

Dear Editors,

Thank you very much for careful evaluation of our manuscript. According to the suggestions by reviewers, we made substantial modifications which are highlighted in red. I hope our manuscript is now improved and suitable for publication.

Sincerely yours

Masashi Suzuki

Modified points:

1. We modified “Belgium” to “Denmark” (page 4, line 12).
2. We modified the explanation about the flow of the paper in “INTRODUCTION” section (page 5, line 17-20).
3. We added the explanation about bacteremia and mortality in Japanese hemodialysis patients (page 6, line 7-22)
4. We changed “CAUSATIVE ORGANISM” to “CAUSATIVE ORGANISMS” (page 6, line 24).
5. We summarized about causative organisms in new Table1 (page 20) and modified to reduce the sentences in “CAUSATIVE ORGANISMS” section (page 7, line 1-20).
6. We changed the title of section “SITES OF INFECTION” to “CAUSES OF BACTEREMIA” (page 7, line 22).
7. We added the explanation of the incidence compared in catheter and arteriovenous fistula and graft in “RISK FACTORS” section (page 8, line 14-20).
8. We added “Antibiotics/antiseptics coated catheters” section (page 11, line 8-11).
9. We added the detail of treatment (page 11, line 15-20).
10. We corrected the title of a reference (page 14, line 5, 6).
11. We corrected the name of an author in references (page 14, line 23, 27).
12. We corrected the name of a journal in references (page 18, line 36).
13. We added Table 1-3 (page 20-21) and Figure 1 (page 23), and changed old Table 1 to Table 4 (page 22).

Reviewer 0050659

Thank you very much for your detailed and kind comments.

1. Thanks for the efforts on this manuscript.
2. Bacteremia in a dialysis patient is a big topic and challenging to cover in a minireview. Perhaps you would be better off focusing on catheter related BSI or something more focused

We appreciate your comment on this point. Catheter related blood stream infection (CRBSI) is the most common and unique feature in hemodialysis patients. However, CRBSI is about 20-30% of causes of bacteremia and other blood accesses including arteriovenous graft and fistula are also important, as you recommended in the 5th comment. And bacteremia in patients with arteriovenous graft and fistula is especially important in the countries that the prevalence of catheter is low, such as in Japan. So we described on the general feature of bacteremia and then discussed the catheter related bacteremia, as a unique feature of bacteremia in hemodialysis patients.

3. Please utilize tables to focus the readers. You could have a table on the drugs and dosing for Locke therapy. You could have a table on the bugs and a few recommendations for therapy. But with limited verbage in a minireview, tables and figures are helpful

We summarized about therapy and antibiotics in Table2, 3 (page 21) and Figure 1 (page 23).

4. I understand you submitted this to the world journal, but your epi data is all over the place which makes it hard for the user to relate to. Not sure that can be fixed, it is just a comment

Thank you for your comments.

5. Under incidence, is there data on HD catheters v fistulas v grafts?

We added the explanation of the incidence compared in catheter and arteriovenous fistula and graft in “Risk factors” section (page 8, line 14-20).

6. Causative organisms could be listed in table format and thus provide more room for expanding other sections

We summarized them in Table 1 (page 20) and reduce the sentences in “causative organisms” section (page 7, line 1-20).

7. Sites of infection....that is not related to bacteremia. I don't think that section fits in the manuscript. You have a few lines discussing BSI and vascular access infection, the the first sections really offer nothing to the paper

Sites of infection stands for causes of bacteremia. We thought that it was important to recognize bacteremia in hemodialysis patients. We changed the title of the section to “causes of bacteremia” (page 7, line 22).

8. I do not get the flow of the paper.....you discuss bacteremia then focus on catheter related BSI's. This makes the paper seem unfocused, would honestly suggest focusing on CRBSI since you are limited in space with a minireview

We described on the general feature of bacteremia and then discussed the catheter related bacteremia, as a unique feature of bacteremia in hemodialysis patients. We added the explanation about the flow of the paper in “INTRODUCTION” section (page 5, line 17-20).

9. Locke therapy is always challenging. Please provide specific dosing recommendations, likely in table format

We summarized them in Table 2 (page 21).

10. I would also provide contraindications to locke therapy and more information on when it will not work

We added the contraindications and the case that does not work, i.e. the cases to require catheter removal in “Treatment of catheter related bacteremia” section (page 11, line 15-20) and Figure 1 (page 23).

11. Any comments on antibiotic impregnated catheters?

We added “Antibiotics/antiseptics coated catheters” section (page 11, line 8-11).

12. Should treatment be broken down into antibiotic management and catheter management?

Generally, the treatment of bacteremia is systemic antibiotic therapy, other than the cases to need drainage or debridement. However catheter management in addition to systemic antibiotics is important in hemodialysis patients using catheter especially in cases the catheter removal is difficult. They should be done together although we described them separately. We described the detail of antibiotics and catheter management in the “Treatment of catheter related bacteremia” section (page 11, line 15-20) and Figure 1 (page 23) and Table 2 and 3 (page 21).

13. Please discuss indications for HD cath removal in more detail. You have about 2 sentences without a lot of details.

We added the explanation of catheter removal in “Treatment of catheter related bacteremia” section (page 11, line 15-20) and Figure 1 (page 23).

14. Reference 2 says "chapter 2" but is in reference to a journal. I think tha needs fixed

We corrected the reference (page 14, line 5, 6).

Reviewer 28383

Thank you very much for your kind comments.

I was expecting to know more about this problem in Japanese hemodialysis population, rather than the international literature

We added the information in “INCIDENCE OF BACTEREMIA IN HEMODIALYSIS PATIENTS” section (page 6, line 7-15).

2- You have in Japan the best hemodialysis survival, how much this is affected by infections

We added the information in “INCIDENCE OF BACTEREMIA IN HEMODIALYSIS PATIENTS” section (page 6, line 16-22).

3- You did not give details about CRBSI management, like empirical AB therapy, duration of therapy, ext...

We added about the therapy of CRBSI in “Treatment of catheter related bacteremia” section (page 11, line 15-20) and Table 2, 3 (page 22) and Figure 1 (page 23).

4- Reference number 7 was mentioned in the introduction as Belgium study, and then as a Danish study

We corrected it (page 4, line 12).

Reviewer 28383

Thank you very much for your kind comments. We corrected all the points according to your suggestion.

The authors comprehensively reviewed clinical and bacteriological features of bacteremia in hemodialysis patients. The paper is well-written and provides valuable information regarding this field. Some points should be revised.

1. page 4, line 19: This cohort study was done in Denmark, not in Belgium.

We corrected it (page 4, line 12).

2. page 5, line 14: “ORGANISM” should be changed to “ORGANISMS”

We corrected it (page 6, line 24).

3. page 13, line 6: “American Journal of Kidney Diseases” should be changed to “Am J Kidney Dis”

We corrected it (page 14, line 6).

4. page 14, line 2: “Sogaard OSs” should be changed to “Sogaard OS”

We corrected it (page 14, line 23, 27).

5. page 19, line 23: “Bmj” should be changed to “BMJ”

We corrected it (page 18, line 36).