

**World Journal of Cardiology – Manuscript No. 50340**  
**Response to reviewers' comments**

We thank the reviewers and the editor for their appreciation of our work, their thorough assessment of our manuscript and the encouraging comments how to improve the manuscript.

Our responses to the reviewers' comments are indicated below and all corresponding changes in the manuscript are highlighted in [blue](#).

**Editor's comments:**

Comment 1: The language of the manuscript is not so good. A Non-Native Speakers of English Editing Certificate is required. We will reject the manuscript if it is not provided.

Response: We have submitted the certificate of Ms. Carole Cürten, who has, as stated in the *Acknowledgments* section, done the English language revision of the manuscript.

Comment 2: In order to attract readers to read your full-text article, we request that the author make an audio file describing your final core tip, it is necessary for final acceptance. Please refer to Instruction to authors on our website or attached Format for detailed information. The accepted formats are mp3 or wma.

Response: We have recorded and submitted the core tip as an audio file, as requested.

Comment 3: Please read these four important guidelines carefully and modify your figure(s) accordingly: First, all submitted figures, including the text contained within the figures, must be editable. Please provide the text in your figure(s) in text boxes. Second, for line drawings that were automatically generated with software, please provide the labels/values of the ordinate and abscissa in text boxes. Third, please prepare and arrange the figures using PowerPoint to ensure that all graphs or text portions can be reprocessed by the editor. Fourth, in consideration of color-blind readers, please avoid using red and green for contrast in vector graphics or images. For pictures with multiple parts, please create text box in the upper left corner with uppercase letters A, B, etc.; please use SmartArt, text box and shape to draw the flowchart directly in PowerPoint.

Response: As requested, we have revised the figures according to the guidelines and have now submitted the figures as editable PowerPoint files.

Comment 4: Please provide the author contributions. See the format in the attachment file-revision policies. The format of this section should be like this:

Author contributions: Wang CL and Liang L contributed equally to this work; Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed research; Wang CL, Zou CC, Hong F and Wu XM performed research; Xue Jz and Lu JR contributed new reagents/analytic tools; Wang CL, Liang L and Fu JF analyzed data; and Wang CL, Liang L and Fu JF wrote the paper.

Response: We have provided the author contributions in the requested format in the manuscript.

Comment 5: Please revise the manuscript according to the review report and my comments. And answer all of the reviewers' comments carefully (point-to-point).

Response: We have revised the manuscript accordingly. The point-by-point answers to the reviewer's comments can be found below.

Comment 6: Please provide all authors abbreviation names and manuscript title here. The abbreviation names should be the same as the copyright. World J Cardiology 2019; In press.

Response: We have included the abbreviated authors' names and title under the abstract section as requested.

Comment 7: Under the heading of Case Presentation, the following seven aspects must be presented in this order: 1) Chief complaints; 2) History of present illness; 3) History of past illness; 4) Personal and family history; 5) Physical examination upon admission; 6) Laboratory examinations—e.g., routine blood tests, routine urine tests and urinary sediment examination, routine fecal tests and occult blood test, blood biochemistry, immune indexes, and infection indexes; and 7) Imaging examinations—e.g., ultrasound, plain abdominal and pelvic CT scan, high-resolution chest CT scan, and head MRI. The patient case presentation should be descriptive, organized chronologically, accurate, salient, and presented in a narrative form. Please change the main body of the case report to the following format.

Response: We have changed the case presentation to meet these formal requirements (changes in the manuscript highlighted in blue).

Comment 8: Please provide the decomposable figure of Figures, whose parts are movable and editable. So you can put the original pictures in PPT and submit it in the system.

Response: See response to the editor's comment 3).

Comment 8: Please check and confirm that there are no repeated references! Please add PubMed citation numbers (PMID NOT PMCID) and DOI citation to the reference list and list all authors. Please revise throughout. The author should provide the first page of the paper without PMID and DOI. PMID (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed>) (Please begin with PMID:) DOI (<http://www.crossref.org/SimpleTextQuery/>) (Please begin with DOI: 10.\*\*) for example:

English-language journal articles (list all authors and include the PMID and DOI, where applicable):

1 Ma L, Chua MS, Andrisani O, So S. Epigenetics in hepatocellular carcinoma: An update and future therapy perspectives. World J Gastroenterol 2014; 20: 333-345 [PMID: 24574704 DOI: 10.3748/wjg.v20.i2.333]

Coding system: The author should number the references in Arabic numerals according to the citation order in the text. The reference numbers will be superscripted in square brackets at the end of the sentence with the citation content or after the cited author's name, with no spaces. For example, "Crohn's disease (CD) is associated with increased intestinal permeability<sup>[1,2]</sup>." If references are cited directly in the text, they should be included with the direct citation content within the text; for example, "From references<sup>[19,22-24]</sup>, we know that...". Before submitting your manuscript, please ensure that the order of citations in the text is the same as in the references section, and also ensure the spelling accuracy of the authors' names. Do not list the same citation twice (i.e., with two different numbers)

Response: We confirm that there are no repeated references in the manuscript. PMID and DOI have been added for all references, where available.

## **Reviewers' comments:**

### Reviewer no. 00227375:

This is a rare case report about the left recurrent laryngeal nerve palsy after aortic arch stenting. This manuscript is nicely structured and well written. I have no questions about this manuscript.

Response: We thank the reviewer for the support regarding our manuscript.

### Reviewer no. 02565578:

Cardiologists are familiar with the Ortner syndrome, which consists in the vocal cord paralysis resulting from the compression of the left recurrent laryngeal nerve by abnormal mediastinal vascular structures, most commonly aortic aneurysm. It is reported extensively in literature. Cardiac surgeons are well aware of the possible complication of the aneurysm or coarctation open repair. And even if "the nerve is generally easily visualized, as is the vagus nerve from which it branches, and injury to both nerves should be assiduously avoided" (Jaquiss RDB. Operative Techniques in Thoracic and Cardiovascular Surgery, 2002;7:2-10), there are numerous case reports describing left recurrent laryngeal nerve injury following these interventions. The present case involves a damage to the same nerve in the same location, but as a complication of a different kind of procedure. Indeed, in the discussion of their case, the Authors focused on the catheterization and stenting, avoiding lengthy and unnecessary references to other procedures and resulting complications. The increased risk of vocal cord paralysis in stenting was previously suggested by Ohta et al. (J Vasc Surg.2007;45:866) who concluded that "even the latest surgical techniques in aortic arch surgery [i.e., stent graft placement or balloon angioplasty] have not eliminated the high risk of surgical vocal cord paralysis." In particular, the ADDITIONAL balloon angioplasty for a stenosed aortic graft were independent risk factors for this complication. These retrospective observations share some similarities with the present case and could be mentioned by the authors. Overall, the case is well presented, the report is very informative and merits publication.

Response: We thank the reviewer for these important comments. We agree that the identification of additional balloon angioplasty of aortic grafts as an independent predictor of LRLN palsy reported after surgical stent-graft placement by Ohta et al. is very much in line with the findings in our patient, as not only the implantation of the second stent, but also the (re-)dilation of the stents may have led to vocal cord palsy. We have included this report in our discussion, which now reads as follows:

[...] We suggest that, due to the course of the LRLN as it passes underneath the aortic arch in close proximity to the pulmonary artery and the ligamentum arteriosum, stent implantation in a severely hypoplastic aortic arch may either stretch the LRLN as the transverse aortic diameter increases, or compress it between the aortic arch and the pulmonary artery, thereby leading to LRLN damage and left vocal cord paresis. Moreover, after surgical aortic stent-graft placement, additional dilation of the graft is a known independent predictor of LRLN palsy <sup>[14]</sup>. Therefore, (re-)dilation of the stents in our patient may also have played a significant role in her having developed post-interventional LRLN palsy. [...]

### Reviewer no. 03722832:

It is an interesting case report but revision is must the following clarification: 1. Language editing. 2. Provide the angles of projection for each angiographic image. 3. 2nd balloon and 2nd stent not visible. 4. Why did author selected such relatively short diameter and short length stent which migrated distally? 5. Provide clear image to left common carotid and left subclavian artery. 6. Provide the CT and MRI before and after procedure to justify your claim. 7. Did author do video recording of LLNP, please provide.

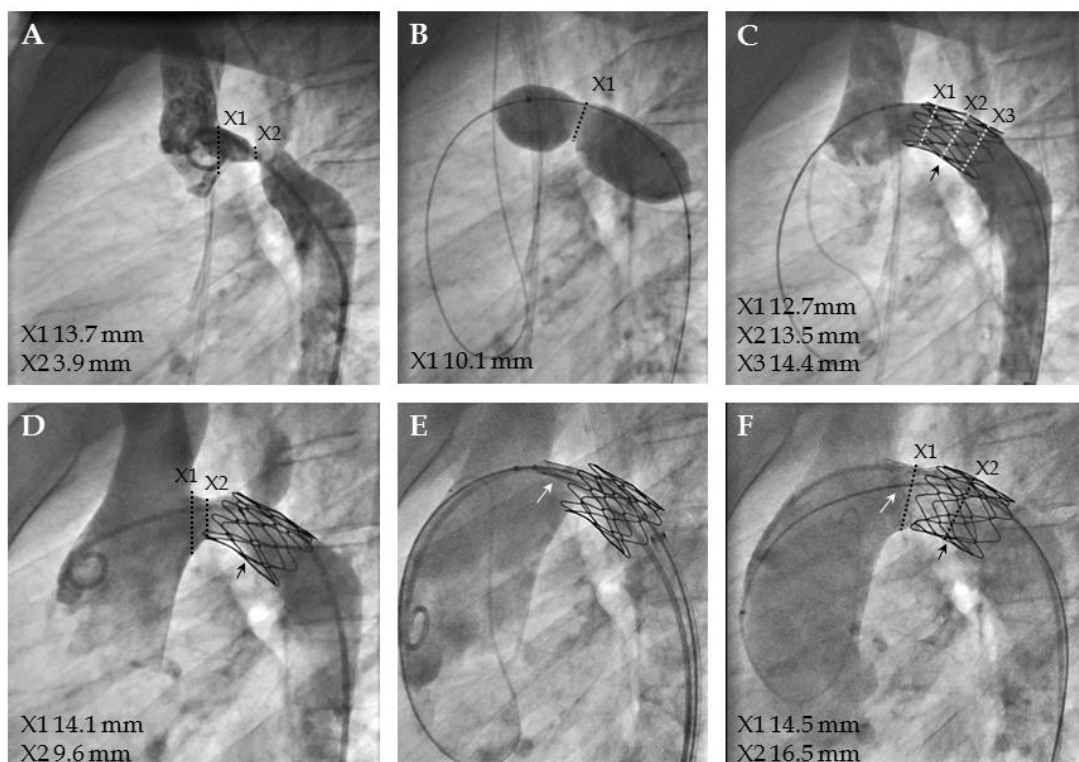
Response: We thank the reviewer for raising these issues. We have answered the seven points separately below.

1. Language editing has been done by us and by Ms. Cürten (see submitted certificate).

2. The angles of projection for Fig. 1 have been added to the figure legend, which now reads as follows:

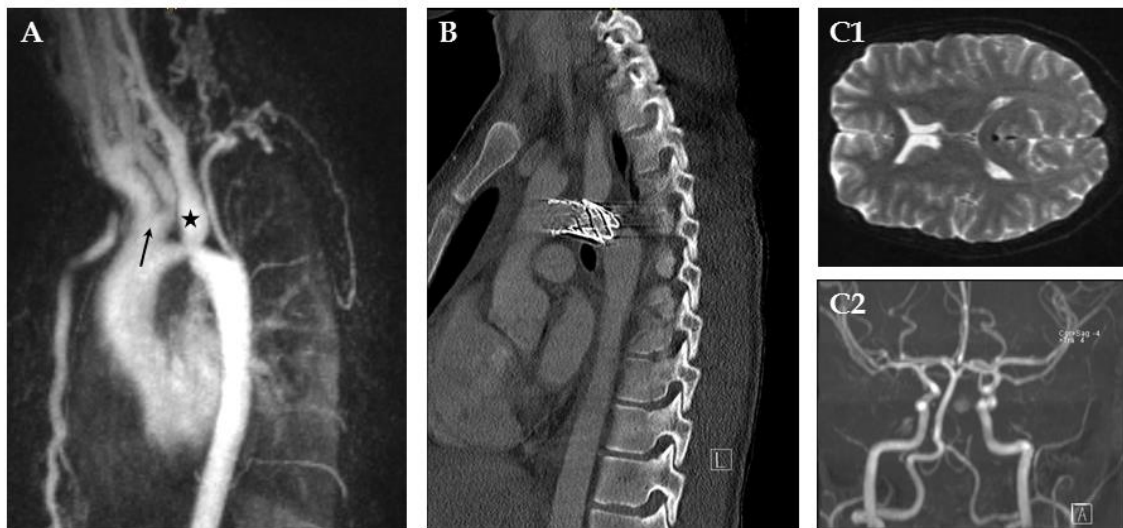
Figure 1: Angiograms in lateral projection (all images, LAO 90°) demonstrating pre-, intra- and post-interventional findings. A) Left aortic arch with bi-carotid trunc and transverse arch hypoplasia with severe native stenosis just proximal to origin of the left subclavian artery. B) Balloon interrogation using an 18 mm Tyshak II that unmasks a relatively high compliance of the stenosis. C) After implantation of a 22 mm CP stent (indicated by black arrow) on 14 mm BiB. D) Re-stenosis proximal of the previously implanted CP stent on follow-up. E) Positioning and implantation of a LD Max 26 mm stent (indicated by white arrow) over the re-stenosis. F) Final result following redilation of both stents with 16 mm Atlas balloon, and proximal stent flaring with 20 mm Cristal balloon.

3. The LD Max stent on the balloon in Fig. 1E and the unfolded stent in Fig. 1F have been indicated with a white arrow. Additionally, the distance measurement previously labelled "X1" in Fig. 1F has been removed for improved visibility of the LD Max stent. The revised Fig. 1 now looks like this:



4. We expanded the bare metal CP stent to the diameter of the aorta surrounding the coarctation, as recommended in the literature (see ref. 6, Gewillig et al. 2012). Especially in the case of a very circumscribed and severe stenosis as presented here, this approach should usually anchor the stent sufficiently while avoiding damage to the vessel itself. That the stent migrated is unusual and was not anticipated. The length of the stent was selected so as to clearly cover the localized stenosis without overstenting the bi-carotid trunc, which may lead to severe complications and should therefore be avoided (Gewillig et al. 2012). Moreover, a longer stent would also induce remodelling incl. reduced elasticity in a larger area of the aortic wall, which could possibly have negative effects for our young patient in the future. Finally, we were not able to avoid stenting over a longer stretch of the aorta, however, we initially tried to avoid this due to the reasons mentioned above.

5. and 6. We have added Suppl. Fig. 1 to show the pre-interventional anatomy with the bi-carotid trunc and the left subclavian artery more clearly, and the post-interventional findings ruling out additional thoracic and intracranial pathologies, as requested.



**Suppl. Fig. 1:** A) Cardiac MRI with hypoplastic native aortic arch and bi-carotid trunk (arrow) with severe stenosis just proximal to the left subclavian artery (star). B) Post-interventional CT-Scan ruling out aortic aneurysm, dissection, hematoma, and thoracic tumour formation. C1 and C2) Post-interventional MRI incl. MR-angiogram ruling out an intracranial pathology such as stroke or tumour.

7. Unfortunately, there is no video of the laryngoscopy demonstrating the left vocal cord palsy available.



**Response to reviewer's comments**

We thank the reviewer for the appreciation of our work, the thorough assessment of our manuscript and the encouraging comments on how to improve the manuscript. Our responses to the reviewer's comments are indicated below and all corresponding changes in the manuscript are highlighted in blue.

**Reviewer's comments:**

*Reviewer's code:* 01293596

*Position:* Editorial Board

*Academic degree:* PhD

*Professional title:* Professor

*Reviewer's country:* Japan

Fürniss et al. demonstrated an interesting case of left recurrent laryngeal nerve (LRLN) palsy after stenting to the aortic arch stenosis. The palsy was a very rare complication of the stenting and in the present case it was fortunately transient.

1. I think the migration of initial CP stent and overlap with the second stent might cause over-dilatation of aortic arch, resulting in LRLN stretch or injury. The authors should discuss more regarding why this rare complication occurred, and describe the points that operators should be careful for aortic arch stenting (e.g. stent diameter, pressure of post dilatation or overlap of stents).

We thank the reviewer for this important comment. As discussed in the manuscript, either stent placement itself, or re-dilatation of the stents with proximal flaring may have led to left recurrent laryngeal nerve (LRLN) palsy. However, which of these aspects was more important in the pathomechanism is not known. The overlap of stents may of course have played a role, however, as the stent material is very thin, we consider this to be less probable.

The discussion of the pathomechanism of LRLN injury reads as follows:

[...] We suggest that, due to the course of the LRLN as it passes underneath the aortic arch in close proximity to the pulmonary artery and the ligamentum arteriosum, stent implantation in a severely hypoplastic aortic arch may either stretch the LRLN as the transverse aortic diameter increases, or compress it between the aortic arch and the pulmonary artery, thereby leading to LRLN damage and left vocal cord paresis.

Moreover, after surgical aortic stent-graft placement, additional dilation of the graft is a known independent predictor of LRLN palsy[14]. Therefore, (re-)dilation of the stents in our patient may also have played a significant role in her having developed post-intervention LRLN palsy. [...]

2. The reason why the LRLN palsy improved after follow up should also be discussed. I wonder whether the stent diameter decreased after the follow up. The authors should mention the findings of aortography and/or laryngoscopy after the follow up if they were re-evaluated.

We thank the reviewer for pointing out this aspect. Echocardiographic follow-up has not shown any indication of stent diameter decrease until now. We assume that LRLN palsy improved due to either growth of the nerve to accommodate the larger aortic diameter or cessation of inflammatory reaction and edema. There was no clinical need to perform re-aortography (with the concomitant radiation exposure) or laryngoscopy.

The discussion about LRLN recovery now reads thus:

[...] Our patient recovered relatively quickly, most likely due to either nerve growth to accommodate the larger aortic diameter, or due to cessation of an inflammatory reaction or edema following either stretch or compression of the nerve. Contrary to this positive clinical course in our patient, previous reports of LRLN after endovascular therapy of patent ductus arteriosus or left pulmonary artery stenosis have documented persistent vocal cord paralysis after six months in over 50% of patients<sup>[8-12]</sup>. However, other than the case by Javois and colleagues, who described coughing after their patient drank water<sup>[12]</sup>, there were no previously reported symptoms of LRLN palsy other than hoarseness after transcatheter interventions<sup>[8-11]</sup>. Presumably due to these relatively mild clinical presentations neither medical therapy nor surgical device removal was performed in any of the cases. Therefore, it remains unclear whether in the case of acute LRLN palsy after aortic arch stent implantation, the administration of medication or decompression of the nerve by surgical stent removal would lead to LRLN recovery. [...]

3. Figure 2 just repeated the contents of manuscript. Is it necessary?

We agree that Figure 2 repeats the contents of the manuscript. However, the World Journal of Cardiology requests adherence to the CARE Checklist, which includes an overview of the case as a time line (or a table), therefore this was included in the manuscript. As we do not consider Figure 2 to be essential either, we ask the editors to decide whether it should remain in the manuscript or not.