 5.7</td>
</tr>
<tr>
<td>FS (%)</td>
<td>38.7 ± 6.9</td>
<td>38.4 ± 8.5</td>
<td>39.2 ± 7.6</td>
</tr>
<tr>
<td>EF (%)</td>
<td>68 ± 9</td>
<td>68 ± 11</td>
<td>69 ± 10</td>
</tr>
<tr>
<td>E (cm/s)</td>
<td>80 ± 20</td>
<td>56 ± 13*</td>
<td>60 ± 18*</td>
</tr>
<tr>
<td>A (cm/s)</td>
<td>80 ± 21</td>
<td>75 ± 15</td>
<td>76 ± 17</td>
</tr>
<tr>
<td>E/A</td>
<td>1.08 ± 0.46</td>
<td>0.77 ± 0.20*</td>
<td>0.81 ± 0.21*</td>
</tr>
</tbody>
</table>

Data are mean ± SD; *p < 0.0167 vs. baseline; †p < 0.0167 vs. early post-operative.
LVDDI: Indexed LV end-diastolic diameter; LVESDI: Indexed LV end-systolic diameter; IVS: interventricular septum; PW: posterior wall thickness; RWT: relative wall thickness; LVMI: indexed LV mass; LAD: left atrial dimension; RVEDD: right ventricular end-diastolic diameter; FS: LV fractional shortening; EF: LV ejection fraction; E: early transmitral velocity; A: late transmitral velocity.

© 2008 Universitair Ziekenhuis Gent

Unger et al, Am J Tranplant, 4: 2038-2044; 2004
CHOICE OF VASCULAR ACCESS
EBPG 2007

CFR GUIDELINE
ADJUSTMENT FOR COMORBIDITIES

Vascular access for hemodialysis: The impact on morbidity and mortality

Di Orio, J Nephrol, 17: 19-25; 2004
LOCKS FOR CVC
EBPG 2007
CATHETER ANTIMICROBIAL LOCK STUDIES

Trisodium citrate 46.7% selectively and safely reduces staphylococcal catheter-related bacteraemia

- **Randomized, Clinical Trial Comparison of Trisodium Citrate 30% and Heparin as Catheter-Locking Solution in Hemodialysis Patients**
  - Georgia Winnett, Jonathan Nolan, Michael Miller, and Neil Ashman

- **Citrate 4% versus Heparin and the Reduction of Thrombosis Study (CHARTS)**
  - Marcel C. Weijmer, Marinus A. van den Dorpel, Peter J.G. Van de Ven, Pieter M. ter Wee, Jos A.C.A. van Geelen, Johannes O. Groeneveld, Brigitte C. van Jaarsveld, Marjon G. Koopmans, Caatje Y. le Poole, Anita M. Schrander-Van der Meer, Carl E.H. Siegert, Koen J.F. Stas for the CITRATE Study Group
CATHETER ANTIMICROBIAL LOCK STUDIES

Sodium citrate 4% locking solution for central venous dialysis catheters—an effective, more cost-efficient alternative to heparin

Trisodium citrate 4%—an alternative to heparin capping of haemodialysis catheters

Prevention of dialysis catheter-related sepsis with a citrate–taurine-containing lock solution

Ethanol lock therapy to treat tunnelled central venous catheter-associated blood stream infections: Results from a prospective trial

Jennifer Broom; Marion Woods; Anthony Allworth; James McCarthy; Joan Faoagali; Sarah Macdonald; Alan Pithie

META-ANALYSIS

Preventing haemodialysis catheter-related bacteraemia with an antimicrobial lock solution: a meta-analysis of prospective randomized trials

Laura Labriola, Ralph Crott, and Michel Jadoul

ATTRIBUTED ADVANTAGES ANTIMICROBIAL LOCKS

- Less catheter exchanges / removals
- Less hospitalizations
- Longer time till need for exchange
- Lower cost (4%)
- No false elevations INR
- Less bacteremia
- Less exit site infections
META-ANALYSIS: QUID ADDITION OF ANTIBIOTICS vs. INFECTION

Study | Treatment or subcategory | Event | Control | RR (fixed) 95% CI | RR (fixed) [95% CI]
--- | --- | --- | --- | --- | ---
01 AB+Heperin | AI-Hwleah 07 VGH | 4/23 | 30/7655 | 0.14 [0.05, 0.40] | 0.13 [0.05, 0.36]
 | Bleyer 05 ME | 0/30 | 1/218 | 0.30 [0.01, 7.42] | 0.15 [0.01, 3.00]
 | Cooper 99 G | 0/19 | 3/1610 | 0.14 [0.02, 1.15] | 0.08 [0.01, 0.59]
 | Kim 06 CefoH | 1/60 | 7/2242 | 0.08 [0.01, 0.59] | 0.09 [0.01, 0.59]
 | McIntyre 04 OH | 1/25 | 10/2470 | 0.08 [0.01, 0.59] | 0.08 [0.01, 0.59]
 | NonIB 06 ME | 1/21 | 4/867 | 0.53 [0.38, 0.73] | 0.53 [0.38, 0.73]
 | Saxena 05 CefoH | 96/58, 035 | 56/17, 885 | 0.46 [0.31, 0.69] | 0.46 [0.31, 0.69]
 | Saxena 06 CefoH | 36/21, 535 | 79/21, 900 | 0.46 [0.31, 0.69] | 0.46 [0.31, 0.69]
 | Zhang 06 GH | 0/5635 | 3/5665 | 0.09 [0.00, 1.80] | 0.09 [0.00, 1.80]
 | Subtotal (95% CI) | 104,204 | 60,412 | 0.39 [0.31, 0.50] | 0.39 [0.31, 0.50]

Total events: 139 (Treatment), 193 (Control)
Test for heterogeneity: $X^2 = 13.88$, df = 8 (P = .09), I² = 42.4%
Test for overall effect: $Z = 7.76$ (P < .0001)

02 AB+citrato
Dogra 02 GC | 0/42 | 7/2643 | 0.05 [0.00, 0.94] | 0.05 [0.00, 0.94]
 | Noria 06 GC | 0/20 | 3/867 | 0.06 [0.00, 1.20] | 0.06 [0.00, 1.20]
 | Pervez 02 GCBag | 1/14 | 4/1311 | 0.20 [0.02, 1.82] | 0.20 [0.02, 1.82]
 | Subtotal (95% CI) | 6959 | 4821 | 0.09 [0.02, 0.41] | 0.09 [0.02, 0.41]

Total events: 1 (Treatment), 14 (Control)
Test for heterogeneity: $X^2 = 0.70$, df = 2 (P = .70), I² = 0%
Test for overall effect: $Z = 3.17$ (P = .002)

Total (95% CI) 111,099 | 65,233 | 0.37 [0.30, 0.47] | 0.37 [0.30, 0.47]

Total events: 140 (Treatment), 207 (Control)
Test for heterogeneity: $X^2 = 18.24$, df = 11 (P = .08), I² = 39.7%
Test for overall effect: $Z = 8.40$ (P < .0001)
CAVE: LOSS OF SUBSTANCE OUT OF CATHETER

ACCOMPANYING EDITORIAL

This important study has immediate implications for clinicians. Nephrologists can be reasonably confident that clopidogrel should not be prescribed for patients undergoing fistula creation because it does not lead to clinically meaningful benefit. In fact, routinely prescribing clopidogrel might actually be counterproductive because it might prolong the survival of immature fistulas that would otherwise have thrombosed, thus delaying referral for a repeat attempt at establishing vascular access. Whether clopidogrel improves patency in fistulas that have already matured is unknown. However, it seems likely that clopidogrel may not prove useful in this setting because thrombosis of an established fistula is almost always a sign of significant underlying stenosis requiring angioplasty. Speculation aside, the findings of Dember et al suggest that clopidogrel cannot currently be recommended to improve maturation or patency of arteriovenous fistulas.

© 2008 Universitair Ziekenhuis Gent

Tonelli, JAMA, 299: 2205-2207; 2008
FISTULA FLOW VS. CARDIAC OUTPUT
EBPG 2007
EFFECT OF FISTULA COMPRESSION

Bos et al, KI, 48: 1641-1645; 1995
The relationship between the flow of arteriovenous fistula and cardiac output in haemodialysis patients

Carlo Basile, Carlo Lomonte, Luigi Vernaglione, Francesco Casucci, Maurizio Antonelli and Nicola Losurdo

Comparison of the cardiac output values among the patients subdivided according to the vascular access flow cut-off values. The horizontal line represents the median, upper and lower limits of the box including the first and third quartiles, and capped bars indicate minimum and maximum value. The one-way ANOVA followed by the Tukey's post-hoc test was performed in order to compare the mean cardiac output values in each access blood flow category identified by the cut-off points previously calculated.

C. Basile et al, NDT, 23: 282-287; 2008
Figure 1. Primary unassisted patency is prolonged in patients on aspirin at baseline. Cumulative incidence of loss of primary unassisted graft patency for baseline aspirin users (dashed line) and nonusers (solid line). The median patency in the baseline aspirin users and nonusers was 5.8 (95% CI, 4.8 to 7.4) and 4.1 months (95% CI, 3.5 to 5.3; P = 0.13), respectively
PREOPERATIVE VASCULAR ULTRASOUND

**Figure 3.** Assisted primary AVF survival for clinical and ultrasound groups.

**Life-table analysis:**
- by patency as intention to treat (n=218): log rank test 6.309, p=0.012
- by AVF use for haemodialysis (n=183): log rank test 6.144, p=0.013

<table>
<thead>
<tr>
<th>Number at risk</th>
<th>Clinical</th>
<th>Ultrasound</th>
</tr>
</thead>
<tbody>
<tr>
<td>60</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>53</td>
<td>64</td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
DAILY HEMODIALYSIS

Adverse Events during the 12-Month Follow-up Period of the Study.*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Conventional Hemodialysis (N = 120)</th>
<th>Frequent Hemodialysis (N = 125)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of events</td>
<td>no. of patients with event</td>
<td>no. of events</td>
<td>no. of patients with event</td>
</tr>
<tr>
<td>Death</td>
<td>9</td>
<td>5</td>
<td>58</td>
<td>2.35 (0.60–1.28)</td>
</tr>
<tr>
<td>All hospitalizations</td>
<td>114</td>
<td>47</td>
<td>109</td>
<td>2.09 (0.53–1.21)</td>
</tr>
<tr>
<td>Unrelated to vascular access</td>
<td>90</td>
<td>44</td>
<td>79</td>
<td>2.11 (0.54–1.82)</td>
</tr>
<tr>
<td>Related to vascular access</td>
<td>24</td>
<td>14</td>
<td>30</td>
<td>2.08 (0.44–1.59)</td>
</tr>
<tr>
<td>Cardiovascular-related</td>
<td>15</td>
<td>12</td>
<td>17</td>
<td>2.08 (0.49–1.49)</td>
</tr>
<tr>
<td>Infection related</td>
<td>27</td>
<td>20</td>
<td>27</td>
<td>2.08 (0.49–1.49)</td>
</tr>
<tr>
<td>All interventions related to vascular access</td>
<td>65</td>
<td>29</td>
<td>95</td>
<td>1.35 (0.84–2.18)</td>
</tr>
<tr>
<td>Correction of access failure</td>
<td>23</td>
<td>15</td>
<td>19</td>
<td>2.08 (0.71–1.44)</td>
</tr>
<tr>
<td>Other procedures</td>
<td>42</td>
<td>21</td>
<td>76</td>
<td>2.08 (1.98–2.97)</td>
</tr>
<tr>
<td>Episodes of hypertension†</td>
<td>470</td>
<td>87</td>
<td>724</td>
<td>2.08 (1.98–2.97)</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potassium &lt;3.0 mmol/liter</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Potassium &lt;3.5 mmol/liter</td>
<td>6</td>
<td>5</td>
<td>13</td>
<td>—</td>
</tr>
<tr>
<td>Hypophosphatemia§</td>
<td>9</td>
<td>7</td>
<td>9</td>
<td>—</td>
</tr>
</tbody>
</table>

* The hazard ratios and P values for rates of events (including multiple events per patient) between the frequent-hemodialysis group and the conventional-hemodialysis group were calculated with the use of the Andersen–Gill model, except where otherwise noted.
† The percentage of dialysis treatments with recorded hypotensive episodes, defined as the need for a lower ultrafiltration rate, reduced blood flow, or saline administration to ameliorate hypotension, was 10.9% in the frequent-hemodialysis group and 13.6% in the conventional-hemodialysis group (P = 0.04 with the use of generalized estimating equations).
‡ The P values for the comparison of the number of patients with at least one event of hypokalemia or hypophosphatemia were calculated with the use of Fisher's exact test.
§ Hypophosphatemia was defined as a phosphorus concentration of less than 2.17 mg per deciliter (0.7 mmol per liter).

Chertow et al, NEJM, 363: 2287-2300; 2010
# DAILY HEMODIALYSIS

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Conventional Hemodialysis (N = 120)</th>
<th>Frequent Hemodialysis (N = 125)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of events</td>
<td>no. of patients with event</td>
<td>no. of events</td>
<td>no. of patients with event</td>
</tr>
<tr>
<td>All interventions related to vascular access</td>
<td>65</td>
<td>29</td>
<td>95</td>
<td>47</td>
</tr>
<tr>
<td>Correction of access failure</td>
<td>23</td>
<td>15</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>Other procedures</td>
<td>42</td>
<td>21</td>
<td>76</td>
<td>38</td>
</tr>
</tbody>
</table>
DAILY HEMODIALYSIS

Benefits

- Less hazard for composite endpoint: death or increase in left ventricular mass
- Less hazard for composite endpoint: death or decrease in physical health score

Chertow et al, NEJM, 363: 2287-2300; 2010
BUTTONHOLE TECHNIQUE

Figure 1 Time to first septic permanent access event in conventional hemodialysis vs. nocturnal hemodialysis (NHD)/rope ladder and NHD/buttonhole cannulation groups (univariable analysis).

Van Eps, Hemodial Int, 14: 451-463; 2010