The Clinical Interface: Research & Vascular Access

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Australian Vascular Access Teaching and Research (AVATAR) Group
Sydney 11th March 2014
Disclosure of Relevant Financial Relationships

I have the following financial relationships to disclose:

- Consultancy research: Analytica, Zychem, BD
- Educational sessions for: BD, Carefusion, Mayo
- Investigator initiated research grant: BD
Why?

Level I Evidence
- Systematic reviews & meta-analysis
- Randomised controlled trials

Foundation Research
- Observational study
- Point prevalence study
- Practice survey
- Laboratory experiments
What?

Cochrane reviews

Pilot trials, simulations

Micro lab studies

Health economics

Practice surveys, cohort studies

Education, knowledge translation

RCTs
Where?
NH&MRC Centre for Research Excellence in Nursing Interventions

Who?
How?
• Networking, email list
• Mentoring, advice on research or publishing
• Research degrees
• Statistics, data management, randomisation service
• Coordinating centre for pilot and multi-site trials
• Training and consultancies
• @AVATAR_Grp
www.avatargroup.org
Previous Studies
Peripheral IV catheters and time...
<table>
<thead>
<tr>
<th>Year</th>
<th>Replacement</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1970</td>
<td>Unlimited</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>1970/71</td>
<td>24h</td>
<td>Expert opinion, response to epidemic</td>
</tr>
<tr>
<td>1981</td>
<td>48-72h</td>
<td>Expert opinion</td>
</tr>
<tr>
<td>1996</td>
<td>48-72h</td>
<td>Collin et al 1975 Cohort study, Band &amp; Maki 1980 Cohort study (n=148)</td>
</tr>
<tr>
<td>2002</td>
<td>At least 72-96h</td>
<td>Lai et al 1998 Cohort Study (N=2503)</td>
</tr>
<tr>
<td>2011</td>
<td>Not more frequently than 72-96h</td>
<td>Maki &amp; Ringer 1991 RCT (N=714), Tager et al 1983 Cohort study (N=3094), Lai et al 1998 Cohort Study (N=2503)</td>
</tr>
</tbody>
</table>
“Consider replacement of the short peripheral catheter when clinically indicated and when infusion treatment does not include peripheral parenteral nutrition. The decision to replace the short PIV should be based on assessment of the patient’s condition; access site; skin and vein integrity; length and type of prescribed therapy; venue of care; integrity and patency of VAD; dressing; and stabilization device.”

Idvall et al. 2006 J Adv Nursing
Webster et al. 2010 Cochrane Database of SRs
Strength of the Evidence

Level I Evidence (INS classification):

- Meta-analyses
- Systematic literature reviews
- Guidelines based on randomised controlled trials (RCTs)
- At least 3 well designed RCTs
Peripheral IV Catheters: The New World of Clinically Indicated Replacement
 Changes for patients & organisations

- 20-25% reduction in cannulation procedures
- Time savings for staff of 20 minutes
- Cost saving per patient up to AUD$10.50
- Cost-effectiveness analysis for Queensland Health
- **AUD$5 million** saved over 5 years

**USA:** Projected savings of 2.5m PIVs/year, 1m of staff time/year & USD$400 million over 5 years


• Rickard CM, McCann D, Munnings J, McGrail MR. Routine resite of PIV devices every 3 days did not reduce complications compared with clinically indicated resite: RCT. BMC Medicine 2010;8:53

• Webster J, Osborne S, Hall J, Rickard CM. Clinically indicated replacement versus routine replacement of peripheral venous catheters. Cochrane Database of Systematic Reviews 2010;3
Routine versus clinically indicated replacement of peripheral intravenous catheters: a randomised controlled equivalence trial.


Lancet 2012; 380: 1066–1074
<table>
<thead>
<tr>
<th></th>
<th>Clinical n=1593</th>
<th>Routine n=1690</th>
<th>Risk (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phlebitis per Patient</td>
<td>114 /1593 (7%)</td>
<td>114/1690 (7%)</td>
<td>RR 1.06 (0.83-1.36)</td>
<td>0.64</td>
</tr>
<tr>
<td>Phlebitis per 1000 days</td>
<td>13.1</td>
<td>13.1</td>
<td>HR 0.94 (0.73-1.23)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

No difference in phlebitis between study groups
Failure over time

Cumulative Hazard

Cumulative time (hours) up to first phlebitis episode

Clin. indicated 66/1590 31/739 10/230 6/91 1/44
Routine replace 70/1686 37/743 5/231 1/90 1/15
<table>
<thead>
<tr>
<th>Per 1000 PIV days</th>
<th>Clinical n=1593</th>
<th>Routine n=1690</th>
<th>HR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIV-BSI</td>
<td>0</td>
<td>0.1 (n=1)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>All-BSI</td>
<td>0.46 (n=4)</td>
<td>1.03 (n=9)</td>
<td>0.46 (0.14-1.48)</td>
<td>0.19</td>
</tr>
<tr>
<td>Local infection</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Colonisation</td>
<td>13.0</td>
<td>12.4</td>
<td>1.05 (0.32-3.68)</td>
<td>NS</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>0.25% (n=4)</td>
<td>0.24% (n=4)</td>
<td>RR 1.06 (0.27-4.23)</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Infection was rare and not different between study groups.
# Bloodstream Infections

<table>
<thead>
<tr>
<th>Type</th>
<th>Clinical n=1593</th>
<th>Routine n=1690</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIV-BSI</td>
<td></td>
<td>1 - <em>Enterobacter cloacae</em></td>
</tr>
<tr>
<td>PIV-(A)BSI</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Any BSI</td>
<td>11 in 9 patients</td>
<td>4 in 4 patients</td>
</tr>
<tr>
<td>Organisms</td>
<td><em>Staph aureus</em> X 2</td>
<td><em>Staph aureus</em></td>
</tr>
<tr>
<td></td>
<td>CNS</td>
<td>CNS X 4</td>
</tr>
<tr>
<td></td>
<td><em>Staph epidermidis</em></td>
<td>*Enterobacter coli X 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Enterobacter cloacae</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Pseudomonas aeruginosa</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Bacteroides fragilis</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Klebsiella oxytoca</em></td>
</tr>
<tr>
<td>Per 1000 PIV days</td>
<td>Clinical n=1593</td>
<td>Routine n=1690</td>
</tr>
<tr>
<td>-------------------</td>
<td>----------------</td>
<td>----------------</td>
</tr>
<tr>
<td>All PIV failure</td>
<td>77 (n=670)</td>
<td>73 (n=636)</td>
</tr>
<tr>
<td>Infiltration</td>
<td>32 (n=279)</td>
<td>27 (n=235)</td>
</tr>
<tr>
<td>Occlusion</td>
<td>40 (n=344)</td>
<td>40 (n=344)</td>
</tr>
<tr>
<td>Accidental removal</td>
<td>19 (n=166)</td>
<td>18 (n=159)</td>
</tr>
</tbody>
</table>

No difference in PIV failure between study groups
Clinically indicated replacement leads to equivalent phlebitis, and no difference in infection or failure.
Twins can still be ugly
26% of PIVs FAIL

• Should 26% of blood glucometers fail?
• Should 26% of hip prostheses fail?
• Should 26% of PICCs fail?

Why should 26% of PIVs fail?
40% of PATIENTS have at least one PIV failure over a course of therapy.
PIVs are failing around the globe
20% develop occlusion/infiltration
10% have their PIV “just fall out”
7% of patients develop phlebitis
One in five PIVs is redundant
Can we do better?
Can we do more?
Securement & dressing

ANTT & Infection Control

Connectors & cleaning

IV lines & solutions

Patency & flushing

Insertion & removal
Risk factors for PIV catheter failure: a multivariate analysis of data from a randomized controlled trial
Infection Control & Hospital Epidemiology. 2014
## Predictors of Occlusion/Infiltration

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR</th>
<th>95%CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand</td>
<td>1.47</td>
<td>1.28-1.68</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>1.44</td>
<td>1.30-1.61</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IV Antibiotics</td>
<td>1.41</td>
<td>1.25-1.59</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IV Hydrocortisone</td>
<td>1.36</td>
<td>1.03-1.80</td>
<td>0.028</td>
</tr>
<tr>
<td>Any infection</td>
<td>1.27</td>
<td>1.12-1.44</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Antecubital fossa</td>
<td>1.27</td>
<td>1.08-1.49</td>
<td>0.004</td>
</tr>
<tr>
<td>Upper arm</td>
<td>1.25</td>
<td>1.04-1.50</td>
<td>0.016</td>
</tr>
<tr>
<td>2\text{nd} or later IV</td>
<td>1.17</td>
<td>1.01-1.35</td>
<td>0.037</td>
</tr>
<tr>
<td>OT/Rad insert</td>
<td>0.80</td>
<td>0.67-0.94</td>
<td>0.009</td>
</tr>
<tr>
<td>IV Antipyretic</td>
<td>0.76</td>
<td>0.59-0.97</td>
<td>0.030</td>
</tr>
</tbody>
</table>
### Predictors of Accidental Removal

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR*</th>
<th>95%CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand</td>
<td>2.45</td>
<td>1.93-3.10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-IV Team insert</td>
<td>1.69</td>
<td>1.30-2.20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Antecubital fossa</td>
<td>1.65</td>
<td>1.23-2.22</td>
<td>0.001</td>
</tr>
<tr>
<td>Smaller than 20G</td>
<td>1.29</td>
<td>1.02-1.61</td>
<td>0.030</td>
</tr>
</tbody>
</table>

*Cox regression*
# Predictors of Phlebitis

<table>
<thead>
<tr>
<th>Predictor</th>
<th>HR*</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>1.64</td>
<td>1.28-2.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Larger than 20G</td>
<td>1.48</td>
<td>1.08-2.03</td>
<td>0.014</td>
</tr>
<tr>
<td>Any infection</td>
<td>1.41</td>
<td>1.05-1.89</td>
<td>0.022</td>
</tr>
<tr>
<td>Age°</td>
<td>0.99</td>
<td>0.98-0.99</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IV ‘Other’ Meds</td>
<td>0.72</td>
<td>0.56-0.92</td>
<td>0.009</td>
</tr>
</tbody>
</table>

*Cox regression

°Each increase in age by 1 year, decreased HR by 1.1%
Change to PIV site placement

Proximal to distal

Forearm as preferred site
Change to PIV Inserter

Any inserter → Expert inserter
Specialist versus non-specialist vascular access insertion for the prevention of access device failure (Protocol).

Cochrane Database of Systematic Reviews


Peter Carr
Change to PIV size

Smaller

Dislodgement

20 gauge

Bigger

Phlebitis
Changes to PIV flushing

• Regular flushing and improved dilution are likely key to reducing PIV failure
• The current evidence base is limited in terms of most aspects of flushing and dilution management
Absolutely FAB research program

**Flushing And Blood sampling**


2. Clinical audit of adult, paeds and NICU

3. State-wide survey N=1,200


Dr Samantha Keogh
Senior Research Fellow
Changes in Monitoring

Regular assessment, documentation and action are still needed

What are we looking for?

1. Does it **hurt**?
2. Does it **work**?
3. Is it **needed**?
4. Does the **wound** look **infected**?
5. Does the **patient** look **infected with the PIV the likely source**?

Changes in Infection Prevention

<table>
<thead>
<tr>
<th>Insertion skin preparation</th>
<th>Regular re-application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clean gloves</td>
<td>Sterile gloves?</td>
</tr>
<tr>
<td>Plain dressing</td>
<td>Antimicrobial dressing??</td>
</tr>
</tbody>
</table>
## SAVE Pilot Trial

<table>
<thead>
<tr>
<th></th>
<th>Standard polyurethane (control)</th>
<th>Bordered polyurethane</th>
<th>Sutureless securement device</th>
<th>Tissue adhesive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure, N</td>
<td>8/21</td>
<td>5/20</td>
<td>5/23</td>
<td>3/21</td>
</tr>
<tr>
<td>Failure, %</td>
<td>38%</td>
<td>25%</td>
<td>22%</td>
<td>14%</td>
</tr>
</tbody>
</table>

**Marsh N, Flynn J, Hewer B, Webster J, Mihala G, Rickard CM.** Tissue Adhesive, Sutureless Securement Devices or Bordered Polyurethane for the securement and dressing of PIV catheters - can we do better at preventing catheter failure? **Submitted.**
The SAVE Trial

- **Securing All intravascular devices Effectively in PIVs**
- Superiority parallel RCT of dressing and securement
- Randomized to 4 groups:
  - Standard polyurethane
  - Bordered polyurethane
  - Sutureless securement device
  - Tissue adhesive
- 1,880 patients (900 recruited)
- $1m NHMRC project grant
Central venous Access device Se Curem ent And Dressing Effectiveness: The CASCADE Trial

<table>
<thead>
<tr>
<th>Total Failure in PIV &amp; IAL pilot trials</th>
<th>Control S-SP</th>
<th>SD-SP</th>
<th>BP</th>
<th>TA-SP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>24/98</td>
<td>18/103</td>
<td>11/93</td>
<td>11/109</td>
</tr>
<tr>
<td></td>
<td>24.5%</td>
<td>17.5%</td>
<td>11.8%</td>
<td>10.1%</td>
</tr>
<tr>
<td></td>
<td>RR 0.71</td>
<td>RR 0.48</td>
<td>RR 0.41</td>
<td></td>
</tr>
<tr>
<td></td>
<td>40/305 (13.1%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RR 0.53
The CASCADE Trial

- 4 group multi-site RCT 2015--2018
- Short term and long term CVADs
- 3,500 patients
1. Sutures + simple polyurethane (controls)
2. Bordered polyurethane
3. Tissue adhesive + simple PU
4. Sutureless securement device + PU

- Brisbane and Sydney sites
- Submitted to NHMRC March 2014
Intravascular administration sets: Replacement after Standard Versus Prolonged use

RSVP Trial
Since 1971, AS have been time limited for use. Firstly 24 hours with gradual extensions since

Replacing AS may remove contaminated sets, or by breaking a closed circuit may allow contamination

Routine AS change involves equipment and nursing time costs, and increases medical waste. It increases profits for manufacturers but increases hospital costs

Routine replacement costs A$1 billion annually, 2 million nursing hours, and does not have a strong evidence base
History of AS replacement

• Pre 1971, AS used until therapy complete
• 1970/71 US epidemic of CRSBI 24h replacement advocated
• Enterobacter agglomerans
• 1970s/80s trials of 24 vs 48, 48 vs 72 etc
• 2002 CDC “Replace no more frequently than 72h (unless blood, lipids)”
• 2011 CDC “Replace between 4 and 7 days”

Meta-analysis of all shorter vs longer durations:
- Longer AS use RR 1.06 (95%CI 0.66-1.68) for IVD-BSI
- Longer AS use RR 1.85 (95%CI 1.01-3.38) mortality
  (Mortality data came from neonatal study)
- Results consistent for subgroup analyses of central vs peripheral IVs, adults vs paeds, TPN vs non-TPN

“It appears that AS that do not contain lipids, blood or blood products may be left in place for up to 96 hrs without increasing infection”
Use beyond 96 hours

- Cochrane review concluded “There are currently an inadequate numbers of trials to examine the effect of AS use beyond 96hrs”

- What evidence is there for use beyond 96hrs?
  - One RCT (2001, N=512) in oncology plain CVCs compared 3 day with ‘between 4 and 7 day’ changes and found no diff in IVD-BSI
  - RBWH RCT (2004, N=404) antiseptic CVCs compared 4 with 7 day changes and found identical rates IVD-BSI (1.5% each group or 2.9/1,000 days)

- Both studies underpowered to study IVD-BSI
ICU practice

• N=180: 58% change AS on day 3-4, 16% Day 7

![Graph showing time limits on central line tubing]
Providing evidence for administration set replacement

The RSVP Trial

• Randomised controlled trial
• Randomized to 2 groups:
  • 4 day AS replacement
  • 7 day AS replacement
• 2011-2015, 6,554 patients
• 7 hospitals – Brisbane, Sydney, Perth
• NHMRC $1.6 million
• Short term CVCs
• Long term CVCs
• PICCs
• IALs (ICU)

• Mainly ICUs and haematology-oncology
• MUST have infusions running for >7 days
Trial design

- Multi-centre, parallel group RCT
  = Equivalence design

Outcome measures

- Primary: IVD-BSI (as per CDC)
- Secondary: IVD colonisation
  AS colonisation
  All cause BSI
  All cause mortality
  Time in situ
  Number of AS per patient
  Costs
Patient criteria

Inclusion criteria

• Informed written or documented verbal consent
• Central venous and/or peripheral arterial IVD in situ with AS
• IVD has been in situ for >24 hours
• IVD scheduled/expected use ≥7 days

Exclusion criteria

• Current bloodstream infection
• Planned removal of device ≤24 hours
• IVD in situ >96 hours
• Original AS already routinely replaced
Approvals in place

- HREC QH multisite + SSA
- HREC WA + SSA (ICU – no consent)
- HREC NSW multisite + SSA
- QCAT etc all done
- Registered on ANZCTR

Feasibility

- Research nurse and PI
- At least 4 hrs Mon, Wed, Fri
- Recruit minimum 5/wk

Funding

- Site start up and per patient payments
Processes

• Screening & recruitment, consent
• Randomisation using central website
• 1:1 ratio, blocked, stratified by site and device type
• Controls: 4 day AS replacement
• Intervention: 7 day replacement
• Only 1 IV device per patient studied
• Chemo, lipids and blood AS still changed 24h
• Training and monitoring by study manager
• DSMB analysis N=1000, 2000, etc
Procedures

Control group - AS changed Day 4

Intervention group - AS changed Day 7

• Research nurses affix a tag to each AS, indicating group and due date for change to alert clinical staff and to monitor how many AS actually last the 4/7 days

• In both groups, additional AS reconfiguration can occur as clinically indicated due to treatment addition/ completion, IVD removal or AS malfunction

• Blood & tip cultures, and line removal should be undertaken by clinical staff as clinically indicated
Data collected

• Baseline: age, sex, diagnosis, infection risk, immunosuppression status, concurrent infection, IVD type, insertion site, inserter discipline & seniority
• On-trial: AS hang time, AS configuration at time of replacement
• On trial: Antibiotics, infusate type, additives
• Bedisde: Reasons for AS replacement or removal
• 48 hour post removal: IVD dwell time, mortality
• Culture data, blinded CRBSI assessment
• SAE monitoring (limited dataset)
• Data collection is on RedCAP through web
Why RSVP to RSVP?

- Will provide definitive evidence whether 4 and 7 day AS use is of equivalent safety for patients
- Find out whether your current policy is correct
- Reduce Australia’s costs & time - estimated at A$1 billion and 2 million nursing hours
- Will lead to at least 3 quality publications, shape international guidelines and receive many citations in the literature
- The trial is funded and has the prestige and quality assurance of NHMRC backing
A worldwide point prevalence study
2014
"A day in the life of
www.omgpivc.org
Evan
Alexandrou
Principal Investigator