Antibiotic-resistant organisms and AML


doi: 10.1093/ndt/gfs081
Advance Access publication 18 April 2012

**Anti-microbial locks increase the prevalence of *Staphylococcus aureus* and antibiotic-resistant *Enterobacter*: observational retrospective cohort study**

John J. Dixon, Maggi Steele and A. David Makanjuola

South West Thames Renal and Transplantation Unit, St. Helier Hospital, Carshalton, Surrey, UK

*Correspondence and offprint requests to:* John J. Dixon; E-mail: johndixon3@nhs.net

**Abstract**

**Background.** Anti-microbial lock solutions (AML), in conjunction with systemic antibiotics, may successfully treat tunnelled haemodialysis catheter-related bloodstream infections (CR-BSI). It is unknown whether AML promote anti-microbial resistance.

**Methods.** This is a retrospective cohort study of all CR-BSI (2003–2006) in our dialysis unit. Controls (n = 265) were treated with systemic vancomycin and gentamicin. In addition to the systemic antibiotics, the study group (n = 662) received AML containing vancomycin and gentamicin during inter-dialytic periods. Antibiotic sensitivity/resistance profiles of all organisms were analysed. Changes in the incidence of infection (chi-square test) and resistant organisms (Fisher’s exact test) were calculated.

**Results.** The incidence of CR-BSI decreased from 8.50/1000 catheter days (controls) to 3.80 (study group; P < 0.0001), and the incidence of relapses decreased (P = 0.0027). The number needed to treat to prevent subsequent bacteraemia using an AML adjunct is 3 ± 0.4. The proportion of Gram-positive cultures increased (P < 0.0001), including *Staphylococcus aureus* (P = 0.03), but the proportion of methicillin-resistant *S. aureus* (P = 0.87) and vancomycin resistance (P = 0.90) did not. Increased gentamicin resistance (P < 0.0001) and ciprofloxacin resistance (P = 0.04) were observed in Gram-negative cultures. Gentamicin resistance [relative risk (RR) > 15.29; P < 0.0001] and ciprofloxacin resistance (RR = 6; P = 0.007) increased in *Enterobacter* species, but not *Pseudomonas* or *Escherichia coli* species.

**Conclusion.** AML decrease CR-BSI incidence, although proportions of *S. aureus* and anti-microbial-resistant *Enterobacter* are increased.

**Keywords:** antibiotic resistance; haemodialysis catheter; line locks

**Introduction**

Tunnelled haemodialysis catheters (THC) are associated with increased bacteraemia when compared with arteriovenous fistulae [1]. Treatment of haemodialysis catheter-related bloodstream infections (CR-BSI) has significant financial costs [2] and associated morbidity [3]. Guidelines recommend empirical systemic treatment with vancomycin and an aminoglycoside for suspected CR-BSI, when THC...
cannot be removed [4]. This regimen provides broad-spectrum cover for Gram-positive and Gram-negative pathogens.

Instillation of concentrated anti-microbial solutions (or ‘lock’; AML) into THC lumens after haemodialysis sessions, in conjunction with systemic antibiotics, may successfully treat CR-BSI and improve rates of catheter salvage [5]. The concentration of anti-microbials in AML exceeds the minimum inhibitory concentration (MIC) needed for bactericidal effect and probably eradicates colonized intra-luminal biofilm [6]. The United Kingdom Renal Association recommend using AML as prophylaxis against CR-BSI [7], as do other authors [8]. The strength of this recommendation, however, is weak because it is based upon evidence of moderate quality. The heterogeneity of previous studies means that the most effective antibiotic regimen remains unclear.

Anti-microbial-resistant organism prevalence increases with greater anti-microbial use [9]. Vancomycin use in haemodialysis patients is of concern because of an increasing prevalence of vancomycin-resistant enterococci (VRE) and vancomycin-resistant Staphylococcus aureus (VRSA) in haemodialysis patients [10]. Recently, reports of gentamicin resistance have emerged in haemodialysis patients receiving AML as prophylactic therapy against CR-BSI [11]. Resistant infections are harder to treat and, as such, have increased costs and morbidity [12]. Organisms resistant to one class of anti-microbial agents may also develop resistance to unrelated agents [13].

Most previous studies regarding AML use in THC focus on prevention of CR-BSI. Those studies assessing treatment efficacy have concentrated on catheter salvage and reduction of infection rates. There is a paucity of studies in the literature investigating the potential harmful effects of AML used in treating CR-BSI, with little work assessing whether their use promotes anti-microbial resistance in subsequent infections. The probability of promoting selective growth may be less with AML than with using systemic antibiotics alone because the concentration of antibiotics is many times higher than the MIC required [14].

Several studies have compared AML with anticoagulant lock controls in preventing CR-BSI, where subsequent CR-BSI were treated with systemic antibiotics. No resistant organisms were observed in some studies [15–17], whereas methicillin-resistant S. aureus (MRSA) was observed in the treatment group in others [18–20]. The follow-up period of each study is short. Although each study reports reduced CR-BSI, they merely compare rates of anti-microbial-resistant infections associated with antibiotic exposure. All patients with CR-BSI will receive systemic antibiotics and are already exposed to an increased risk of developing subsequent resistant organisms [12]. To determine the additional risk associated with AML, one should compare patients treated with systemic antibiotics alone with patients treated with systemic antibiotics and AML. There are, however, no randomized trials investigating this risk.

In 2004, our treatment policy for CR-BSI changed from a 2-week course of systemic vancomycin and gentamicin to adding an AML, containing vancomycin, gentamicin and heparin, in the inter-dialytic period during the 2-week period of treatment with the systemic antibiotics. The chemical stability of prolonged AML containing vancomycin, gentamicin and heparin has been confirmed [21]. The concentration of antibiotics in our AML far exceeds the MIC for the organisms responsible for CR-BSI in the 2003 cohort.

The primary aims of this retrospective observational cohort study are to establish an association between AML use as a treatment adjunct for CR-BSI and: (i) the incidence of CR-BSI and (ii) the incidence of anti-microbial resistance, in our haemodialysis population dialysing with THC. The study end points were (i) the need for removal of THC due to CR-BSI, (ii) relapse rates and (iii) culture of anti-microbial-resistant organisms.

**Materials and methods**

**Setting**

This study was undertaken in the South West Thames Renal and Transplantation Centre, based at St. Helier University Hospital, Carshalton, Surrey, UK, and its five regional satellite units. During the study period, our haemodialysis population increased from 573 patients on 1 April 2003 to 698 patients on 31 December 2006. The proportion of patients dialysing via THC decreased from 33.7% to 23.1% throughout the study period.

The THC (Permcath® or Tesio®) were inserted by senior nephrology trainees or consultants using sterile equipment, operator gowns, face masks and gloves. The skin was cleansed with chlorhexidine beforehand. Ultrasound guidance was used. The insertion sites were, in order of preference, right internal jugular vein, left internal jugular vein, right femoral vein and left femoral vein. Staff who handled THC during haemodialysis sessions used standard infection control procedures. Each THC was cleaned with 2% chlorhexidine and 70% alcohol wipes upon connecting to the haemodialysis machines. No additional prophylactic measures (e.g. intra-nasal mupirocin) were used. Haemodialysis was performed thrice weekly for a mean of 3.76 ± 0.34 h (SD).

**Data collection**

Data regarding CR-BSI have been collected prospectively, since 2003, at weekly meetings between hospital nephrology and microbiology staff. All blood cultures taken from patients receiving haemodialysis, the organism/s grown and anti-microbial sensitivities and resistances were discussed. To the best of our knowledge, data collection is complete, thus reducing the possibility of selection bias.

**Definitions**

CR-BSI was defined as a positive bacterial culture in blood associated with clinical and/or laboratory markers of infection (e.g. elevated C-reactive protein or leucocyte counts) [6]. ‘Treatment failure’ was defined as failure of pyrexia or laboratory markers of infection to improve within 48 h or culture of the same organism in the 2-week period following eradication therapy. ‘Contaminant’ was defined as culture of a skin commensal with no clinical or laboratory stigmata of infection following eradication therapy, providing that this was not the presenting organism. ‘Relapse’ was defined as a positive blood culture with the same organism occurring at any time in the life of the THC after the 2-week period following completion of eradication therapy.

**Anti-microbial techniques**

Blood cultures were taken peripherally and from the dialysis circuit. Historical controls, between April and December 2003, were treated with a 2-week course of intravenous vancomycin and gentamicin, calculated by body weight. The study group, between January 2004 and December 2006, was treated with the same regimen and an additional AML containing vancomycin (10 mg), gentamicin (8 mg) with heparin (5000 units/mL) added to the remaining volume in the THC lumens between each inter-dialytic period for 2 weeks. No other anti-microbials were used as AML. Systemic antibiotics were changed, and the AML stopped, if subsequent culture and sensitivity profiles suggested alternative anti-microbials were more appropriate. Patients were treated with 3-weeks antibiotics if the CR-BSI was due to S. aureus or 6 weeks if metastatic complications occurred. Eradication was confirmed by a negative blood culture and absence of clinical/laboratory markers of infection between 1 and 2 weeks after the end of the treatment period.
Participant selection

All positive blood cultures in patients dialysing via a THC were reviewed. Bacteraemia were excluded if from an alternative source (e.g. pneumonia) or if a contaminant was cultured in the post-eradication therapy sample. Treatment failures were not counted as new cases, whereas relapses were.

THC removal

THC were removed, if possible, and temporary non-cuffed catheters were used when clinically indicated: if mechanical failure occurred (i.e. blood flows < 250 mL/min or physical damage to the THC); when the THC were not needed (e.g. commencing another mode of renal replacement therapy or recovery of renal function) or if severe CR-BSI occurred (i.e. haemodynamic instability, treatment failure, relapse, if the CR-BSI was due to S. aureus or MRSA or if a metastatic complication had occurred).

Study variables

Positive blood cultures were categorized as Gram-positive organisms, Gram-negative or others. Gram-positive organisms were classified as vancomycin-sensitive or -resistant. Staphylococcus aureus was classified as sensitive or resistant to methicillin (MRSA). Gram-negative organisms were classified according to sensitivity or resistance to gentamicin, ciprofloxacin or both. Data were examined in two groups: the study group was treated with systemic antibiotics and an AML and a historical control group (treated with systemic antibiotics only).

Study size

The sample size needed in the study group to achieve 80% power with a statistical significance of 5% was calculated using the historical 2003 data as a baseline. To determine a 50% decrease in CR-BSI, 61 positive cultures were needed in the group treated with AML. The number of CR-BSI needed in the study group to demonstrate a 50% increase in the following resistant organisms was (i) overall anti-microbial resistance (n = 87), (ii) MRSA (n = 427), (iii) VRE (n = 1196), (iv) resistant Escherichia coli (n = 366), (v) resistant Pseudomonas (n = 49) and (vi) resistant Enterobacter species (n = 4672).

Ethics

Data were anonymized in accordance with South West London Research Ethics Committee guidelines. Informed consent was not obtained from individual participants because this was a retrospective review of previously collected and anonymized data.

Statistical methods

GraphPad QuickCals® (GraphPad Software, Inc.) was used for statistical calculations. Demographic data were compared using Fisher’s exact test; the t-test compared age. The chi-square test calculated changes in the prevalence of CR-BSI. Fisher’s exact test compared rates of relapse and antibiotic resistance. Relative risk (RR) and numbers needed to treat were calculated.

Results

Demographic details

Differences between the two populations studied are listed in Table 1. This shows no difference in age, gender, ethnic origin, primary renal diagnosis, THC insertion site or mean duration of catheter.

Number of participants and positive blood cultures

The number of study participants and description of positive blood cultures are summarized in Table 2. Following introduction of AML, the incidence of THC with CR-BSI significantly decreased, and continued to fall throughout the study period, reaching 2.16 episodes per 1000 catheter days in the final year of analysis. The proportion of THC removed due to CR-BSI and the proportion of relapses was less in the study group (Table 2). The RR of developing subsequent CR-BSI using AML was 0.50 ± 0.03 (P < 0.0001). 66.3% of controls developed CR-BSI, and 32% of the study group developed subsequent infections. The absolute risk reduction was 34 ± 4.2% [95% confidence interval (95% CI)]. The number needed to treat (NNT) to prevent subsequent CR-BSI with AML is 3 ± 4 (95% CI).

Anti-microbial-resistant organisms

The risk of developing further resistant infections when treated with an AML adjunct is RR = 1.07 (CI 0.27–4.75; P = 0.56). 19.6% of controls had a resistant organism and 21.5% of those treated with AML cultured a resistant organism. The absolute risk increase (ARI) is 1.85% (CI –3.15 to 6.85). The number needed to harm is 54—i.e. 1 in 54 patients with a CR-BSI will be subsequently infected with a resistant organism due to AML.

Gram-positive organisms

The range of Gram-positive organisms and antibiotic-resistant Gram-positive organisms is summarized in Table 3. The proportion of S. aureus increased, although the proportion of MRSA did not change. The proportion of Enterococci, the largest non-staphylococcal subgroup of Gram-positive organisms, did not change, nor did the proportion of VRE. No VRSA were identified. There was no statistically significant risk of developing vancomycin resistance or MRSA with AML (Table 4). The RR of developing a Gram-positive-resistant organism is 0.89 (95% CI 0.62–1.30; P = 0.57).

Gram-negative organisms

The range of antibiotic-sensitive and -resistant Gram-negative organisms is summarized in Table 3. A significant increase in gentamicin resistance was found overall. Subgroup analysis revealed gentamicin resistance in Enterobacter species. Increased ciprofloxacin resistance was observed (P = 0.04), particularly in Enterobacter species. There is a statistically significant risk associated with developing antibiotic resistance if Enterobacter is cultured. This finding is not observed with other Gram-negative species (Table 4). The RR of developing Gram-negative-resistant organisms is 1.60 (CI 1.18–2.18; P = 0.002).

Patients with acute kidney injury

The proportion of patients with acute kidney injury (AKI) developing CR-BSI in THC was lower than expected in both groups (P < 0.0001). In the control group, all relapses and CR-BSI requiring THC removal were in patients with chronic kidney disease (CKD); in the treatments group, three THC were removed in patients with AKI and no relapses occurred (Table 1). There was no difference in the proportion of MRSA occurring in patients with CKD and AKI in both groups, although less VRE and Gram-negative-resistant organisms were identified in patients with AKI (Table 3).

Discussion

Key findings

This study demonstrates a significant reduction in subsequent CR-BSI following adjunctive AML therapy; the incidence reduced by over 50%, and a significant reduction in the
The proportion of treatment failure or relapses was observed. Although the proportion of CR-BSI in the study group was still high at 3.80 episodes per 1000 catheter days, it had progressively decreased throughout the study period, reaching 2.16 episodes per 1000 catheter days in the final year of analysis. The NNT to prevent subsequent CR-BSI with AML is 3 ± 0.4. This is similar to the NNT of three observed in a meta-analysis where AML were used prophylactically [22]. Our study is the first to calculate the NNT where AML are used as part of treatment.

Our study demonstrates no overall increased risk of developing further resistant CR-BSI when treated with our AML adjunct. The ARI of the organism becoming resistant is non-significant. Our results show that the organisms subsequently cultured are, however, different in their antibiotic resistance profiles.

The proportion of Gram-positive cultures significantly increased in the study group, especially *S. aureus*. The proportion of Gram-negative cultures significantly decreased, although there was no change in the proportion of the commonest organisms. The proportion of Gram-positive and Gram-negative organisms appears to be reduced equally in a meta-analysis of studies where AML were used prophylactically [22]. This contrasts with our study, where an increased proportion of Gram-positive organisms was observed in the study group despite the fact that vancomycin was a constituent of our AML.

There was no significant change in the proportion of MRSA or VRE as a result of AML in our study. We found that if a Gram-positive organism is cultured following treatment with AML, the RR of antimicrobial resistance is not significant. No VRSA were isolated in either population.

Although the overall proportion of Gram-negative organisms decreased significantly, a significant increase in Gram-negative antibiotic-resistant organisms occurred following AML therapy. The RR of a Gram-negative organism developing

### Table 1. Demographic differences between the two study groups

<table>
<thead>
<tr>
<th>Details</th>
<th>Systemic antibiotics only (2003; 8 months), n = 265</th>
<th>Systemic antibiotics and AML (2004–2006; 36 months), n = 662</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>61.1% (162)</td>
<td>60.7% (402)</td>
<td>0.94</td>
</tr>
<tr>
<td>Age ± SD, years</td>
<td>63.8 ± 12.8</td>
<td>65.5 ± 15.7</td>
<td>0.12</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>72.9% (193)</td>
<td>71.0% (470)</td>
<td>0.63</td>
</tr>
<tr>
<td>Black</td>
<td>8.7% (23)</td>
<td>10.0% (66)</td>
<td>0.71</td>
</tr>
<tr>
<td>South Asian</td>
<td></td>
<td></td>
<td>0.90</td>
</tr>
<tr>
<td>Oriental</td>
<td>1.1% (3)</td>
<td>1.0% (7)</td>
<td>1.00</td>
</tr>
<tr>
<td>Other</td>
<td>7.9% (21)</td>
<td>8.0% (53)</td>
<td>1.00</td>
</tr>
<tr>
<td>Primary Renal Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>25.3 % (67)</td>
<td>24.2% (160)</td>
<td>0.80</td>
</tr>
<tr>
<td>GN</td>
<td>10.9% (29)</td>
<td>11.3% (75)</td>
<td>0.91</td>
</tr>
<tr>
<td>HTN/RVD</td>
<td>14.0% (37)</td>
<td>15.0% (99)</td>
<td>0.76</td>
</tr>
<tr>
<td>PCKD</td>
<td>4.2% (11)</td>
<td>4.5% (30)</td>
<td>0.86</td>
</tr>
<tr>
<td>PN</td>
<td>7.5% (20)</td>
<td>8.6% (57)</td>
<td>0.69</td>
</tr>
<tr>
<td>Unclear</td>
<td>18.9% (50)</td>
<td>18.1% (120)</td>
<td>0.78</td>
</tr>
<tr>
<td>Others</td>
<td>19.2% (51)</td>
<td>18.3% (121)</td>
<td>0.78</td>
</tr>
<tr>
<td>THC insertion site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RIJ/LIJ</td>
<td>93.6% (248)</td>
<td>94.3% (624)</td>
<td>0.56</td>
</tr>
<tr>
<td>Femoral</td>
<td>6.4 % (17)</td>
<td>5.7% (38)</td>
<td></td>
</tr>
<tr>
<td>Mean duration of catheter days (95% CI)</td>
<td>88.00 (80.30–95.69)</td>
<td>77.99 (65.33–90.65)</td>
<td>0.14</td>
</tr>
</tbody>
</table>

aNumbers in parentheses are raw data. P-values were calculated by Fisher’s exact test, except for age, where the t-test was used. GN = glomerulonephritis; HTN = hypertension; LIJ = left internal jugular vein; PCKD = polycystic kidney disease; PN = pyelonephritis; RIJ = right internal jugular vein; RVD = renovascular disease.

### Table 2. Number of trial participants, number of positive blood cultures and their subgroups

<table>
<thead>
<tr>
<th></th>
<th>Systemic antibiotics only (2003; 8 months)</th>
<th>Systemic antibiotics and antibiotic lock (2004–2006; 36 months)</th>
<th>Difference (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of THC</td>
<td>400</td>
<td>2057</td>
<td>0.79</td>
</tr>
<tr>
<td>CKD patients</td>
<td>318</td>
<td>1621</td>
<td></td>
</tr>
<tr>
<td>AKI patients</td>
<td>82 (20.5%)</td>
<td>436 (21.2%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total positive blood cultures</td>
<td>265</td>
<td>662</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CKD patients</td>
<td>258</td>
<td>617</td>
<td>0.84</td>
</tr>
<tr>
<td>AKI patients</td>
<td>7 (2.6%)</td>
<td>45 (6.8%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CR-BSI episodes per 1000 catheter days</td>
<td>8.50</td>
<td>3.80</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CR-BSI requiring THC removal, %</td>
<td>182 (68.7%)</td>
<td>213 (32.3%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Relapses</td>
<td>35 (13.2%)</td>
<td>45 (6.8%)</td>
<td>0.0027</td>
</tr>
<tr>
<td>Gram-positive</td>
<td>171 (64.5%)</td>
<td>504 (76.1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gram-negative</td>
<td>88 (33.2%)</td>
<td>154 (23.3%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fungi</td>
<td>6 (2.3%)</td>
<td>4 (0.6%)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

aFigures in parentheses are the percentage of total infections. P-values were calculated using Fisher’s exact test.
resistance is significant. An overall increase in gentamicin resistance was found in the study group; this was mainly accounted for by the increase in gentamicin-resistant *Enterobacter*. The RR of gentamicin resistance in the study group approaches significance and was mainly accounted for by the increase in antibiotic-resistant *Enterobacter*. Ciprofloxacin resistance significantly increased in the study group. This risk is increased for *Enterobacter* but not other Gram-negative species. A possible mechanism for these findings is that genetic mutation of the microbe occurs, altering the binding capacity of the anti-microbial to the microbe [13].

**Clinical implications**

Our study population was ethnically diverse, with similar distributions of age and primary renal disease to the range...
seen in many cities with large dialysis units. A significantly smaller proportion of patients with AKI developed CR-BSI with THC than patients with CKD. No firm conclusions can be made, however, because the majority of our patients with AKI received temporary non-cuffed catheters and were not included in our study. Further studies are needed because this population of patients may have a different susceptibility to infection [23].

Irreversible sensorineural hearing loss has been associated with aminoglycoside-containing AML [24]. The mechanisms involve leaking of the AML into the systemic circulation [25]. The NNT observed in our study and reduction in the incidence of CR-BSI by > 50% are similar to that in a meta-analysis [22] of prophylactic AML use. A potential advantage of using AML as a treatment adjunct, and not prophylactically, may be that similar improvements in rates of CR-BSI can be achieved, but with reduced exposure to antibiotics.

Although our study demonstrates no increased risk of developing subsequent CR-BSI with resistant organisms following treatment with AML, the risk is not completely eliminated. The most important predictor of early treatment failure of CR-BSI appears to be the organism responsible [26]. Our study shows increased prevalence of S. aureus and anti-microbial-resistant Enterobacter following AML therapy. Staphylococcus aureus CR-BSI is highly pathogenic [27] with 22% in-hospital mortality, rising to 32% at 90 days [28]. The odds ratio of mortality with MRSA is 2.6 (CI 1.4–4.9) [28]. 60% of CR-BSI due to S. aureus have an un-complicated course, however, 16% develop endocarditis or metastatic complications [29]. It is recommended that THC are removed if CR-BSI are due to S. aureus [30]. Enterobacter bacteraemia has a mortality of 5–20%, rising to 44% in those who develop endocarditis [31]. It seems logical that resistant Enterobacter will be harder to treat with consequent higher mortality.

The clinical cost of reduced CR-BSI needs to be weighted against the increased proportion of pathogenic organisms and less common Gram-negative organisms being subsequently cultured. Given the increased prevalence of S. aureus and resistant Enterobacter, there is a need for a trial directly comparing the effectiveness of AML with non-antibiotic locks (e.g. citrate) in reducing CR-BSI. Non-antibiotic locks do not promote antimicrobial resistance and may be more cost-effective.

**Limitations**

This is a single-centre study. Microbial profiles differ between centres [9]. It is possible that our study results are limited to the population of our individual centre. Controls and the study group are demographically similar. (Table 1). There are, however, a large percentage of patients with an unknown cause of renal failure in both groups. They are statistically similar, although the potential exists for mis-classification of, for example, diabetic nephropathy into one of the ‘unknown’ groups, which could result in a statistically and clinically significant difference.

The major limitation of our study is its retrospective nature. The data collection method and contemporary analysis were, however, robust enough to have not missed any data. Data were discussed between a panel of senior nephrologists and microbiologists, thus minimizing the risk of mis-classification. Controls and the study group were not treated contiguously and had follow-up periods of different durations; the changing antibiotic sensitivity/resistance profile in the study group may be due to unaddressed confounding factors within our study (e.g. a change in the microbial profile over time), rather than associated with treatment changes.

Systemic antibiotic concentrations were not measured. If the study population had a lower mean antibiotic concentration, a different sensitivity/resistance profile could have resulted with a MIC too low for our AML to exert its full anti-microbial effect. Our study is under powered to detect a significant increase in VRE. The risk is likely to be underestimated in our study, although VRE is presumed to be less pathogenic in patients with an intact immune system [32]. Our study demonstrates that ciprofloxacin resistance occurs following treatment with a vancomycin/gentamicin–AML, resistance to other antimicrobial agents potentially exists [13].

**Acknowledgements.** The authors thank the patients whose anonymous data were used in this study and Chris Kingswood and Carmel Keller, of Brighton and Sussex Medical School, East Sussex, UK, for reviewing aspects of this manuscript.

**Conflict of interest statement.** None declared.

**References**

Survival of elderly dialysis patients is predicted by both patient and practice characteristics

Celine Foote1, Toshiharu Ninomiya1, Martin Gallagher1,2, Vlado Perkovic1, Alan Cass1,3, Stephen P. McDonald4,5 and Meg Jardine1,2

1Renal and Metabolic Division, The George Institute for Global Health, Sydney, Australia, 2Renal Medicine, Concord General Repatriation Hospital, Sydney, Australia, 3Sydney Medical School, University of Sydney, Sydney, Australia, 4Australia and New Zealand Dialysis and Transplantation Registry (ANZDATA), Adelaide, Australia and 5Discipline of Medicine, University of Adelaide, Adelaide, Australia

Correspondence and offprint requests to: Meg Jardine; E-mail: mjardine@georgeinstitute.org.au

Abstract

Background. Increasing numbers of elderly patients face decisions about the management of end-stage kidney disease. Improved understanding of contemporary patient and practice factors influencing prognosis may assist decision making for individual patients and their care providers.

Methods. This is a prospective registry study using multi-variable proportional hazards models. A total of 1781 patients aged ≥75 years at dialysis initiation recorded in ANZDATA, the Australia and New Zealand renal replacement registry, between January 2002 and December 2005. The patient characteristics were demographic and comorbid conditions. The practice characteristics were late

doi: 10.1093/ndt/gfs096
Advance Access publication 7 May 2012