

## The Essence of Clinical Practice Guidelines for Ossification of Spinal Ligaments, 2019: 2. Pathology of OPLL

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### Pathology of OPLL

#### Summary

Although it has been suggested that dietary habits, comorbidities, and dynamic factors might be involved in the onset and progression of OPLL, the causal relationship remains to be determined.

#### Commentary

##### 1. Relationship between dietary habits and OPLL

Serum estrogen level, which is affected by vegetable protein intake, and estrogen receptor gene polymorphism have been compared between patients with OPLL and healthy individuals, but the results are inconsistent among reports<sup>1-9</sup>. The association between vitamin A intake and OPLL was also investigated from the aspect of vitamin A receptor, but the abnormality of vitamin A receptor in patients with OPLL has not been demonstrated<sup>10</sup>. Recently, the association between retinoic acid receptor gamma and ossification was reported<sup>11</sup>.

##### 2. Relationship between comorbidities and OPLL

The relationship between diabetes<sup>12</sup> and insulin secretory response<sup>13</sup> is reported. Especially, OPLL at thoracic and/or lumbar spine is reported to strongly correlate with diabetes,

obesity, and hyperleptinemia<sup>14</sup>. Conversely, another report concluded that diabetes has no direct relationship with the incidence of OPLL and ossification progression<sup>15</sup>. The relationships between OPLL and Ca and P metabolism disorders, vitamin D-resistant rickets<sup>16-18</sup>, and hypo-hyperparathyroidism<sup>19-22</sup> are also reported, but the causal relationships between OPLL and these disorders have not been fully elucidated. As for the relationship between OPLL and myotonic dystrophy, abnormally expanded mRNA in myotonic dystrophy is thought to affect the splicing of other mRNA, leading to effects on glucose and lipid metabolism, which might indirectly affect the onset of OPLL<sup>23-27</sup>. Thus, abnormal glycolipid metabolism is involved in the onset of OPLL; however, the detailed mechanism remains to be elucidated.

##### 3. Relationship between mechanical factors and OPLL

Mechanical loading applied to the cervical spine is reported to contribute to the onset of OPLL and progression<sup>28-30</sup>, although the relationship between job type and OPLL has not been demonstrated<sup>31-34</sup>. In an analysis of the cells of posterior longitudinal ligament and other ligaments in patients with OPLL, mechanical stimulation was shown to increase the gene expression relating bone differentiation in the cells of patients with OPLL than those of patients without OPLL<sup>35</sup>. The involvement of elevated expression of BMP2<sup>36</sup>, prostaglandin I2<sup>37</sup>, and connexin-43 has been suggested as the underlying mechanism<sup>38,39</sup>.

**Conflicts of Interest:** The author declares that there are no relevant conflicts of interest.

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1. Epidemiology of OPLL, written by Tomohiko Hasegawa, MD, PhD, Hamamatsu University, School of Medicine, Japan. <https://doi.org/10.22603/ssrr.2021-0096>
2. Pathology of OPLL, written by Takashi Kaito, MD, PhD, Osaka University Graduate School of Medicine, Japan. <https://doi.org/10.22603/ssrr.2021-0074>
3. Diagnosis of OPLL, written by Hirotaka Chikuda, MD, PhD, Gumma University, School of Medicine, Japan. <https://doi.org/10.22603/ssrr.2021-0118>
4. Treatment of Cervical OPLL, written by Toshitaka Yoshii, MD, PhD, Tokyo Medical and Dental University Hospital, Japan. <https://doi.org/10.22603/ssrr.2021-0100>
5. Treatment of Thoracic OPLL, written by Shiro Imagama, MD, PhD, Nagoya University Graduate School of Medicine, Japan. <https://doi.org/10.22603/ssrr.2021-0095>
6. Diagnosis of OLF, written by Masao Koda, MD, PhD, University of Tsukuba, Japan. <https://doi.org/10.22603/ssrr.2021-0116>
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