Author's response to reviews

Title: Bradycardia meets arteriosclerosis: oliguric acute kidney injury as main symptom resolved by pacemaker implantation.

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Author's response to reviews: see over
Re: Submission of a revised case report ("Bradycardia meets arteriosclerosis: oliguric acute kidney injury as main symptom resolved by pacemaker implantation")

Dear Prof. Kidd,

Thanks to all reviewers and editors for the review. We addressed all points (below). In addition, all changes can be traced in the manuscript (attachment). As a result, we resubmit a revised version of the case report and look forward to seeing it published soon.

1st Reviewer (nd):
The subject is an important one. In general, it was found that the publication of the article is suitable in the Journal of Medical Case Reports. The abstract gives an adequate picture of the entire report. The Introduction of the study is written clear. In this chapter, the sufficient literature data were given. The case design is appropriate and clearly explained. It was written well manner.
Thanks for the review. There is no issue that requires further clarification.

2nd Reviewer (raag)
The authors have attempted to demonstrate the link between the treatment of heart block and improvement in kidney function. Unfortunately I find the latter unconvincingly associated with the pacemaker insertion for the following reasons:

1. The cessation in oliguria seemed to occur prior to the insertion of pacemaker (table 1)
   Thanks for this comment. As Table 1 indicates, oliguria was resolved following cessation of beta-blocker treatment, i.e. before pacemaker insertion. This treatment effect is in line with bradycardia-related AKI. It is also stated in the text that rehydration did not alleviate AKI, that oliguria even occurred during intravenous rehydration: page 5, lines 5-8: “For suspected, however clinically inapparent hypovolemia, an intravenous fluid challenge using sterile saline was performed. Despite fluid challenge, oliguria suddenly developed shortly after admission,
serum creatinine remained high (Table 1), "Propanolol was discontinued at once, thereafter urine output improved (Table 1)."

To improve graspability and understanding, Conclusion Section was modified:

**Old (Page 7, lines 2-4):** "Creatinine did not further rise due to countermeasures taken including intravenous rehydration, pause of antihypertensive medication and pacemaker insertion."

**New (Page 7, lines 2-4):** "In fact, intravenous rehydration therapy did not improve oliguric AKI both in terms of diuresis or creatinine levels. However, cessation of beta-blocker treatment resolved oliguria. By discharge, antihypertensive medication was modified, i.e. the dose of spironolactone and amlodipine was reduced, torasemide and the ACE-inhibitor ramipril were introduced. Lastly, pacemaker insertion led to a long-term recovery of AKI as judged on laboratory findings, diuresis and overall condition."

### 2. Improvement in creatinine level also seemed to have occurred prior to the pacemaker insertion.

We respectfully disagree. Serum creatinine ameliorated more slowly during the index hospitalization (on admission: 200 µmol/l, by discharge: 162 µmol/l). There was no clear tendency regarding serum creatinine prior to pacemaker implantation or cessation of propanolol, given the cut-off used for definition of 1st-degree AKI (26.5 µmol/l or 0.3 g/dl). As discussed in the Conclusion section, oliguria is more sensitive for AKI diagnosis than the observed rise in serum creatinine. As long as an AKI is not long-standing leading to acute tubular necrosis, it is fair to assume that resolution of oliguria precedes a fall in serum creatinine during AKI recovery.

### 2. Unclear of the indication for so many antihypertensive drugs which may be Nephrotoxic like ACE-I, spironolactone and diuretics in a patient with resolving AKI.

Clearly, as stated in the Case Presentation, antihypertensive medication at admission and at discharge was nearly equipotent: ramipril (5 mg/d) and torasemide (20 mg/d) were added at discharge, beta-blocker was reinstated before discharge after pacemaker implant (original dosage), both spironolactone and amlodipine were maintained at a lower dose. Specifically, ACE-inhibitor ramipril was not prescribed prior to index hospital admission. Therefore, nephrotoxic effects conveyed by ACE inhibitors are not applicable. As antihypertensive medication was prescribed for at least 2 years without change, drug-induced AKI as a whole is unlikely. During the 4 months follow-up after pacemaker implant, however, antihypertensive medication was reduced which is attributed to the resolution of (repeat) AKI.

### 3. The language used need to be improved to ease understanding of the manuscript.

Efforts have been taken to improve understanding and readability. Changes can be traced in the manuscript attachment.

All authors read and approved the revised manuscript.
Kind regards,

Rainer U. Pliquett, MD