Interestingly, however, among the ‘low’ cardiovascular risk participants 7 had an elevated TnT and 35 had a normal TnT.

Although the numbers of patients are small, these data suggest that an elevated TnT in ‘low’ cardiovascular risk renal transplant recipients identifies a group who are at increased risk of all-cause mortality.

Undoubtedly, renal transplant recipients with high cardiovascular risk profiles should undergo aggressive risk-factor modification irrespective of their TnT level. However, the results of our study suggest that an elevated TnT level identifies a group of renal transplant recipients who are at increased risk of all-cause mortality and who may be overlooked if the risk assessment is based on the presence of traditional cardiovascular risk factors. TnT is a biochemical marker readily available in clinical practice that can enhance the current methods used to stratify risk in renal transplant recipients. An elevated TnT level can identify a subgroup of patients who may well benefit from more aggressive cardiovascular risk-factor modification.

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Letters
Advance Access publication 10 June 2008

Catheter locks, heparin and biofilm: what is the risk?

Sir,
Dr Onder’s work [1] once again demonstrates the efficacy of the value of antimicrobial catheter lock solutions (ALS) [2–6]; however, their work may add additional insight into the pathophysiology of biofilm. We have often speculated that the success of ALS over the traditional heparin lock might be possibly related to the fact that heparin itself may promote biofilm production [7] of most Staphylococcus through aiding quorum sensing [8]. If so, then the systemic heparin that flows through the catheter may also be a risk factor. We have recently evaluated risk factors for catheter-related sepsis (CRS) in 559 patients undergoing chronic maintenance haemodialysis and found that a prolonged duration of catheter use ($P < 0.0001$), a depressed serum albumin ($P < 0.001$), intravenous iron ($P = 0.001$) and a mid-treatment dose of heparin ($P = 0.046$) were the only variables that were associated with increased risk of sepsis (which was predominantly Staphylococcus, Table 1) [9]. While our data were not perfect, it may still lend some clinical evidence that the heparin itself is the risk factor for biofilm production and sepsis. The effect of heparin on biofilm, however, might vary for various strains of Staphylococcus. Onder’s work now suggests that such may not be the case, since elimination of heparin did not improve the successful eradication of sepsis but actually tended to decrease it.

Does this suggest that heparin may not be a pathologic factor? Perhaps, yet unlike most series of CRS, Staphylococcus aureus was relatively uncommon in Onder’s study and indeed only one case was assigned to the heparin arm. In contrast, both coagulase negative Staphylococcus and Enterobacter were four times as common infecting agents in the heparin arm as Staphylococcus aureus. Another investigator recently found that in vitro heparin caused detachment of Staphylococcus lugdunensis from catheter walls [10], which could theoretically either inhibit biofilm formation [11] or alternatively promote sepsis through systemic dispersal of biofilm [12]. The unusual distribution of bacterial pathogens in Dr Onder’s work may have therefore either distorted his results, or alternatively may have given us valuable insight into the lack of an effect heparin on CRS.

Editorial Note: Dr Onder et al. declined the opportunity to reply to this letter.

Conflict of interest statement. All authors have no conflicts of interest.

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Table 1. Organisms responsible for the catheter-related sepsis ($N = 141$) [7]

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number</th>
<th>% of total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>76</td>
<td>53.9</td>
</tr>
<tr>
<td>Methicillin resistant Staphylococcus aureus</td>
<td>20</td>
<td>14.2</td>
</tr>
<tr>
<td>Methicillin resistant Staphylococcus epidermidis</td>
<td>10</td>
<td>7.1</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>7</td>
<td>5.0</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>6</td>
<td>4.3</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>4</td>
<td>2.8</td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>3</td>
<td>2.1</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>3</td>
<td>2.1</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>2</td>
<td>1.4</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>2</td>
<td>1.4</td>
</tr>
<tr>
<td>Staphylococcus hemolyticus</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>Torulopsis glabrata</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>Versinia entercollitica</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>Corynibacterium jekium</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>Streptobacillus moniliformis</td>
<td>1</td>
<td>0.7</td>
</tr>
</tbody>
</table>
1. Onder AM, Chandar J, Simon N et al. Comparison of tissue plasmino-


4. Poole CV, Carlton D, Bimbo L et al. Treatment of catheter-related bac-


8. Shanks RM, Donegan NP, Graber ML et al. Heparin stimulates *Staphy-


11. Diskin CJ. Heparin, biofilm, and catheter-related sepsis. *Diagn Micro-
bioi Infect Dis* 2008

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Advance Access publication 13 June 2008

Reply to Dr S.C. Palmer and co-workers

We thank Dr Palmer and co-workers for their careful response to our Editorial Comments in the June issue of *NDT* [1] to their meta-analysis: ‘Vitamin D Compounds in Chronic Kidney Disease,’ published in *Ann Intern Med* 2007 [2].

1. We certainly do agree with Dr Palmer’s last remark in the reply on the need for further large-scale research on mineral and bone disorders in CKD, as also clearly stated in our Editorial Comments [1].

2. It now appears in their reply that some of the rather strong conclusions in their meta-analysis, which we opposed, are modified and less strongly promoted.

3. Both Dr Palmer and Dr M. Tonelli refer in their reply to our Editorial Comment to situations, where therapeutic replacement may be harmful and they both mention ‘e.g. oestrogen plus progestin after menopause.’ We do agree with that, but it is, however, not the correct clinical situation to use for comparison with vitamin D deficiency in uraemic patients, as neither calcitriol nor EPO replacement therapy of uraemic patients should be compared to pharmacological hormone replacement therapy for post-menopausal women. Vitamin D deficiency should rather be compared with hormone substitution therapy of ovariectomized young women.

4. As pointed out in our editorial, Dr Palmer et al. correctly mentioned in their meta-analysis a number of limitations to their study [2]. In spite of this, and in spite of the fact that none of the studies in the meta-analysis were either powered or designed to evaluate clinically relevant outcomes, such as mortality, Dr Palmer et al. continued to draw some rather powerful conclusions. In our opinion, their conclusions should have been much more moderate or maybe the authors should even have considered, whether the data in their meta-analysis were of too poor quality to warrant publication. It could instead have been turned into a Letter to the Editor and/or to the authorities stressing the need for good RCTs in this scientific field.

Reply to Dr M. Tonelli

We thank Dr Tonelli for his response to our critical editorial Comments [1] to his editorial on: ‘Vitamin D in patients with CKD: nothing new under the sun,’ published in *Ann Intern Med*, 2007 [3]. We do have some comments to Dr Tonelli’s response, which was published together with our Editorial Comments [1] in the June issue of *NDT*:

1. Unfortunately, and strangely, there is a world in between what Dr M. Tonelli and we consider as good scientific quality. From Dr Tonelli’s reply, it is clear that he only finds that scientific evidence exists, if proven by randomized controlled trials (RCTs), optimally supported by meta-analyses, while we also do accept the results of good clinical investigations and of well-performed experimental studies. Without such studies no ideas would be created that later could form the basis for subsequent RCTs. As such, we do accept the importance of RCTs and meta-analyses, but do not accept that ‘very little evidence exists to support or advocate for such unproven therapies in the absence of good quality evidence,’ [3] when dealing with the topic of vitamin D.

2. As mentioned above to Dr Palmer, neither calcitriol nor EPO therapy of uraemic patients should be compared with pharmacological hormone replacement therapy for post-menopausal women, but vitamin D deficiency should rather be compared with hormone substitution therapy of ovariectomized young women. We agree with Dr Tonelli that physiology and pathophysiology are difficult issues to perceive.

3. Of course it is not the call for RCTs that is characterized as ‘potentially dangerous’; we do agree with the need for more RCTs, as concluded in our editorial, but as also stated in our editorial [1], we strongly disagree with Dr Tonelli’s statement: ‘In the meantime, it is hard to argue strongly for the use of vitamin D in patients receiving dialysis’ [3], which means that until RCTs and meta-analyses are created, we should withhold