

Reviewer #1:

**Scientific Quality:** Grade D (Fair)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Major revision

**Specific Comments to Authors:** In this scoping review, the authors introduced radiographic evaluation of congenital transverse limb deficiencies. This scoping review summarized the current state of knowledge on congenital transverse limb deficiencies and to provide an update regarding the radiographic evaluation of congenital transverse limb deficiencies. The specific review comments: (1) How many researchers are involved in the full-text screening process? If it is done by one researcher, how do you determine the effect of offset error caused by the operation of one researcher on the screening results?

- Thank you for pointing this out. The following sentences were added for increased clarity regarding the screening process.
- Page 1, line 13: “Four authors reviewed these during the screening process.”
- Page 3, line 63: “Four of the authors (N.V., A.L, S.Y., M.B.) screened the article by title and abstract.”
- Page 3, lines 70-71: “These articles then underwent a full-text screening process by the same four authors (N.V., A.L, S.Y., M.B.).”

2) In this review, the authors refer to the embryology of limb development and the etiology of congenital transverse limb deficiencies. Please add a description of the main mechanisms of etiology at the embryological level of congenital transverse limb deficiencies.

- Based on this comment, the sections ‘Etiology’ and ‘Embryology’ were combined into ‘Etiology & Embryology’.
- Further, the following sentences were added to better describe the main mechanisms of the etiology at the embryological level.
  - Page 4, lines 86 – 92: “The main mechanism of the etiology and embryological level is the disruption of growth of the Apical Epidermal Ridge (AER) along the proximodistal plane.<sup>14</sup> The subsequent result is that the interaxial signaling that is responsible for normal limb development is disrupted and causes a deficiency in the plane orthogonal to the developing limb bud, that is, transversely. There are several proposed causes for this disruption of the AER. The leading theory includes hypoperfusion, which leads to apoptosis of the AER.”

(3) In the section on the natural history of congenital transverse limb deficiencies, it is recommended that the second paragraph about treatment be placed in the treatment section.

- This has been done and this paragraph is now presented on page 8, lines 171 – 174.

(4) Regarding the screening and diagnosis of congenital transverse limb deficiencies, are there other forms of screening and diagnosis available besides prenatal testing? Please add.

- To the best of our knowledge there are no other forms of definitive diagnosis outside of prenatal imaging and one can suppose postnatal physical exam/post natal imaging in cases of missed diagnosis. The focus of this article is to highlight the use of standard and novel prenatal imaging techniques with the purpose being to encourage the development of standardized prenatal guidelines to encourage earlier diagnosis and earlier treatment of

transverse limb deficiencies. For this reason, the title has been changed to: 'Prenatal Radiographic Evaluation of Congenital Transverse Limb Deficiencies: A Scoping Review'.

Reviewer #2:

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** This is an interesting and meaningful study, and I recommend accept.

***(1) Science editor:***

The manuscript has been peer-reviewed, and it's ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade D (Fair)

***(2) Company editor-in-chief:***

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Orthopedics, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.

- The figures have been re-prepared in powerpoint as requested. The captions have been rewritten in the standard format above with similar contents (i.e. the same patient at the same prenatal time frame) have been described as above.
  - Example: **“Figure 1: Prenatal imaging at 24 weeks and 5 days demonstrating a transverse limb deficiency of the right forearm.**
  - **A:** 2D ultrasound showing markedly shortened right ulna (bone between "+" crosshairs) and radius (bone between "x" crosshairs) secondary to a transverse limb reduction defect (arrow).
  - **B:** High-resolution 2D ultrasound with high-frequency 4-18 Megahertz probe demonstrating a hyperechogenic thin line (arrow) representing a visualized amniotic band attached to the forearm defect.
  - **C:** 3D US rendered image showing the terminal transverse limb defect below the elbow (arrow).

- **D:** 3D US reconstructed image using the maximum intensity projection (MIP) to demonstrate the markedly short ulna (arrows) and radius (arrowhead). The advantage of 3D US in this case is that the normal humerus and elbow (which are not in the same plane of section in Figure 1A) as well as their relationship with the amputated distal forearm can be appreciated in a single image. The 3D rendered images (Figures 1C and 1D) are easier to understand for both the referring providers and parents.
- **E:** Axial balanced turbo field echo (BTFE) fetal MRI slice showing the deficiency (arrow).”
- The arrows and panel labels are now editable.

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- We can confirm that all pictures are original and were generated de novo by the authors for this manuscript. Thus, ‘Copyright©PhoenixChildrensRadiology2023’ has been added to each image.

Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

- The bullet points were removed from the contents of each cell so that the lines were aligned. The cell content is unsegmented.

Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the RCA. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

- Upon search of this very helpful resource, the following articles were selected as relevant and added to the section pertaining to results of treatment. They have also been added as References 41, 43, and 44.
  - **Mano H, Fujiwara S, Takamura K, Kitoh H, Takayama S, Ogata T, Hashimoto S, Haga N.** Congenital **limb deficiency** in Japan: a cross-sectional nationwide survey on its epidemiology. *BMC Musculoskelet Disord* 2018;**19**:262. [PMID: [30053842](#) DOI: [10.1186/s12891-018-2195-3](#)] [Cited by in Crossref: 11] [Cited by in RCA: 11] [Impact Index Per Article: 2.2] [Reference Citation Analysis] [What about the content of this article? (0)] [Abstract] [Track Full Text] [Download PDF] [Figures] Open
  - **Datta D, Selvarajah K, Davey N.** Functional outcome of patients with proximal upper **limb deficiency**–acquired and congenital. *Clin Rehabil* 2004;**18**:172-7. [DOI: [10.1191/0269215504cr716oa](#)] [Cited by in Crossref: 138] [Cited by in RCA: 139] [Impact Index Per Article: 19.7] [Reference Citation Analysis] [What about the content of this article? (0)] [Abstract] [Track Full Text]
  - **Burger H, Vidmar G.** A survey of overuse problems in patients with acquired or congenital upper **limb deficiency**. *Prosthet Orthot Int* 2016;**40**:497-502. [DOI: [10.1177/0309364615584658](#)] [Cited by in Crossref: 31] [Cited by in RCA: 34] [Impact Index Per Article: 4.4] [Reference Citation Analysis] [What about the content of this article? (0)] [Track Full Text]
- The new sentences resulting from these references are as below.
  - Page 8, line 184: “Upper extremity defects are more common and the choice and fit of prosthesis is rapidly evolving.”<sup>41</sup>”
  - Page 8, lines 188-189: “Generally, the outcome of prosthesis use in patients with proximal upper limb deficiencies is good.”<sup>43</sup>”
  - Page 8, lines 191 – 193: “However, it is important to consider that prosthesis choice and fit needs to be individualized based on the level of amputation and stump choice to prevent the nerve entrapment syndromes associated with prosthesis overuse.”<sup>44</sup>”