Radial Longitudinal Deficiency: Recent Developments, Controversies, and an Evidence-Based Guide to Treatment

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Continuing Medical Education

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Learning Objectives

Upon completion of this CME activity, the learner should achieve an understanding of:

- Embryology of upper limb development in relation to radial longitudinal deficiency and thumb hypoplasia
- Relative benefits and risks of wrist centralization on the ulna
- Recent alternatives to wrist centralization
- Classification and surgical indications for thumb hypoplasia
- Reconstructive options and outcomes for thumb hypoplasia

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Radial longitudinal deficiency (RLD) is the most common congenital longitudinal deficiency at birth and represents a wide spectrum of upper extremity anomalies, from mild thumb hypoplasia to absent radius. Radial dysplasia may be isolated or associated with an array of systemic anomalies that should be familiar to pediatric hand surgeons. The management

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of RLD has evolved greatly since its inception in the late 19th century, largely due to decades of innovation that followed the thalidomide catastrophe of the 1960s. Yet controversy still exists regarding many aspects of RLD. Traditional treatments of radial dysplasia (ie, centralization) are unfortunately wrought with poor outcomes and high rates of recurrence, leading some authors to recommend alternative techniques for this condition. Reconstruction of the hypoplastic thumb, although less controversial, is just starting to see long-term outcomes. This article reviews the etiology, classification, and treatment options for RLD, highlighting recent developments and outcomes. *(J Hand Surg Am. 2017;42(7):546–563.*

Key words Radial dysplasia, radial longitudinal deficiency, centralization, thumb hypoplasia, pollicization.

RADIAL LONGITUDINAL DEFICIENCY (RLD), or radial dysplasia, is the most common congenital longitudinal deficiency of the upper extremity (1 in 5,000 live births)[1] and is characterized by a spectrum of dysplastic development along the radial column and includes thumb hypoplasia. The thalidomide-induced epidemic of phocomelia of the 1960s turned limb hypoplasia into a widespread congenital anomaly and spurred advances in the treatment of RLD. The decades that followed saw important innovations in the surgical treatment of RLD. Two landmark articles were published in the 1970s that established principles of surgical management. Dieter Buck-Gramcko[2] published a series of 100 index pollicizations for congenital thumb hypoplasia in 1971 based on the procedure conceived by Littler[3] and Riordan.[4] In 1972, Lamb[5] published his experience in 41 children and stressed the importance of early orthosis fabrication to stretch the fibrotic radial anlage and centralizing the carpus over the ulna with Kirschner wire fixation. Important innovations and follow-up studies over the past few years have both clarified and called into question several of these principles. In this article, we review current literature and updated recommendations for the treatment of RLD.

ETIOLOGY

Embryological development of the upper extremity occurs along 3 axes of the limb bud: proximal/distal (longitudinal), anterior/posterior (radial/ulnar), and dorsal/ventral. According to the Oberg-Manske-Tonkin classification, RLD is a malformation caused by disrupted development along the radial/ulnar axis.[6,7] The developmental biochemical pathways of these 3 axes are complex and intricately interrelated,[8] and the more severe forms of RLD have a proximal/distal component of dysplasia as well.

Growth and patterning along the longitudinal axis of the upper extremity is primarily the result of fibroblast growth factors (FGF) secreted in the apical ectodermal ridge in the distal limb bud. Fibroblast growth factors, primarily FGF8, stimulate cell proliferation and survival for nearby mesodermal cells, inducing and maintaining outgrowth of the limb bud. The apical ectodermal ridge is also maintained, not only by FGF signaling via FGFR1&2, but also by Wnt/beta-catenin, bone morphogenic protein (BMP)/BMPR1a, retinoic acid, and Sonic hedgehog (Shh).[8]

The anterior-posterior axis differentiates due to Shh expression in the zone of polarizing activity (ZPA), a region of the distal posterior (ulnar) limb mesenchyme. The ZPA is established owing to FGF signaling via FGFR2. The Shh produced by the ZPA induces development of posterior (ulnar) structures via Gli-3 and is thought to induce patterning from an ulnar to a radial direction due to an Shh gradient, with development of the anteriormost digit (ie, thumb) occurring independent of Shh signaling[8] (Fig. 1). Recently, Iroquois homeodomain transcription factors 3 and 5 (IRX 3/5) have also been implicated as the driver of anterior limb development. A double knockout murine model produced a phenotype of RLD and current thought is that Shh has an inhibitory role on IRX 3/5[9] (Fig. 2). Alternatively, aberrant expression of *hairy2*, a limb molecular clock gene that is regulated both instructively by FGF and permissively by Shh, may be involved in deficient radial ray development.[8]

RADIAL LONGITUDINAL DEFICIENCY

Classification and diagnosis

Although not commonly screened for, it is possible to diagnose RLD prenatally with obstetric ultrasound (sensitivity, 75%; specificity, 100%).[10] Radial longitudinal deficiency commonly occurs in conjunction with other congenital anomalies. One-third of patients have a named syndrome (Table 1), and 67% of RLD