

VASCULAR ACCESS/ THE VIEW OF THE NEPHROLOGIST

R Vanholder,
University Hospital,
Gent, Belgium

ISSN 0931-0509

NDT

Official Publication of the European Renal Association – European Dialysis and Transplant Association


Volume 22 Supplement 2
May 2007
www.ndt.oxfordjournals.org

Nephrology Dialysis Transplantation


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.




EUROPEAN RENAL ASSOCIATION
MEMBER OF DIALYSIS AND TRANSPLANT ASSOCIATION



OXFORD JOURNALS
A HARTMAN PUBLICATION

EBPG

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

TOPICS

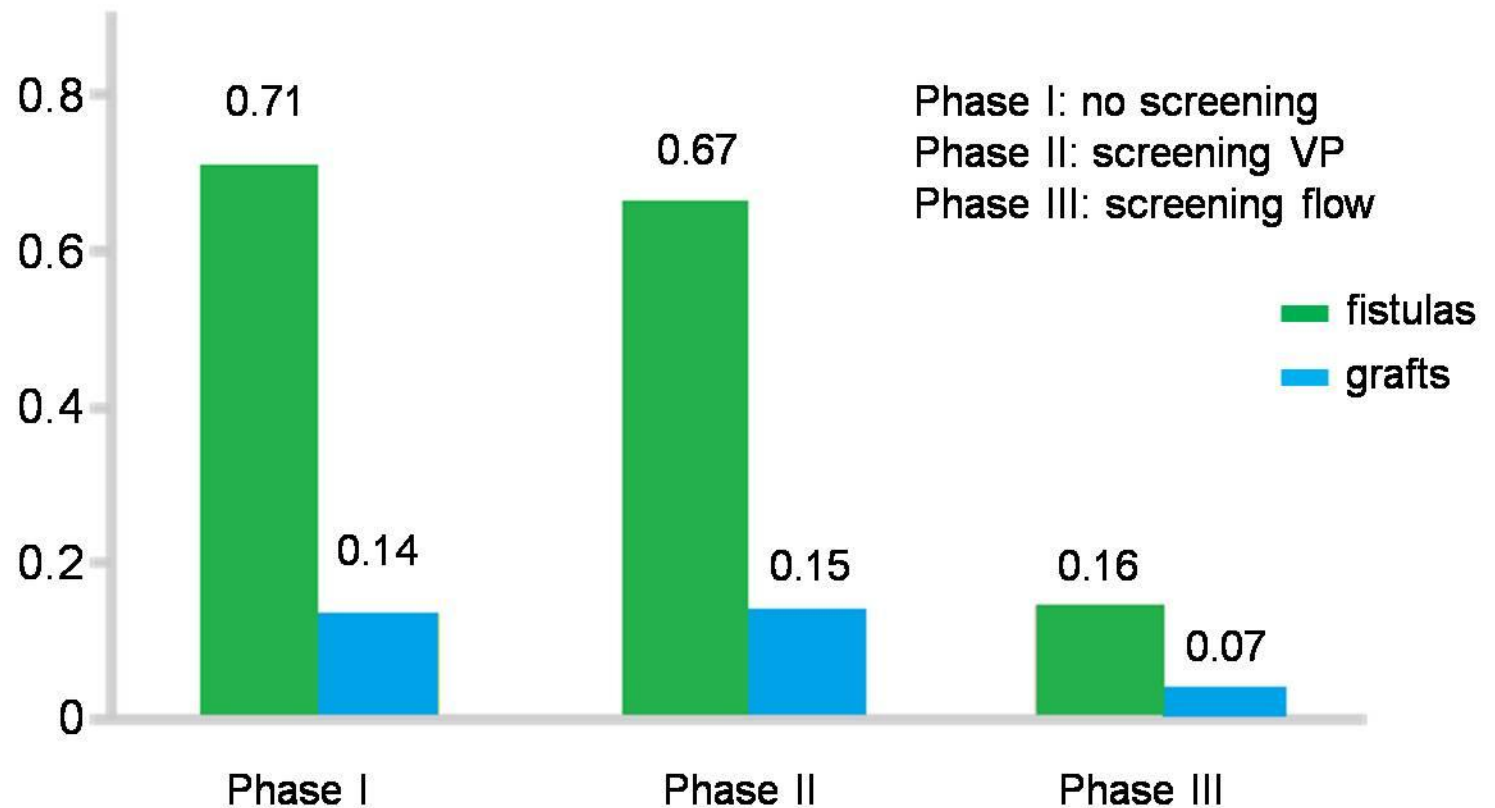
- ➔ **Access flow as predictor of thrombosis**
- ➔ **Preventive antiaggregation / anticoagulation**
- ➔ **Various novel aspects**
- ➔ **Central vein catheter infections**

ACCESS FLOW AS A PREDICTOR OF THROMBOSIS

EBPG 2007

- ➔ **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



IN-DEPTH CLINICAL REVIEW

NDT PLUS
Nephrology Dialysis Transplantation

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

IN-DEPTH CLINICAL REVIEW

NDT PLUS
Nephrology Dialysis Transplantation

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.

IN-DEPTH CLINICAL REVIEW

NDT PLUS
Nephrology Dialysis Transplantation

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. More-over, 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.

IN-DEPTH CLINICAL REVIEW



Abstract

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

monit

Meth

flow s

frequ

Resu

indivi

most

the re

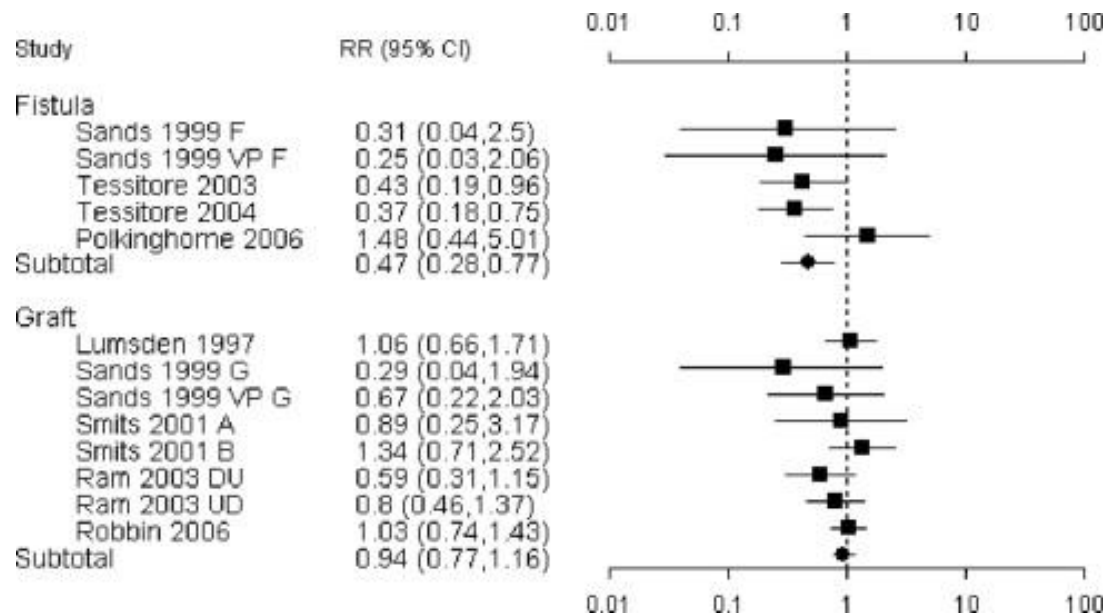
Conc

evalu

Retrospective	1/8
Historic control	2/8
Observational	5/8
Sequential	2/8
RCT	2/8 (in one no difference)

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

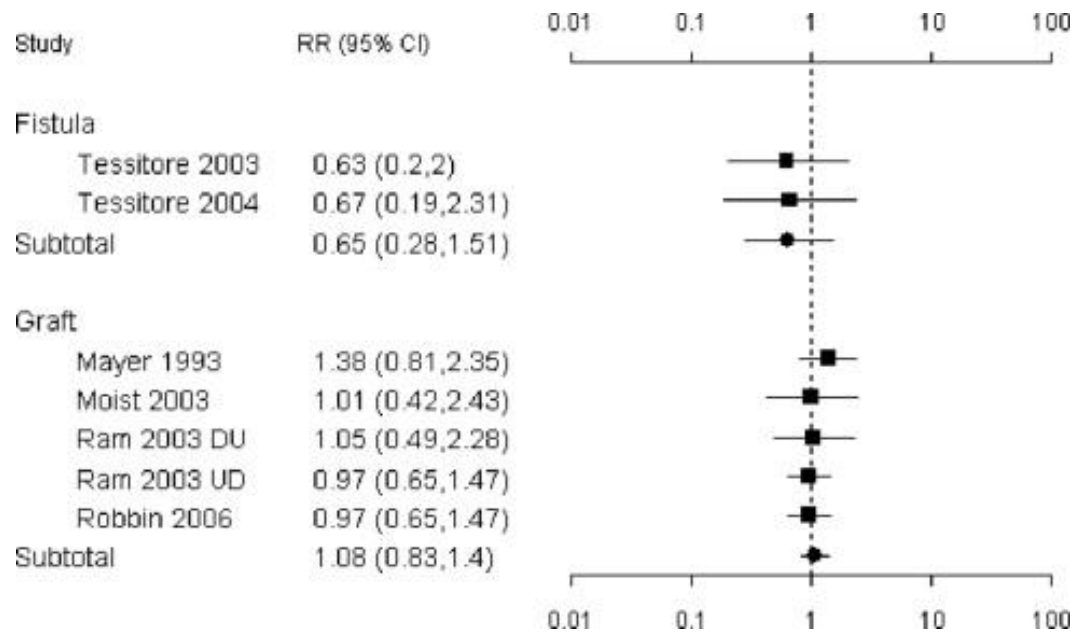
THROMBOSIS WITH ACCESS BLOOD FLOW SURVEILLANCE VS. STANDARD CARE



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.

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

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

	No. (%) of Patients		Relative Risk (95% Confidence Interval) ^b
	Clopidogrel (n = 435) ^a	Placebo (n = 431) ^a	
Thrombosis at 6 wk (all patients)	53 (12.2)	84 (19.5)	0.63 (0.46-0.97) ^c
By location			
Forearm fistula	31 (12.9)	60 (24.7)	0.53 (0.36-0.77)
Upper arm fistula	22 (11.3)	24 (12.8)	0.89 (0.52-1.53)

^aSix of the 441 patients randomized to clopidogrel and 5 of the 436 patients randomized to placebo were not included because patency was not evaluated.

^bRelative risks were stratified for fistula location and center.

^cThe 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, Escofet 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

ASPIRIN AND PATENCY GRAFTS

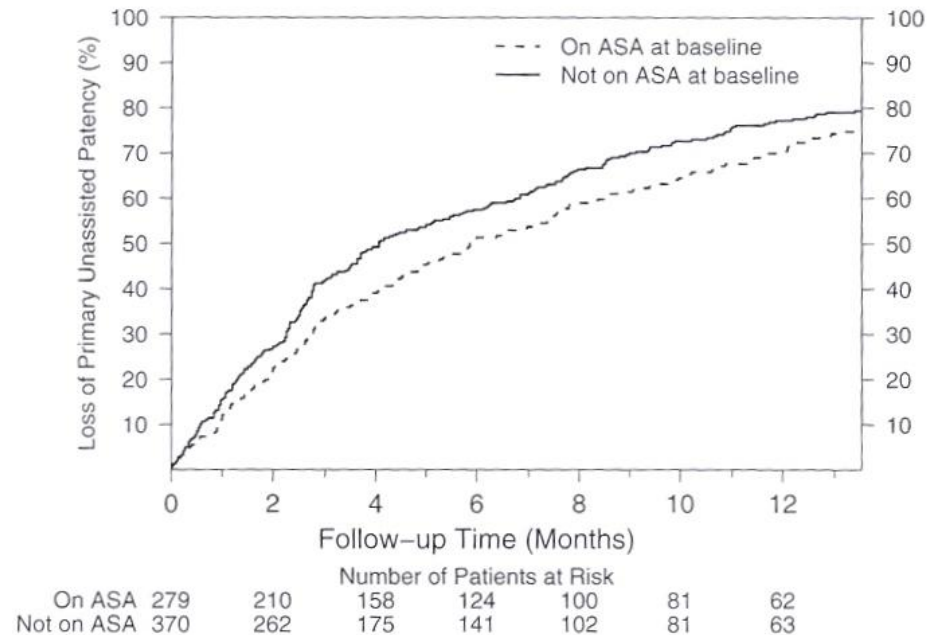
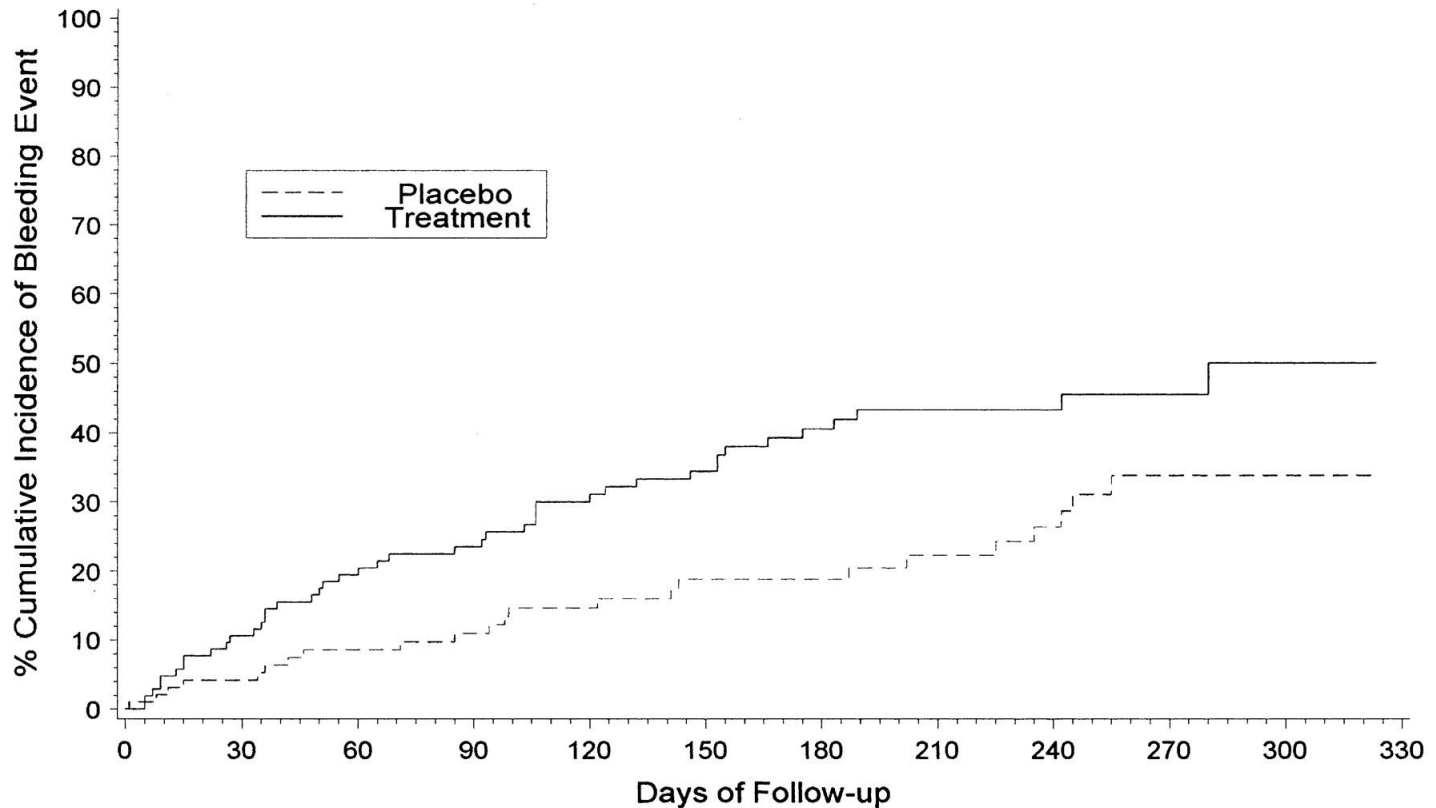


Figure 1. Primary unassisted patency is prolonged in patients on aspirin at baseline. Cumulative incidence of loss of primary unassisted graft patency for baseline aspirin users (dashed line) and nonusers (solid line). The median patency in the baseline aspirin users and nonusers was 5.8 (95% CI, 4.8 to 7.4) and 4.1 months (95% CI, 3.5 to 5.3; $P = 0.13$), respectively

BLEEDING AS A COUNTERBALANCE



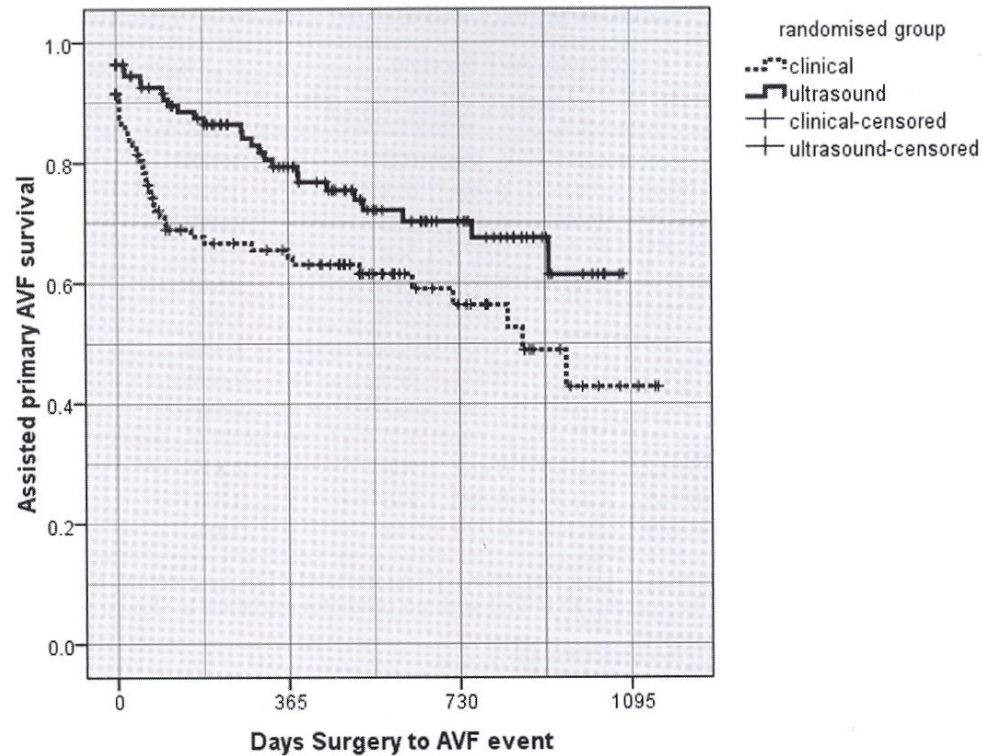
No. at risk

Pbo	96	72	50	15	3
Trt	104	72	45	18	2

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



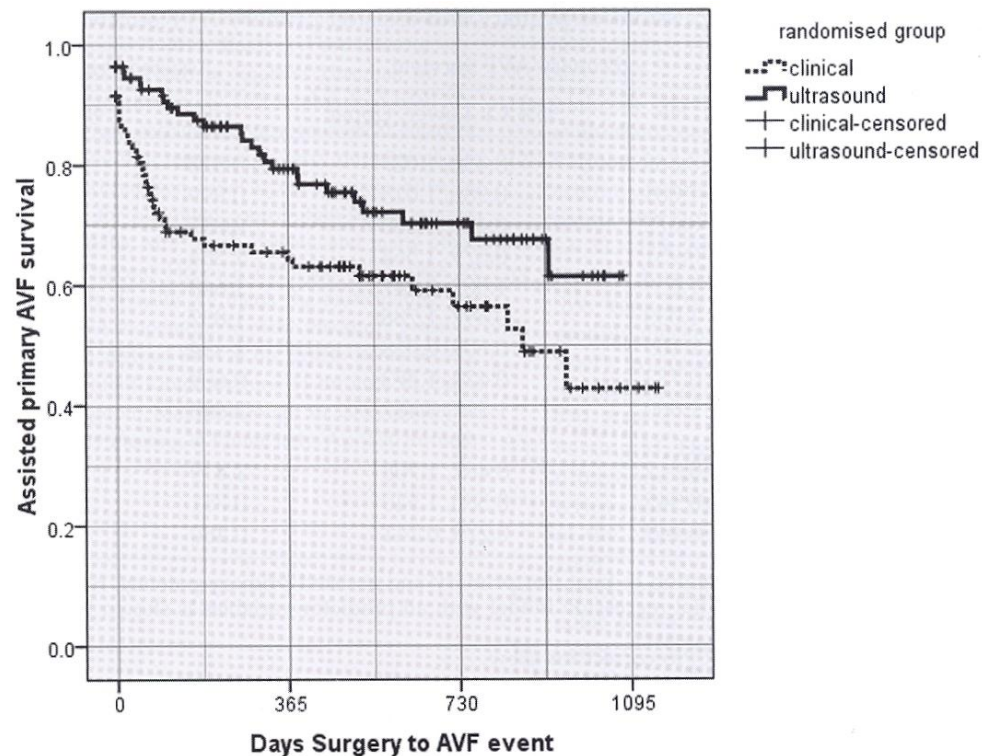
Number at risk	0	365	730	1095
clinical	60	53	34	20
ultrasound	83	64	41	29

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.



Number at risk	0	365	730	1095
clinical	60	53	34	20
ultrasound	83	64	41	29

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.*

Outcome	Conventional Hemodialysis (N = 120)		Frequent Hemodialysis (N = 125)		Hazard Ratio (95% CI)	P Value
	no. of events	no. of patients with event	no. of events	no. of patients with event		
Death	9		5		—	—
All hospitalizations	114	47	109	58	0.88 (0.60–1.28)	0.50
Unrelated to vascular access	90	44	79	47	0.80 (0.53–1.21)	0.30
Related to vascular access	24	14	30	20	0.99 (0.54–1.82)	0.97
Cardiovascular-related	15	12	17	15	0.83 (0.44–1.59)	—
Infection related	27	20	27	23	0.83 (0.49–1.40)	—
All interventions related to vascular access	65	29	95	47	1.35 (0.84–2.18)	0.22
Correction of access failure	23	15	19	15	0.71 (0.35–1.44)	0.35
Other procedures	42	21	76	38	1.71 (0.98–2.97)	0.06
Episodes of hypertension [†]	470	87	724	99	—	—
Hypokalemia						
Potassium <3.0 mmol/liter	0	0	0	0	—	—
Potassium <3.5 mmol/liter	6	5	13	8	—	0.57 [‡]
Hypophosphatemia [§]	9	7	15	9	—	0.80 [‡]

* 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

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

Outcome	Conventional Hemodialysis (N = 120)		Frequent Hemodialysis (N = 125)		Hazard Ratio (95% CI)	P Value
	<i>no. of events</i>	<i>no. of patients with event</i>	<i>no. of events</i>	<i>no. of patients with event</i>		
All interventions related to vascular access	65	29	95	47	1.35 (0.84–2.18)	0.22
Correction of access failure	23	15	19	15	0.71 (0.35–1.44)	0.35
Other procedures	42	21	76	38	1.71 (0.98–2.97)	0.06

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

BUTTONHOLE TECHNIQUE

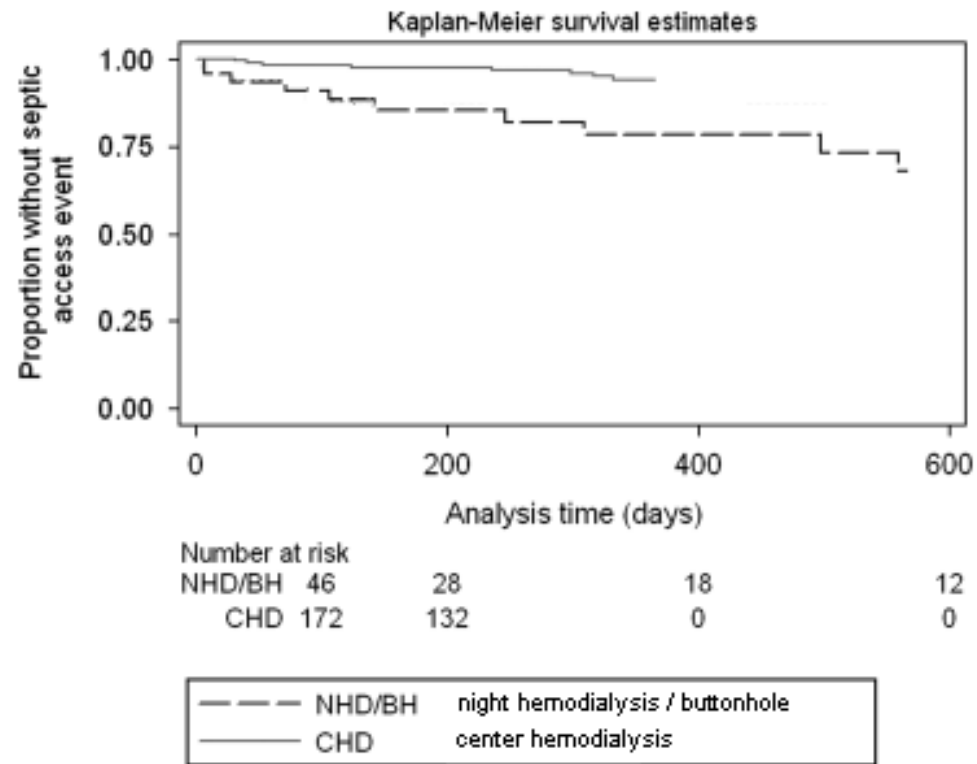


Figure 1 Time to first septic permanent access event in conventional hemodialysis vs. nocturnal hemodialysis (NHD)/rope ladder and NHD/buttonhole cannulation groups (univariable analysis).

BUTTONHOLE TECHNIQUE

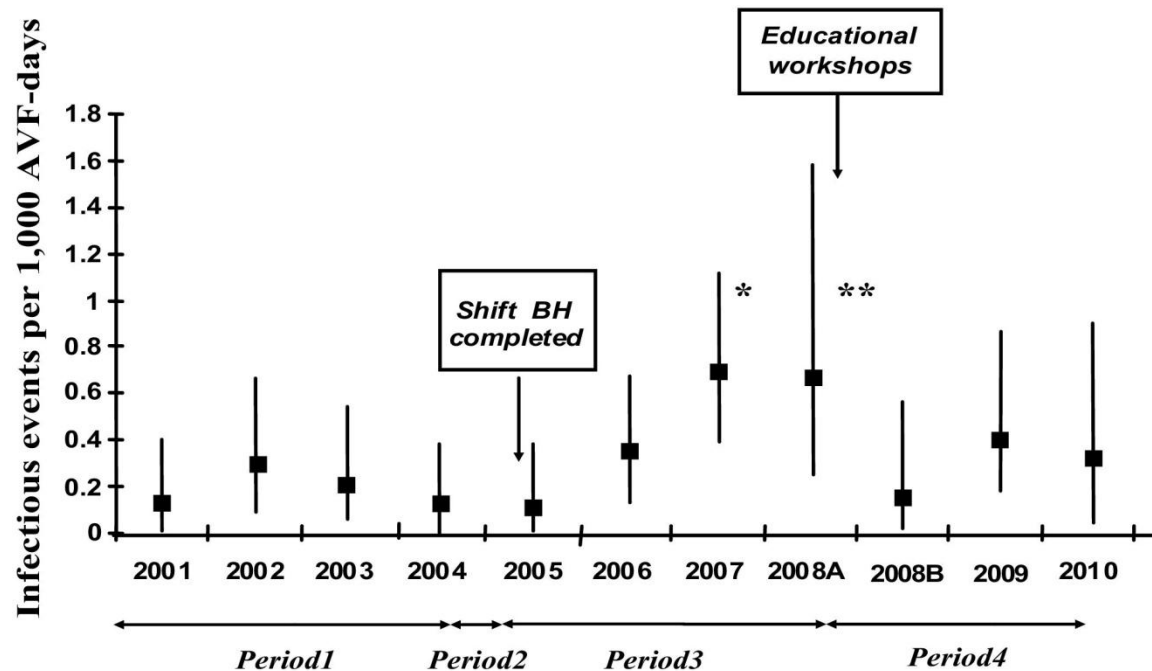


Figure 1. Annual incidence of infectious events. Lines around the squares indicate 95% confidence intervals; * $P < 0.05$ (compared with 2001, 2002, 2003, 2004, 2005, 2006, and 2008B); ** $P < 0.05$ (compared with 2001, 2003, 2004, 2005, and 2008B). Period 1 (January 1, 2001, to August 3, 2004): all patients using rope-ladder technique with sharp needles; period 2 (August 4, 2004, to January 31, 2005): progressive switch to buttonhole (BH) method using blunt needles; period 3 (February 1, 2005, to May 19, 2008): all patients using BH method, before educational workshops; and period 4 (May 20, 2008, to June 30, 2010): all patients using BH method, after educational workshops. Abbreviation: AVF, arteriovenous fistula.

ERBP POSITION STATEMENT on CATHETER RELATED BLOOD STREAM INFECTIONS (CRBSI)

R Vanholder,
University Hospital,
Gent, Belgium

NDT Plus (2010) 3: 234–246
doi: 10.1093/ndtplus/sfq041

Special Feature

NDT PLUS
Nephrology Dialysis Transplantation

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

NDT Advance Access published April 19, 2010

Nephrol Dial Transplant (2010) 1 of 4
doi: 10.1093/ndt/gfq205

NDT
Nephrology Dialysis Transplantation

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 Tordoir⁶ and Wim Van Biesen¹

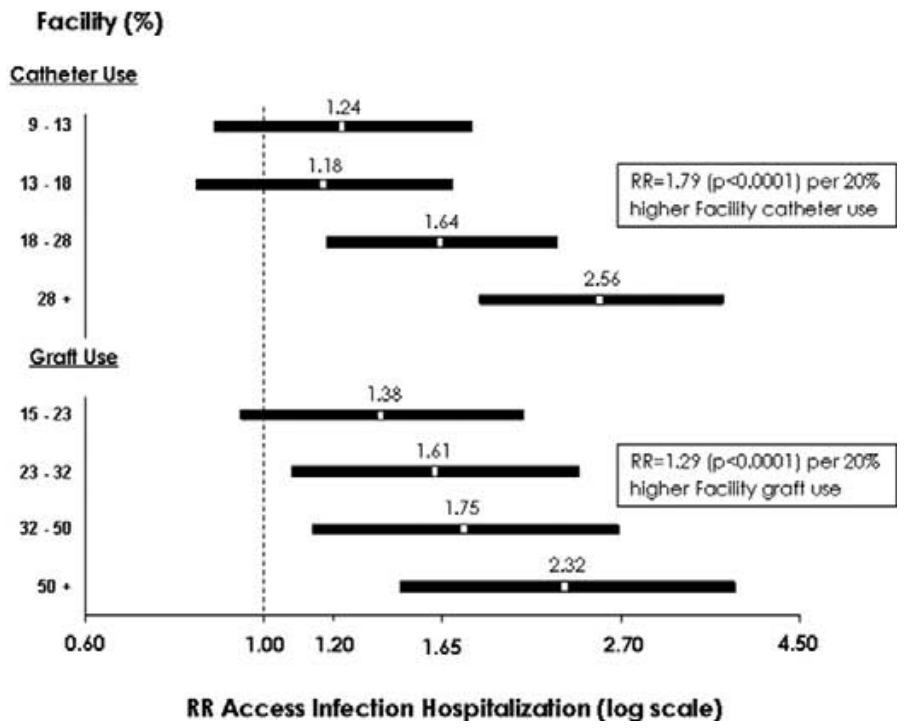
¹Nephrology Section, Department of Internal Medicine, University Hospital, Gent, Belgium, ²Nephrology, Dialysis and Intensive Care Unit, Lapeyronie University Hospital, Montpellier, France, ³Department of Renal Medicine, Royal Derby Hospital, Derby, UK, ⁴Nephrology, Cliniques Universitaires Saint-Luc, 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

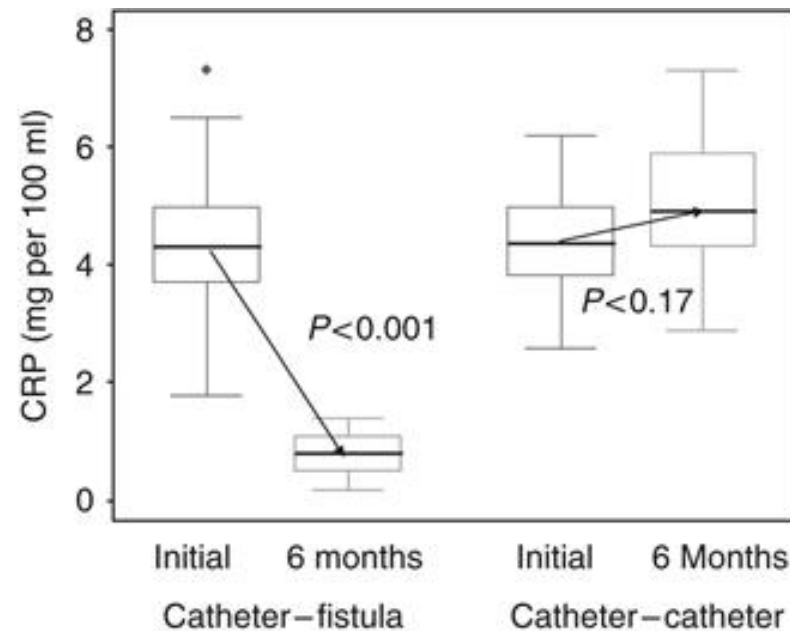
TUNNELED VS. NON-TUNNELED CATHETERS

- ↻ 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

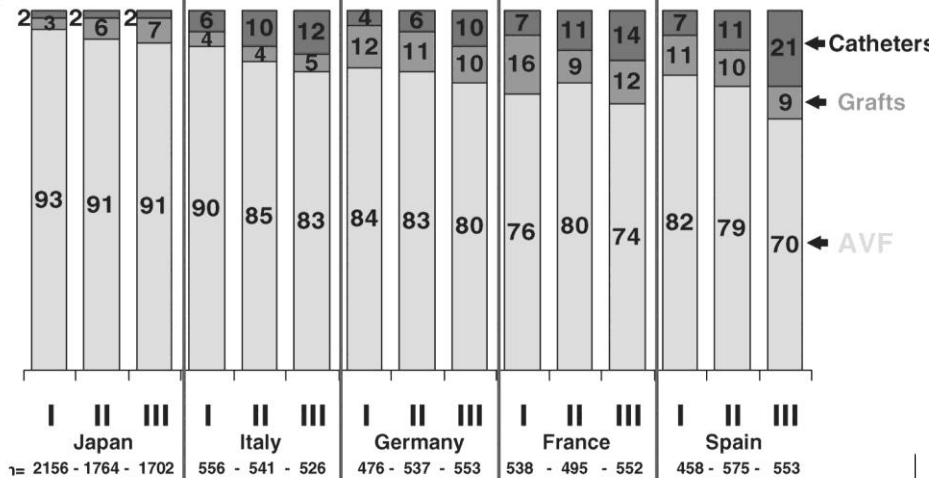


NON-INFECTED ACCESS CATHETERS AND INFLAMMATION

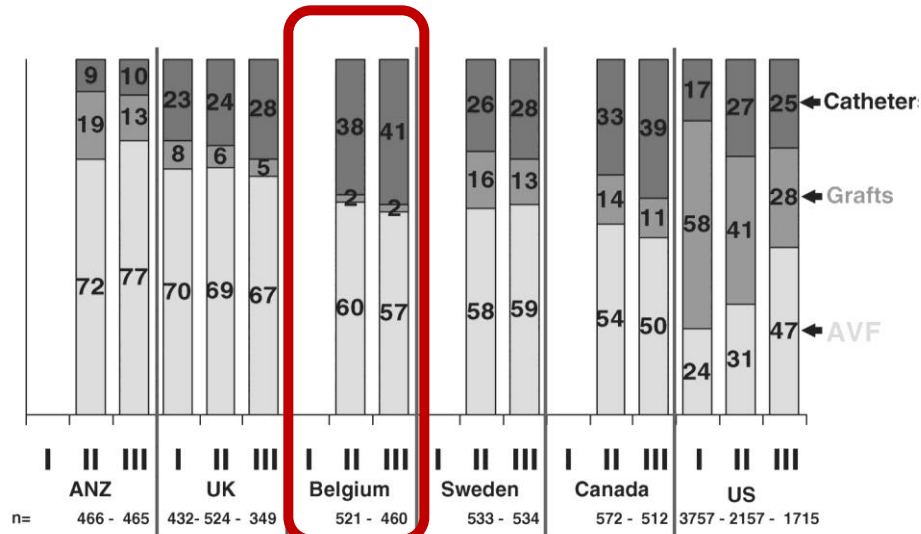


C-reactive protein (CRP) levels (mg per 100 ml) decrease significantly in incident maintenance hemodialysis patients who initially dialyze with a non-infected catheter but with a fistula at 6 months ($P<0.0001$). By contrast, no change in CRP is observed in incident maintenance hemodialysis patients 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.

CATHETER USE IN DOPPS OVER TIME



Prevalent patient cross-sections; cuffed catheters comprise 80-95% of catheter use in countries; DOPPS I (1996-2000), DOPPS II (2002-2003), DOPPS III (2005-2007)



Prevalent patient cross-sections; cuffed catheters comprise 80-95% of catheter use in countries; DOPPS I (1996-2000), DOPPS II (2002-2003), DOPPS III (2005-2007)

- (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

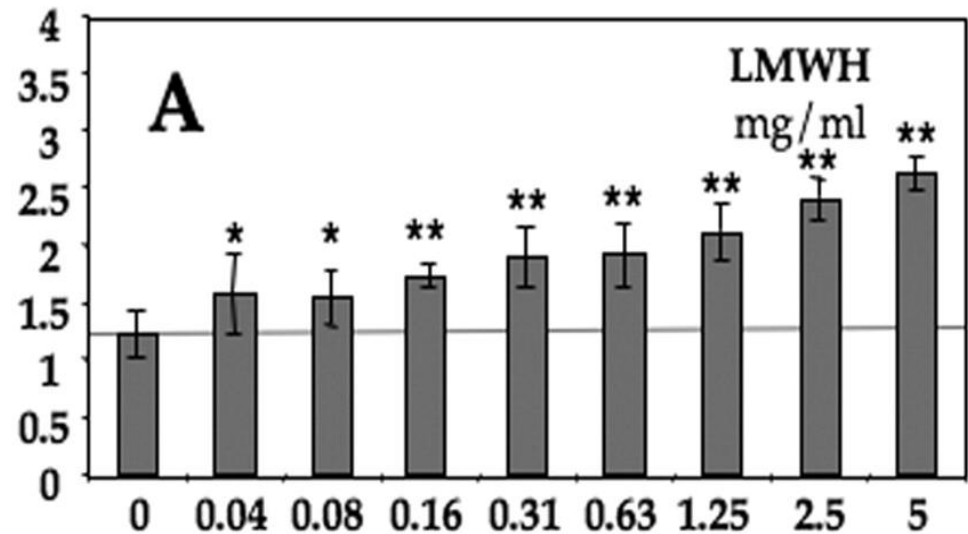
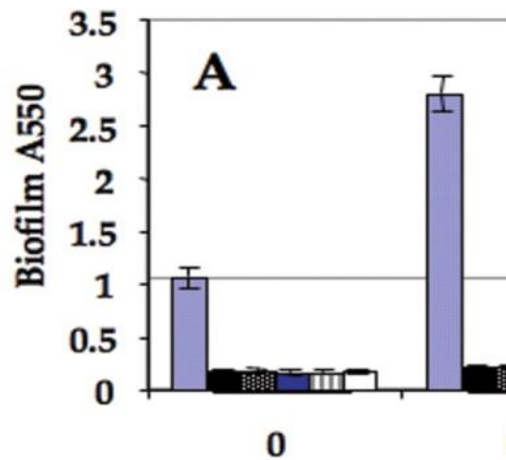
A

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

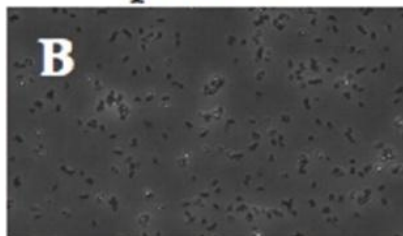
Laura Labriola, Ralph Crott, and Michel Jadoul

Nephrol. Dial. Transplant. 2008 23: 1666-1672

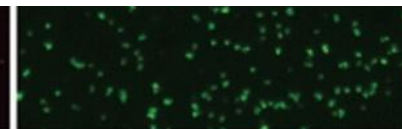
HEPARIN PROMOTES AND CITRATE COUNTERACTS BIOFILM FORMATION



phase 2

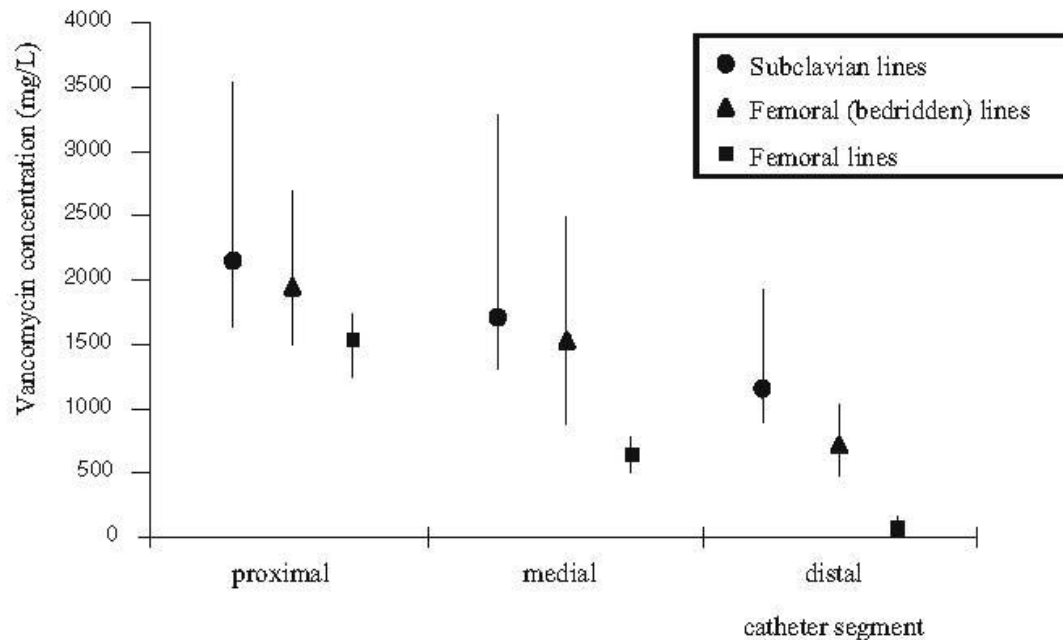


The effect of other anticoagulants on *S. aureus* biofilm formation (A-D)



Gentamicin and citrate together strongly inhibit biofilm formation

CAVE: LOSS OF SUBSTANCE OUT OF CATHETER



FDA WARNING AGAINST CITRATE AT HIGH CONCENTRATIONS

FDA Issues Urgent Warning On TriCitrasol Dialysis Catheter Anticoagulant

The screenshot shows the 'Doctor's Guide' website interface. At the top, it says 'Unregistered User' with a 'personalise' link. Below this is a navigation bar with links for 'Contact Us', 'Order Now', 'Journals', 'Bookstore', and 'Register a colleague'. A search bar is visible on the left. The main content area displays the article title 'FDA Issues Urgent Warning On TriCitrasol Dialysis Catheter Anticoagulant' and the start of the text: '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 bloodlines open, may cause death when infused into patients. TriCitrasol is marketed in individual, sterile, 30ml glass vials, distributed both individually and in hemodialysis kits.' Below the text, there are links for 'Warning', 'Privacy', and 'Awards'. On the left sidebar, there are sections for 'EXPLORE', 'Favourite Journals', 'Favourite Sites', and 'Languages'.

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 bloodlines 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 rhythm disruption, seizures or bleeding due to loss of blood calcium.

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

TriCitrasol 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 triCitrasol 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 triCitrasol and the Medcomp

FDA WARNING AGAINST CITRATE AT HIGH CONCENTRATIONS

FDA Issues Urgent Warning On TriCitrasol Dialysis Catheter Anticoagulant

The screenshot shows the 'Doctor's Guide' website interface. At the top, it identifies the user as an 'Unregistered User' and offers a 'personalise' option. Navigation links include 'Contact Us', 'Order Now', 'Journals', 'Bookstore', and 'Register a colleague'. A search bar is present with a 'Go' button. Below the search bar, there are radio buttons for 'News', 'Medline', 'Bookstore', 'The Web', 'Meetings & Congresses', and 'Complete Doctor's Guide'. An 'EXPLORE' section lists 'All News', 'All Webcasts', 'All Cases', 'All Meetings & Congresses', and 'All Medical Resources'. A 'get mail' button and a 'remind me' button are also visible. The main content area displays the article title 'FDA Issues Urgent Warning On TriCitrasol Dialysis Catheter Anticoagulant' and the beginning of the text: '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 bloodlines 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'.

In an April 9, 2000 letter to its customers, Medcomp announced a recall of its kits (or trays) containing triCitrasol and the Medcomp

AMERICAN SOCIETY FOR DIAGNOSTIC AND INTERVENTIONAL NEPHROLOGY



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

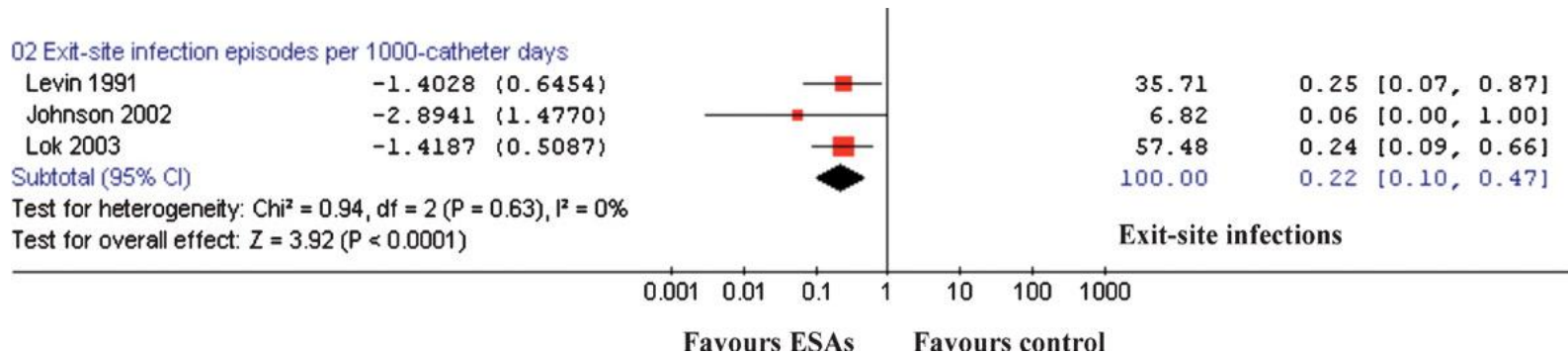
There is wide variation in the use of solutions to “lock” or fill tunneled central venous catheters for dialysis. Some centers use undiluted heparin concentrations ranging from 1000 to 10,000 U/ml and other centers place from 1000 to 10,000 U per lumen. Based on available evidence, it appears that heparin 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



MUPIROCIN RESISTANCE

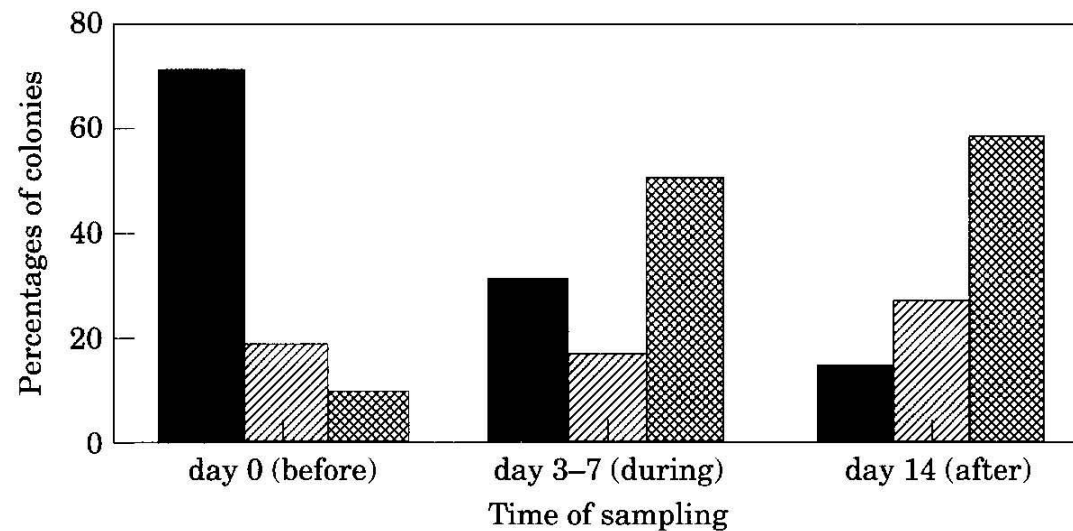


Figure 1. Selection of mupirocin resistance. Changes in coagulase-negative staphylococci of skin flora over time. (■), Susceptible; (▨), low resistance; (▩), high resistance.

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

Treatment of Dialysis Catheter–Related *Staphylococcus aureus* Bacteremia With an Antibiotic Lock: A Quality Improvement Report

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. *Am J Kidney Dis* 50:289-295. © 2007 by the National Kidney Foundation, Inc.

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

NDT
Nephrology Dialysis Transplantation

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

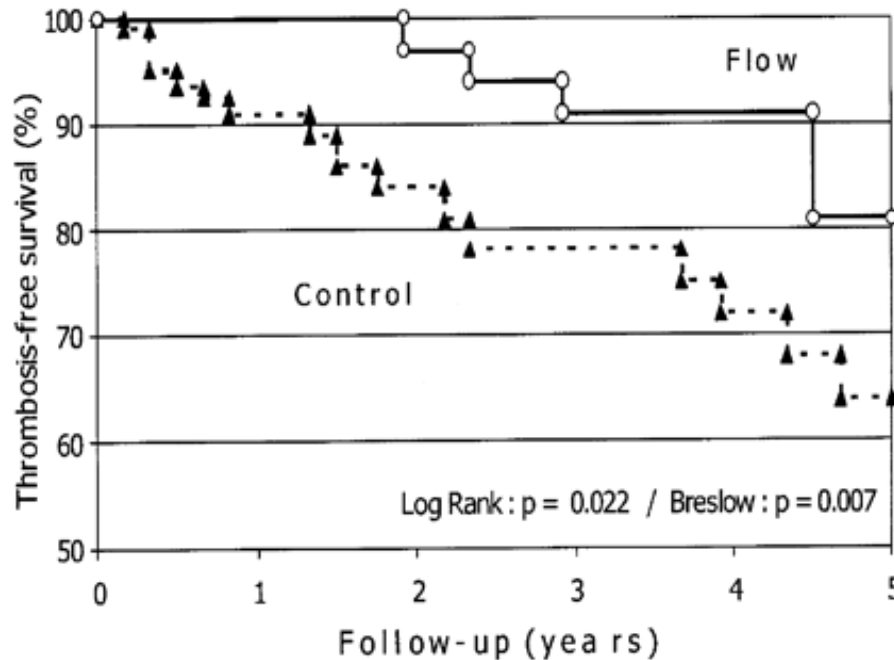
C. Zoccali, K.-U. Garg, F. Locatelli, R. Vanholder, *Nephrol. Dial. Transplant.* 2009; 24: 719-727
Anaemia management in patients with chronic kidney disease: a position statement by the Anaemia Working Group of European Renal Best Practice (ERBP)

K.-U. Garg, F. Locatelli, R. Vanholder, *Nephrol. Dial. Transplant.* 2009; 24: 719-727
Endorsement of the Kidney Disease Improving Global Outcomes (KDIGO) hepatitis C guidelines: a European Renal Best Practice (ERBP) position statement

Nephrol. Dial. Transplant. 2009; 24: 719-727
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

Nephrol. Dial. Transplant., March 2009; 24: 719 - 727

COMPARISON OF CENTERS WITH DIFFERENT POLITICS

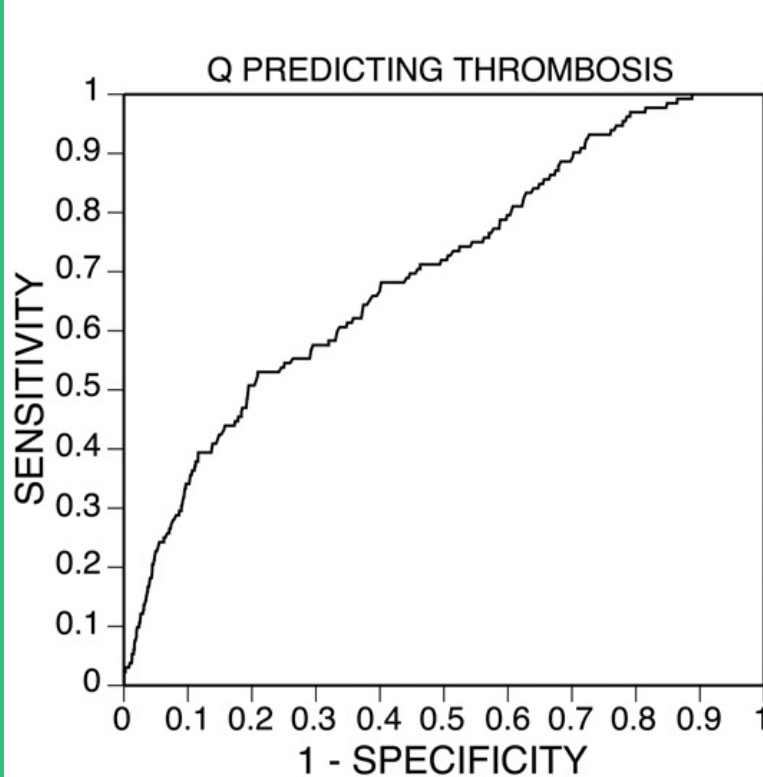


AVFs at risk:

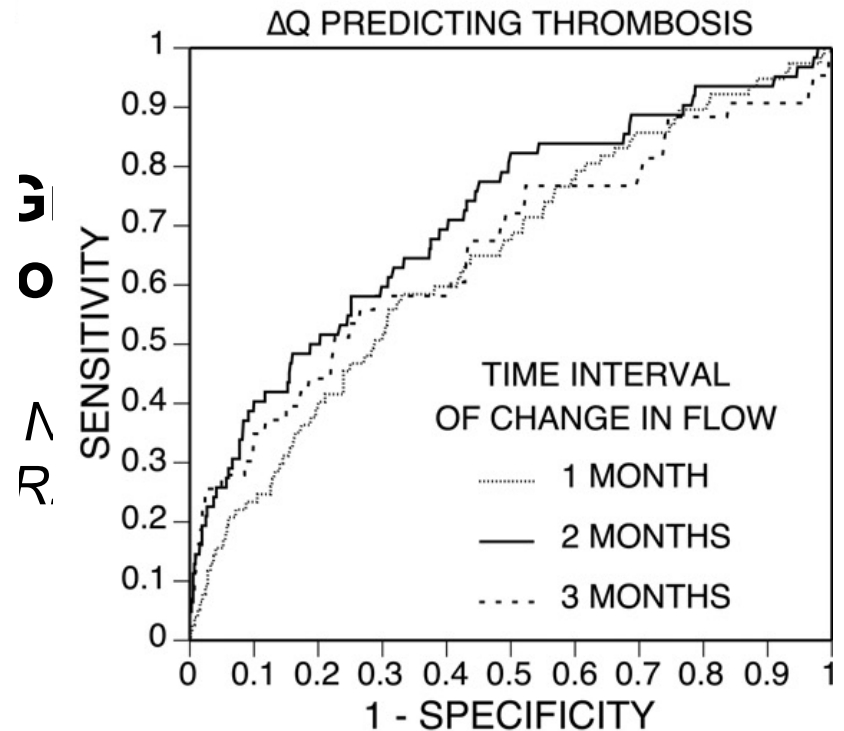
Control	97	72	44	30	21
Flow	62	53	33	21	13

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%.

RCT: MONTHLY FLOW SURVEILLANCE IN GRAFTS



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



	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%

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

	GF-PP	GF-SP	FF-PP	FF-SP
ACEi	1.02	1.16	0.77	0.56
CCBs	0.86	0.88	1.14	1.16
Asp	0.84	0.70	0.89	1.15
A-plat	1.00	1.10	1.06	0.73
Warf	1.33	1.22	0.95	1.12

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

Variables	Patients			
	Baseline	Early post-AVF closure	Late post-AVF closure	
Req LVDDI (mm/m ²)	29.5 ± 3.4	26.9 ± 2.9*	26.2 ± 3.2*	phy After llow-Up rne
Art LVESDI (mm/m ²)	18.1 ± 3.2	16.6 ± 3.4*	16.0 ± 3.5*	
Tra IVS (mm)	12.4 ± 3.0	12.8 ± 3.1	12.2 ± 2.1	
Phili PW (mm)	11.2 ± 1.7	11.6 ± 1.7	11.4 ± 1.7	
Wis RWT (%)	46.9 ± 10.6	52.7 ± 10.2*	51.7 ± 7.6*	
Median	44.1	50.1	49.7	
LVMI (g/m ²)	139 ± 44	127 ± 45*	117 ± 40*†	
Median	135	110	107	
LAD (mm)	45.2 ± 6.0	42.0 ± 5.7*	42.2 ± 5.8*	
RVEDD (mm)	30.1 ± 4.6	30.2 ± 4.1	27.8 ± 5.7	
FS (%)	38.7 ± 6.9	38.4 ± 8.5	39.2 ± 7.6	
EF (%)	68 ± 9	68 ± 11	69 ± 10	
E (cm/s)	80 ± 20	56 ± 13*	60 ± 18*	
A (cm/s)	80 ± 21	75 ± 15	76 ± 17	
E/A	1.08 ± 0.46	0.77 ± 0.20*	0.81 ± 0.21*	

Data are mean ± SD; *p < 0.0167 vs. baseline; †p < 0.0167 vs. early post-operative.

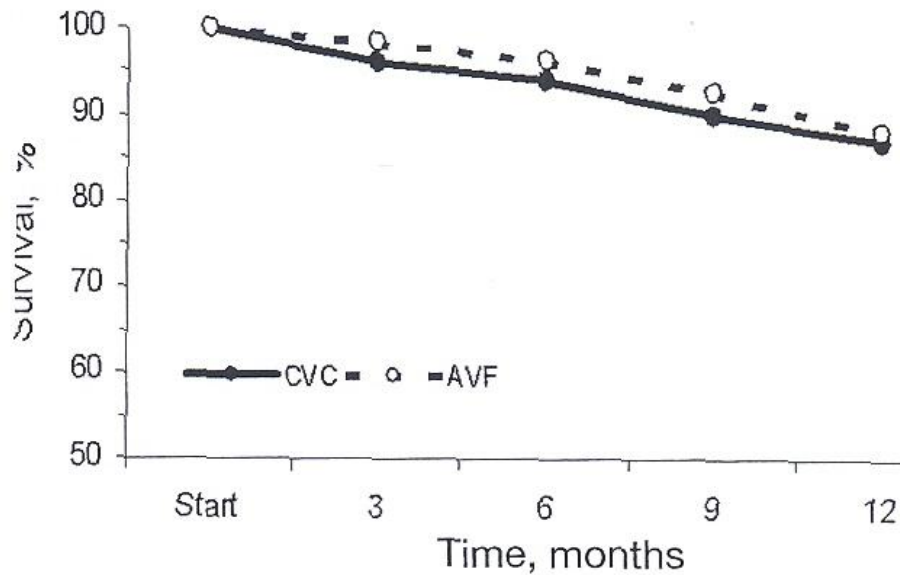
LVEDDI: Indexed LV end-diastolic diameter; LVESDI: Indexed LV end-systolic diameter; IVS: interventricular septum; PW: posterior wall thickness; RWT: relative wall thickness; LVMI: indexed LV mass; LAD: left atrial dimension; RVEDD: right ventricular end-diastolic diameter; FS: LV fractional shortening; EF: LV ejection fraction; E: early transmitral velocity; A: late transmitral velocity.

CHOICE OF VASCULAR ACCESS

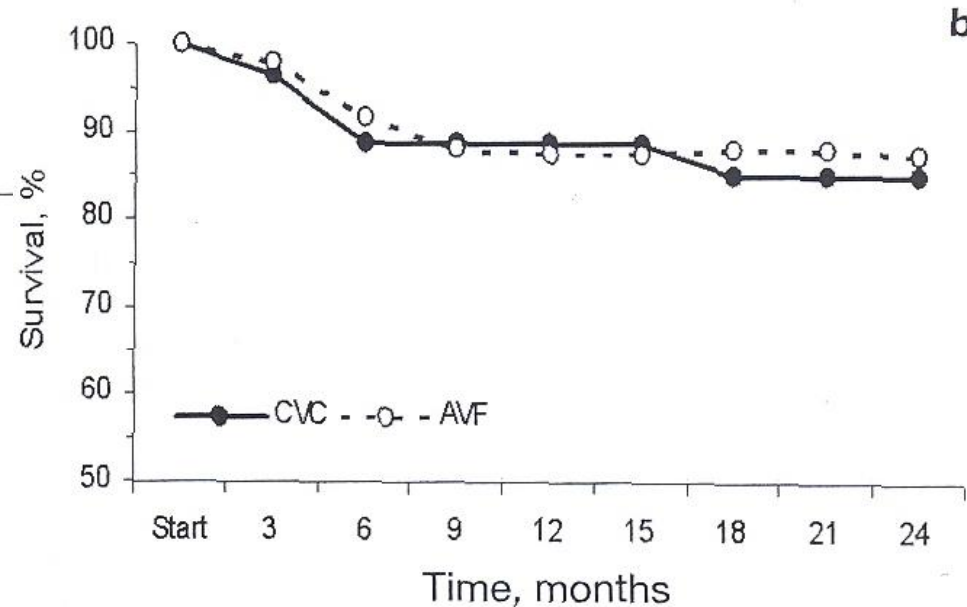
EBPG 2007

➔ CFR GUIDELINE

ADJUSTMENT FOR COMORBIDITIES



hemodialysis: The impact of comorbidity



LOCKS FOR CVC

EBPG 2007

➔ ?

CATHETER ANTIMICROBIAL LOCK STUDIES

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

Ge Randomized, Clinical Trial Comparison of Trisodium Citrate
As 30% and Heparin as Catheter-Locking Solution in Hemodialysis
Ne Patients

Me Citrate 4% versus Heparin and the Reduction of Thrombosis
Pie Study (CHARTS)
Br
Sc
St

Jennifer M. MacRae, Ivana Dojcinovic, Ognjenka Djurdjev, Beverly Jung, Steven Shalansky, Adeera Levin, and Mercedeh Kiaii

J A
Clin J Am Soc Nephrol 2008 3: 369-374

CATHETER ANTIMICROBIAL LOCK STUDIES

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

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

Nep
Chai
Rich **Prevention of dialysis catheter-related sepsis with a citrate–taurolidine-containing lock solution**

Neph *M*
Ne **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

Scandinavian Journal of Infectious Diseases, Volume 40, Issue 5 2008 , pages 399 - 406

META-ANALYSIS

A

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

Laura Labriola, Ralph Crott, and Michel Jadoul

Nephrol. Dial. Transplant. 2008 23: 1666-1672

ATTRIBUTED ADVANTAGES ANTIMICROBIAL LOCKS

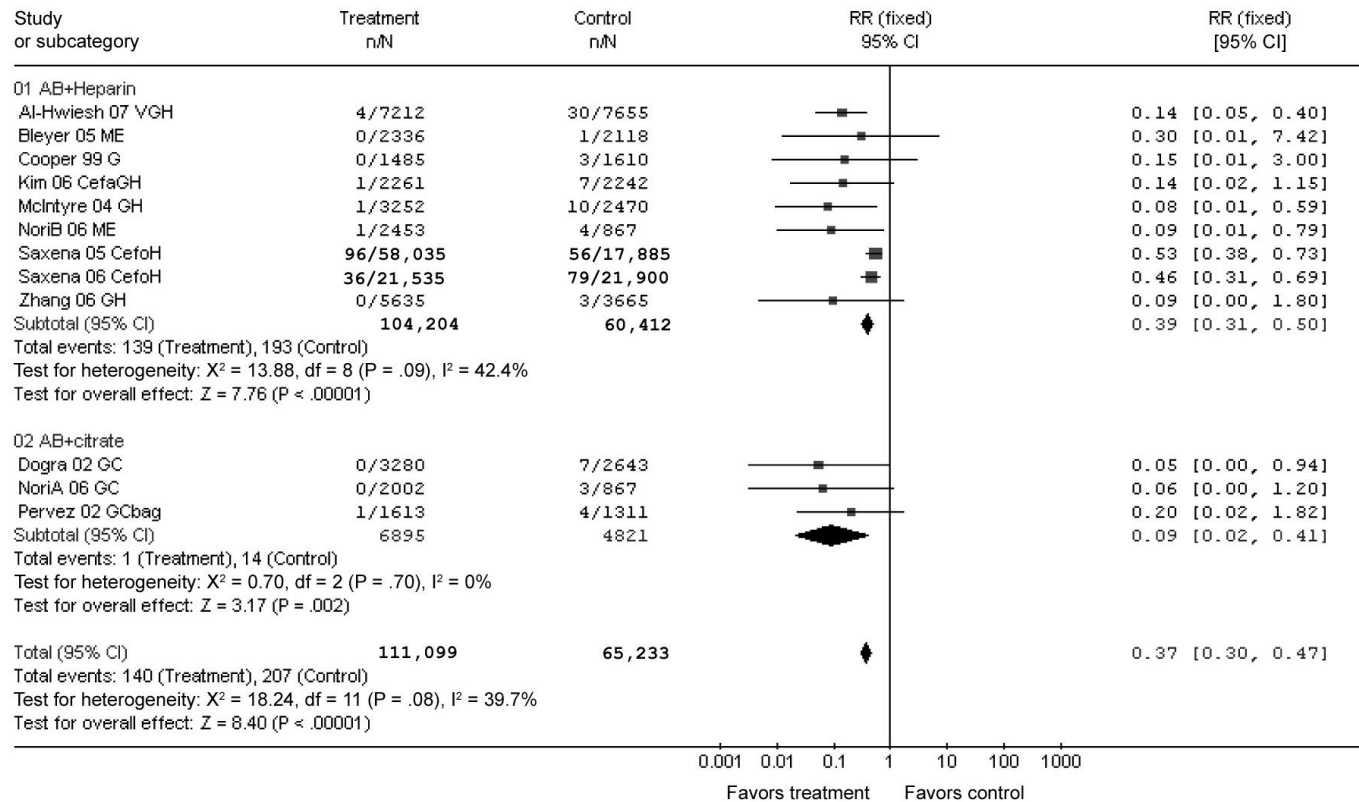
- ➔ **Less catheter exchanges / removals**
- ➔ **Less hospitalizations**
- ➔ **Longer time till need for exchange**
- ➔ **Lower cost (4%)**
- ➔ **No false elevations INR**
- ➔ **Less bacteremia**
- ➔ **Less exit site infections**

META-ANALYSIS: QUID ADDITION OF ANTIBIOTICS vs. INFECTION

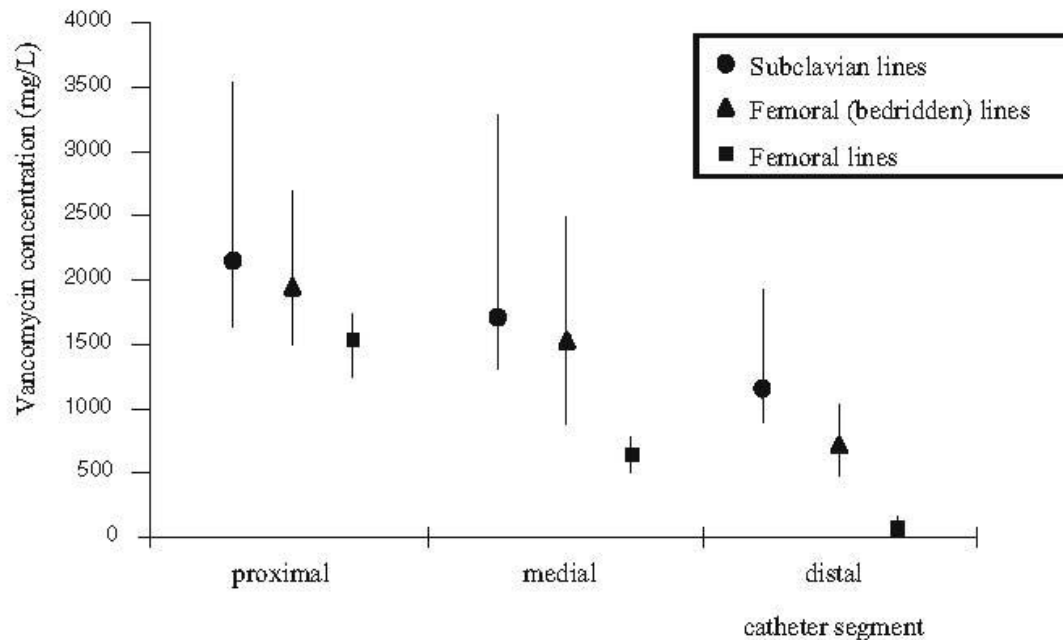
A

Study or subcategory	Treatment n/N
01 AB+Heparin	
Al-Hwiesh 07 VGH	4/33
Bleyer 05 ME	0/30
Cooper 99 G	0/19
Kim 06 CefaGH	1/60
McIntyre 04 GH	1/25
NoriB 06 ME	1/21
Saxena 05 CefoH	96/159
Saxena 06 CefoH	36/58
Zhang 06 GH	0/49
Subtotal (95% CI)	454
Total events: 139 (Treatment), 162 (Control)	
Test for heterogeneity: $X^2 = 41.37$, $df = 8$ ($P < .00001$)	
Test for overall effect: $Z = 10.59$ ($P < .00001$)	
02 AB+Citrate	
Dogra 02 GC	0/42
NoriA 06 GC	0/20
Pervez 02 GCbag	1/14
Subtotal (95% CI)	76
Total events: 1 (Treatment), 14 (Control)	
Test for heterogeneity: $X^2 = 1.52$, $df = 2$ ($P = .47$)	
Test for overall effect: $Z = 2.93$ ($P = .003$)	
Total (95% CI)	530
Total events: 140 (Treatment), 176 (Control)	
Test for heterogeneity: $X^2 = 54.78$, $df = 11$ ($P < .00001$)	
Test for overall effect: $Z = 11.04$ ($P < .00001$)	

B



CAVE: LOSS OF SUBSTANCE OUT OF CATHETER



Soriano et al, Eur J Microbiol Infect Dis, 26: 659-661; 2007

ACCOMPANYING EDITORIAL

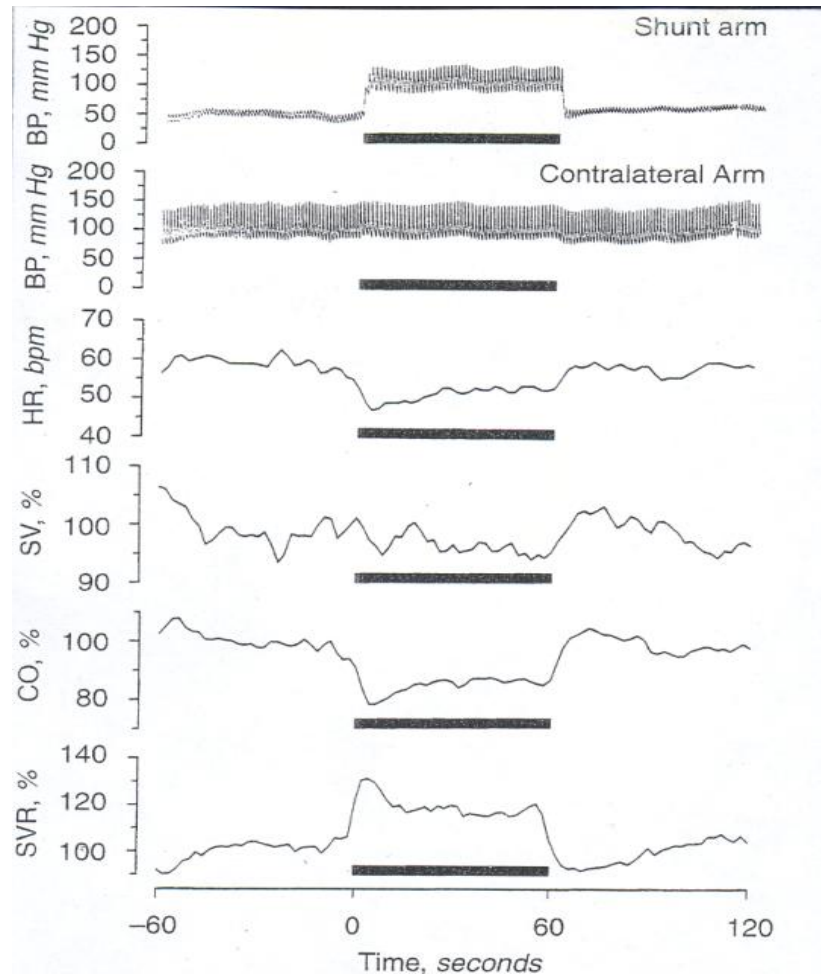
This important study has immediate implications for clinicians. Nephrologists can be reasonably confident that clopidogrel should not be prescribed for patients undergoing fistula creation because it does not lead to clinically meaningful benefit. In fact, routinely prescribing clopidogrel might actually 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.¹² Speculation aside, the findings of Dember et al suggest that clopidogrel cannot currently be recommended to improve maturation or patency of arteriovenous fistulas.

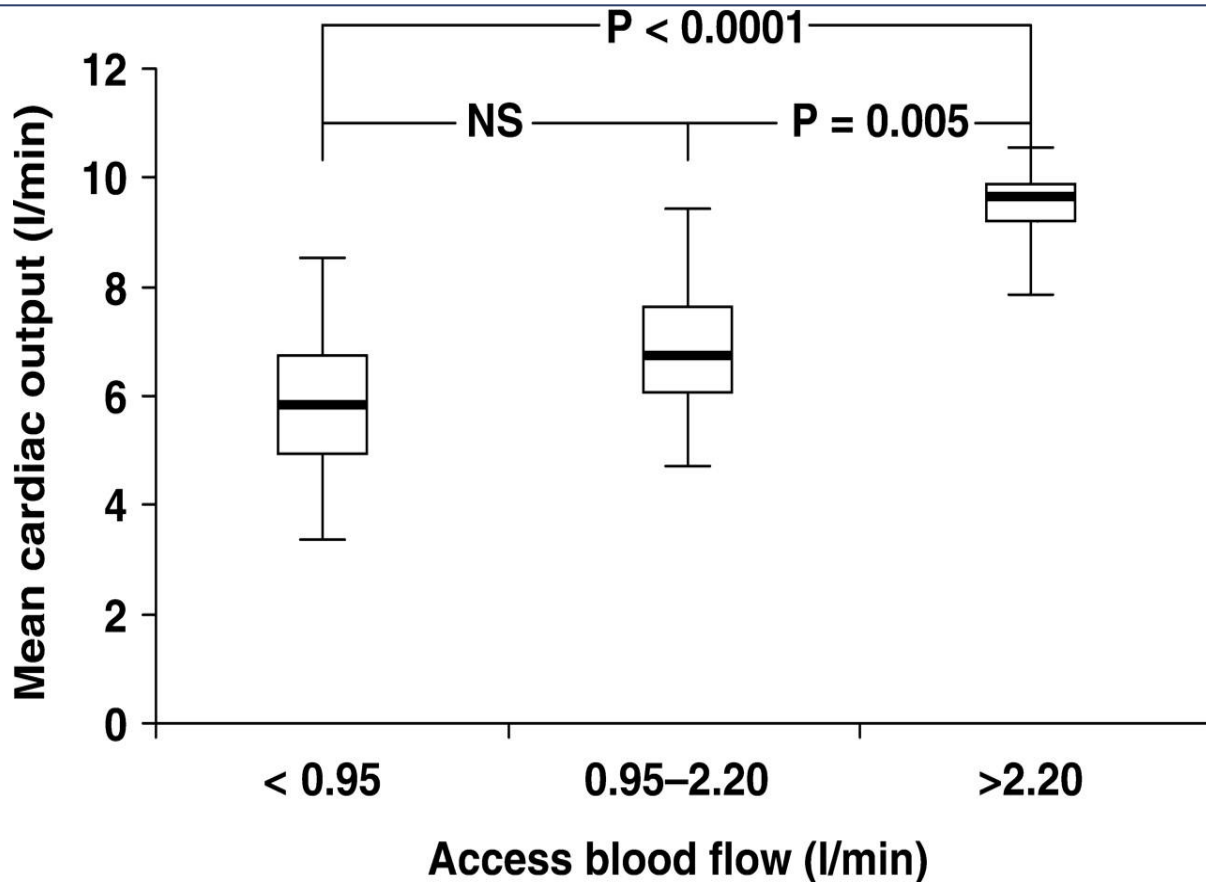
FISTULA FLOW VS. CARDIAC OUTPUT

EBPG 2007

➔ ?

EFFECT OF FISTULA COMPRESSION





out in

la 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.

ASPIRIN AND PATENCY GRAFTS

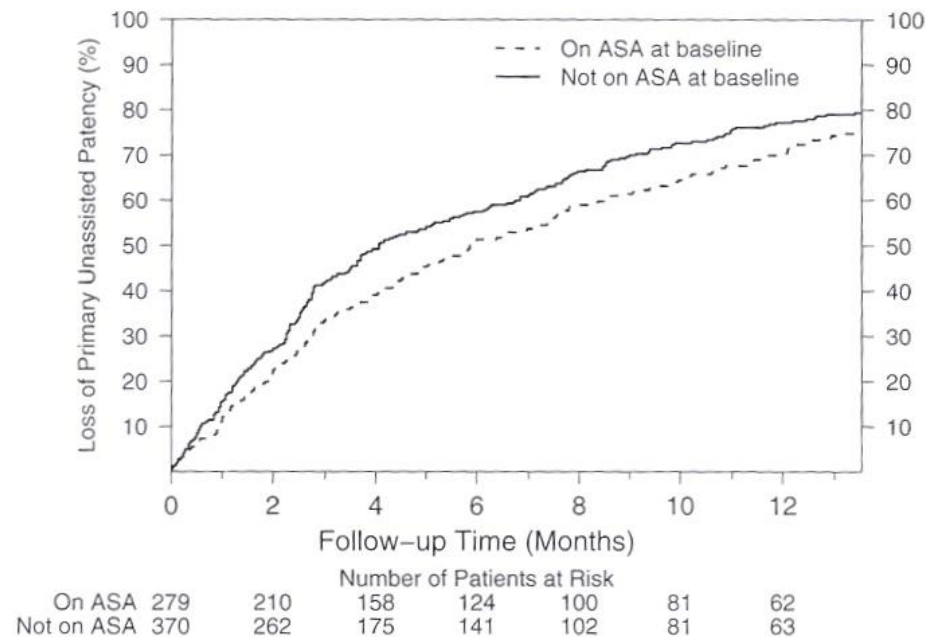
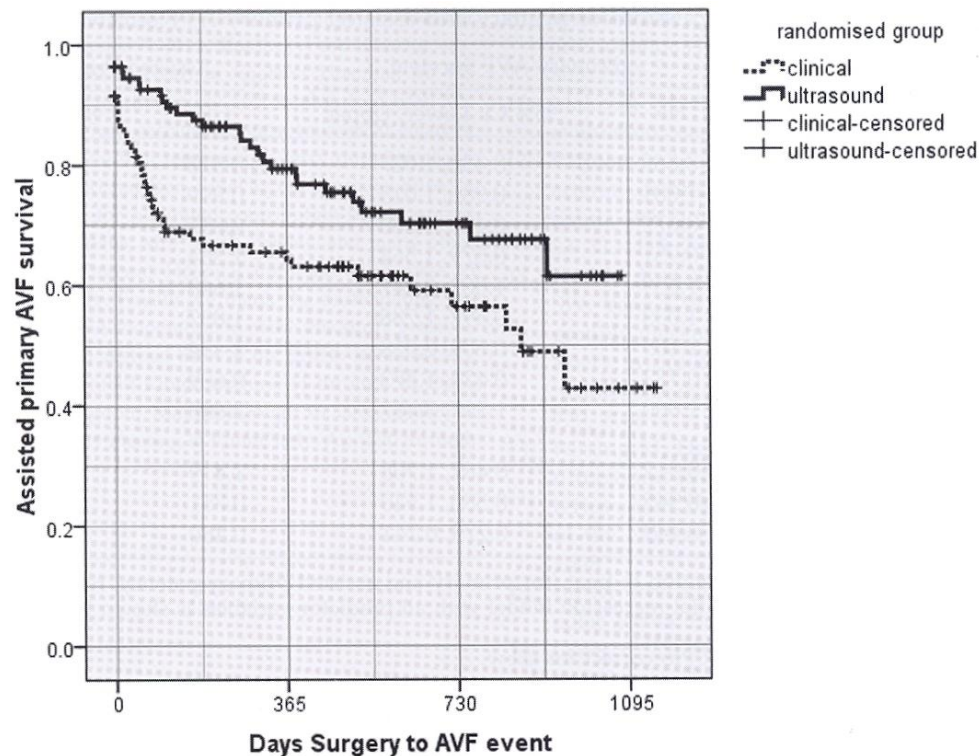


Figure 1. Primary unassisted patency is prolonged in patients on aspirin at baseline. Cumulative incidence of loss of primary unassisted graft patency for baseline aspirin users (dashed line) and nonusers (solid line). The median patency in the baseline aspirin users and nonusers was 5.8 (95% CI, 4.8 to 7.4) and 4.1 months (95% CI, 3.5 to 5.3; $P = 0.13$), respectively



Number at risk	0	365	730	1095
clinical	60	53	34	20
ultrasound	83	64	41	29

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.*

Outcome	Conventional Hemodialysis (N = 120)		Frequent Hemodialysis (N = 125)		Hazard Ratio (95% CI)	P Value
	no. of events	no. of patients with event	no. of events	no. of patients with event		
Death	9		5		—	—
All hospitalizations	114	47	109	58	0.88 (0.60–1.28)	0.50
Unrelated to vascular access	90	44	79	47	0.80 (0.53–1.21)	0.30
Related to vascular access	24	14	30	20	0.99 (0.54–1.82)	0.97
Cardiovascular-related	15	12	17	15	0.83 (0.44–1.59)	—
Infection related	27	20	27	23	0.83 (0.49–1.40)	—
All interventions related to vascular access	65	29	95	47	1.35 (0.84–2.18)	0.22
Correction of access failure	23	15	19	15	0.71 (0.35–1.44)	0.35
Other procedures	42	21	76	38	1.71 (0.98–2.97)	0.06
Episodes of hypertension [†]	470	87	724	99	—	—
Hypokalemia						
Potassium <3.0 mmol/liter	0	0	0	0	—	—
Potassium <3.5 mmol/liter	6	5	13	8	—	0.57 [‡]
Hypophosphatemia [§]	9	7	15	9	—	0.80 [‡]

* 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

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

Outcome	Conventional Hemodialysis (N = 120)		Frequent Hemodialysis (N = 125)		Hazard Ratio (95% CI)	P Value
	<i>no. of events</i>	<i>no. of patients with event</i>	<i>no. of events</i>	<i>no. of patients with event</i>		
All interventions related to vascular access	65	29	95	47	1.35 (0.84–2.18)	0.22
Correction of access failure	23	15	19	15	0.71 (0.35–1.44)	0.35
Other procedures	42	21	76	38	1.71 (0.98–2.97)	0.06

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

BUTTONHOLE TECHNIQUE

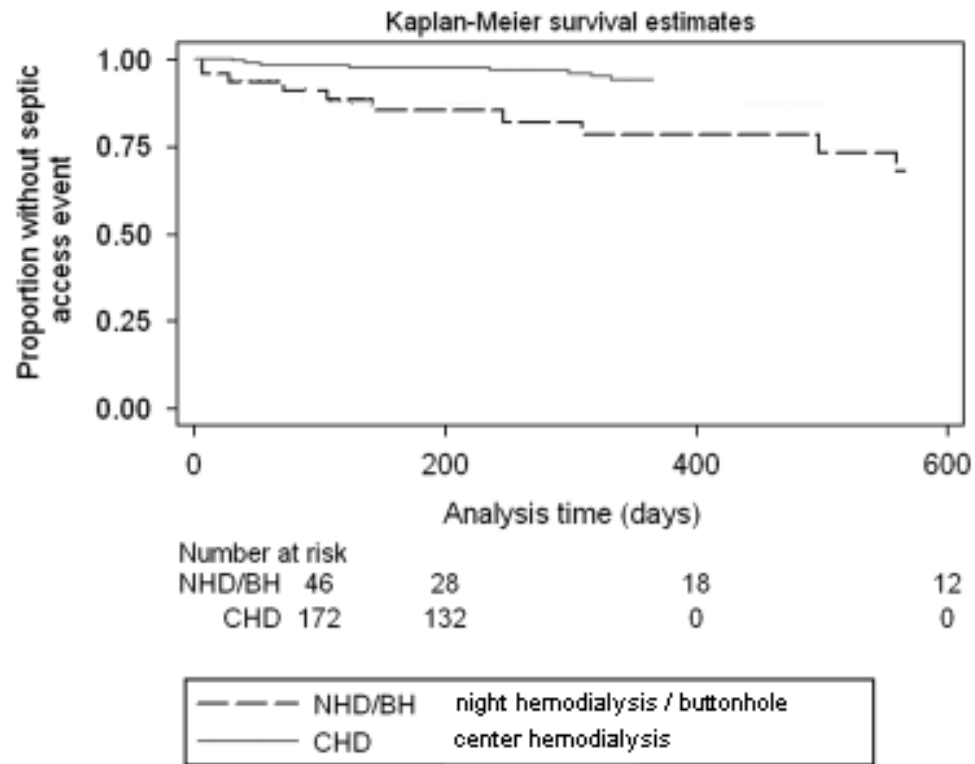


Figure 1 Time to first septic permanent access event in conventional hemodialysis vs. nocturnal hemodialysis (NHD)/rope ladder and NHD/buttonhole cannulation groups (univariable analysis).