Author’s response to reviews

Title: Unilateral pedal lymphangiography plus computed tomography angiography for location of persistent idiopathic chyle leakage not detectable by ordinary contrast computed tomography

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Author’s response to reviewers:

Responses to Reviewers:
Dear editor:

I am very grateful for the comments from two reviewers. We revised the manuscript in accordance with the reviewers’ comments, and carefully proof-read the manuscript. Here below
is our reply according to the reviewers’ comments. We really appreciate if you accept our manuscript for publication.

Best regards.

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1. Hans Heinzer (Reviewer 1):

   ① The authors present an interesting diagnostic tool for a rare disease. My main concern is the low number of patients and the missing control group. The success rate by 100% is notable. The question is not answered by the data, if this is due to the sensitivity of the diagnostic tool or would surgery alone lead to the same results.

   Thank you for your careful review of our manuscript. The patient number is limited because of idiopathic chyluria is a rare disease in recent years. Thus randomized controlled study is not available.

   Successful rate of 100% may be related to accurate location of chyle leaks by LPG + CTA, probably also due to the limited patient number.

2. Panagiotis Kallidonis (Reviewer 2):

   The authors present any interesting study aiming to evaluate the efficacy of unilateral pedal lymphangiography in conjunction with CT angiography. The number of patients is high considering the rarity of the condition. The approach seems to be efficient in detecting and guiding the surgery. Nevertheless, some issues were raised while studying the manuscript.

   ① When the authors are referring to the method of cystoscopy they should refer to "cystoscopy" and not "cystoscope". Please correct the term in the text and abstract. Although I am not native English speaking myself, the authors should consider revising the manuscript with the aid of a native English speaking person. There are numerous expression errors.
Thank you for your careful work. According to your comment, we have corrected this mistake through the whole manuscript. Furthermore, we have had the manuscript polished with professional language editing.

② Patients and methods

Patients:

What was the nature of the current study? Retrospective or prospective? If the study is prospective, did the authors consider to do sample size calculation? Would it be possible with the available evidence in the literature?

Actually, it’s a retrospective study, because idiopathic chyluria is a rare disease. We have collected all patients available in 5 years and we are still anticipating a bigger sample size.

③ The authors should be clear in the evaluation that was done and concluded to the final diagnosis of "idiopathic" chyluria. In example, were any tumors excluded?

As mentioned in the manuscript, detectable etiologies such as thoracic duct stenosis, tuberculosis, cancer or tumor, trauma, pregnancy, filariasis were ruled out through the whole study. （Patients section, line 7, page 3）

④ The performance of "renal pelvic instillation" should be explained.

The renal pelvic instillation was taken via retrograde ureteral perfusion. We had added this in manuscript (Patients section, line 8, page 3).

⑤ Sclerotherapy as a treatment option would be more accurate to be supported by an appropriate publication.

Sclerotherapy has been used in clinical practice for years. We had added an appropriate publication (Discussion section, line 3, page 5, References 8).

⑥ It is important to present the population as accurately as possible since the decision of clinician to follow the suggestions of the authors is based on the ability to select the appropriate patients.
It is not clear why endoscopy of the upper tract did not take place. In the time of endourology, a flexible renoureteroscopy could provide information on the side of the chyluria and exclude conditions such as tumors. Especially in the case of patients with hematuria were included in the study.

Thank you for your valuable advice. Flexible renoureteroscopy is a good examination choice for the upper urinary tract disease. However, it was not available at the beginning of the present study.

Moreover, flexible renoureteroscopy needs general anesthesia and sometimes it is difficult to observe the occurrence of chyluria when the chyle urine was not obvious.

For patients with hematuria, flexible renoureteroscopy is necessary to exclude other disease such as tumors. But we arrange this examination after LPG+CTA in consideration of its invasiveness and cost.

In our opinion, LPG+CTA could be a priority choice for chyluria patients.

7 Lymphangiography technique:

Were the patients sedated for the performance of the approach?

Local subcutaneous anesthesia was performed on the foot before lymphangiography with no sedation.

8 Follow-up treatment:

What approach was selected to do the renal lymphatic stripping and ligation? Laparoscopy? Did the surgeons prepare the kidney? Please be more specific.

Surgical approach was decided according to the patient's condition, and both laparoscopy (4 cases) and open surgery (14 cases) were performed. (Surgical treatment section, line 2-3, page 4)

We removed all perirenal fatty tissue with ligation or stripping of all visible lymphatic ducts.

9 Results:

Please provide in table 1 the statistical test that was used.
Qualitative variables were compared using the $\chi^2$ test. P-values < 0.05 considered statistically significant. The statistical analysis was performed with SPSS 20.0 (SPSS Inc., Chicago, IL, USA).

Table 2 is not accurate since the presence of "+" or a number of "+" is not supported by the current investigation. The authors could be more descriptive in the table in order to provide the appropriate information to the reader. Reference to the literature could also be useful. Otherwise, the table is more or less not accurate.

Thank you for your instructive suggestions. Table 2 has been corrected according to your comments. Y and N represent for positive and negative results in our study. (Table 2)

Discussion:
"Actually, the radiation exposure was more in LPG + CTA than LPG alone (Table 2)." Did the authors measure the radiation exposure? Table 2 does not provide any specific information. Please rephrase.

The exact amount of radiation exposure was difficult to measure. But the LPG + CTA contains two radioactive examinations, it is obviously that the radiation exposure was more than LPG or CT alone. We have modified the Table 2 to make it more accurate. (Table 2)

Conclusion:
The conclusion should provide a summary of the findings of the study. The current conclusion states that presented approach could replace LPG. My impression is that the authors provided an interesting approach which seems to be effective (and more effective than the common approaches) in detecting the sites of the lymphatics that may be related to chyluria. More extensive research would provide the evidence for the establishment of the approach.

Our previous conclusion may not be convincing enough because of the limited patient number. So we have rewritten the conclusion. (Conclusion section, line 3, page 7) Hopefully it is adequate.