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Epidemiology of congenital upper limb anomalies in Korea: A nationwide population-based study

선천성 상지 기형의 역학: 대한민국 전인구 기반 연구

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서울대학교 대학원

의학과 정형외과학 전공

신 영 호

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지도 교수 백 구 현

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위 원 장 권 성 택

부위원장 백 구 현

위 원 정 선 근

위 원 이 영 호

위 원 김 재 광

Abstract

Background: An understanding of the epidemiology of congenital anomalies is important for public health. The epidemiology of congenital upper limb anomalies (CULA) has been studied previously, but there were several limitations to consider it as definite epidemiologic information. The purpose of this study was to analyze the epidemiology of CULA in Korea. More specifically, we evaluated the incidence of each type of CULA, the presence of coexisting anomalies and the surgical treatment status in CULA patients.

Materials and methods: We conducted a retrospective cohort study of patients aged < 1 year between 2007 and 2016 who were registered with CULA in the Health Insurance Review and Assessment Service of Korea. First, patients aged < 1 year with CULA were identified using ICD-10 (International Classification of Diseases, 10th revision) codes. Second, other accompanying congenital anomalies were analyzed for CULA patients. Patients who were diagnosed and registered as having other anomalies within one year of birth, were considered to have other congenital anomalies. Third, the surgical treatment status for CULA patients was analyzed. Since the data were collected until the end of 2019, surgical treatments conducted within minimum three years of the initial diagnosis of CULA were included.

Results: In total, 10,704 patients had CULA, including 6,174 boys (57.7%) and 4,530 girls (42.3%). The mean annual incidence of CULA was 23.5 per 10,000 live births; it was significantly higher in boys than in girls (26.3 vs. 20.5, $p < 0.001$).

Among the four categories of CULA—polydactyly, syndactyly, limb deficiency, and other anomalies—polydactyly was the most common. In total, 4,149 patients (38.8%) had other congenital anomalies and coexisting anomalies of the circulatory system (24.9%) were the most common. In total 4,776 patients (44.6%) underwent operative treatment for CULA within minimum three years of the diagnosis. The proportion of patients who underwent surgical treatment was significantly higher for polydactyly (73.4% vs. 16.8%, $p < 0.001$) and syndactyly (65.3% vs. 41.5%, $p < 0.001$), but it was significantly lower in limb deficiency (27.6% vs. 45.4%, $p < 0.001$) and other anomalies (10.0% vs. 69.8%, $p < 0.001$) than rest of CULA patients. Among the patients who had operations, 21.5% underwent multiple operations. The proportion of patients who underwent multiple operations was significantly higher in syndactyly (35.6% vs. 18.1%, $p < 0.001$), but it was significantly lower in polydactyly (4.0% vs. 95.5%, $p < 0.001$) and other anomalies (17.9% vs. 21.9%, $p < 0.001$) than rest of CULA patients.

Conclusions: The incidence of CULA to be 23.5 per 10,000 for 10 years and the incidence increased slightly over a 10-year period. Among the four categories, polydactyly was the most common type of CULA. A total of 38.8% of patients with CULA had other congenital anomalies with anomalies of the circulatory system being the most associated. A total of 44.6% of patients with CULA underwent operative treatment for CULA and the proportion was significantly higher in polydactyly and syndactyly. Among the patients who underwent operations, 21.5% of the patients underwent multiple operations. The portion of patients who had multiple operations was significantly higher in syndactyly. These results could facilitate an understanding of the epidemiology of CULA in an Asian population

and provide a basis for estimating the national healthcare costs for CULA and the number of specialists needed to treat CULA.

Keywords: congenital anomalies; limb deficiency; polydactyly; syndactyly

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Introduction

An understanding of the epidemiology of congenital anomalies is important for public health. This information provides a basis for estimating the national healthcare costs and the number of required specialists. In addition, monitoring the changes in the incidence and patterns of congenital anomalies may alert us to new teratogens such as thalidomide in the 1960s (Mellin and Katzenstein, 1962).

The epidemiology of congenital upper limb anomalies (CULA) has been studied previously, but there were several limitations to consider it as definite epidemiologic information. Some studies have focused on regional, not national populations (Ekblom et al., 2014; Giele et al., 2001; Goldfarb et al., 2017; Goldfarb et al., 2015), or evaluated the prevalence of CULA, not incidence (Ekblom et al., 2014; Goldfarb et al., 2017; Goldfarb et al., 2015), or only examined for one specific anomaly such as limb deficiency (Klungsøyr et al., 2019; Koskimies et al., 2011). In addition, there are only two old regional studies that have evaluated the epidemiology of CULA in an Asian population (Leung et al., 1982; Ogino et al., 1986) and no national studies.

Korea has been implementing a health insurance system for all citizens since 1989. Since the medical data of the whole population in Korea are managed at the Health Insurance Review and Assessment Service (HIRA), the HIRA dataset makes it easy to retrieve and analyze data to understand the medical status of the whole country. In addition, due to the wide coverage of the national insurance

system, medical access for Korean citizens is the best among the Organization for Economic Cooperation and Development (OECD) countries (Organisation for Economic Co-operation and Development, 2020). Therefore, we could evaluate the epidemiology of CULA in whole nationwide population by analyzing HIRA data. The purpose of this study was to analyze the epidemiology of CULA in Korea. More specifically, we evaluated the incidence of each type of CULA, the presence of coexisting anomalies and the surgical treatment status in CULA patients.

Materials and methods

Data source

In Korea, the National Health Insurance Service (NHIS) covers 100% of the population; 97% have health insurance and 3% have medical aid (Jo et al., 2017). All healthcare providers submit claims data for inpatient and outpatient management to the HIRA for reimbursement of medical costs. These include diagnostic codes (classified according to the International Classification of Diseases, 10th revision [ICD-10]), procedure codes, and demographic information. HIRA provides some of this national data to support public policy developments and research activities when requested. This study protocol was exempted for review by the Institutional Review Board of Asan Medical Center (No. 2020-0124) in accordance with the exemption criteria.

Data acquisition

After confirming the study design and population for candidate, we registered our study plan and applied the right to assess the data at web site of HIRA (https://opendata.hira.or.kr/). At the web site, researchers should describe the search formula mainly composed of diagnosis and performance codes which include all candidate they want to enroll. The details of diagnosis and procedure codes are also available at HIRA web site.

Due to the limited source for web-based search and high demand of many researchers, we waited six months until receiving the right to assess the data server. All data analyses were performed on the web based virtual space with use of statistical program. Since the number of enrolled patients and their medical data

were huge, it took about two months to fully analyze the whole data. All available data could not be downloaded or retrieved. Instead, limited volume of selected and refined data could be retrieved from the data server under permission of HIRA. The time limit of data analysis is originally three months for each study, but could be extended two months more. The cost for utilizing the data is about 300 USD per month.

Data collection

We conducted a retrospective cohort study of CULA patients between 2007 and 2016. First, patients aged < 1 year with CULA were identified using ICD-10 codes (Table 1). The ICD-10 codes for CULA were divided into four categories: polydactyly, syndactyly, limb deficiency and other anomalies (World Health Organization, 2020). For patients who identified several times with the same code, the timing of the first diagnosis was the criterion used for the calculation of annual incidence. If one patient had multiple CULA codes, each code was counted separately for initial analysis, but when calculating the annual incidence of all CULA and each category of anomaly, it was considered as a single case. For

Table 1. Total number of patients who were registered with each diagnostic code for congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016.

Diagnostic code	Number of patients	Incidence per 10,000 live births (95% CI)
Total	10,704	23.52 (23.08–23.97)
Polydactyly	5,264	11.57 (11.26–11.89)
Q690. Accessory finger(s)	1,545	3.40 (3.23–3.57)
Q691. Accessory thumb(s)	2,424	5.33 (5.12–5.54)
Q699. Polydactyly unspecified*	2,495	5.48 (5.27–5.70)
Syndactyly	1,405	3.09 (2.93–3.25)
Q700. Fused fingers	352	0.77 (0.69–0.86)
Q701. Webbed fingers	236	0.52 (0.45–0.59)
Q704. Polysyndactyly*	435	0.96 (0.87–1.05)
Q709. Syndactyly, unspecified*	613	1.35 (1.24–1.46)

Limb deficiency	490	1.08 (0.98–1.18)
Q710. Congenital complete absence of upper limb(s)	6	0.01 (0.00–0.03)
Q711. Congenital absence of upper arm and forearm with hand present	10	0.02 (0.01–0.04)
Q712. Congenital absence of both forearm and hand	8	0.02 (0.01–0.03)
Q713. Congenital absence of hand and finger(s)	251	0.55 (0.49–0.62)
Q714. Longitudinal reduction defect of radius	40	0.09 (0.06–0.12)
Q715. Longitudinal reduction defect of ulna	5	0.01 (0.00–0.03)
Q716. Lobster–claw hand	23	0.05 (0.03–0.08)
Q718. Other reduction defects of upper limb(s)	118	0.26 (0.21–0.31)
Q719. Reduction defect of upper limb, unspecified	45	0.10 (0.07–0.13)
Q730. Congenital absence of unspecified limb(s)*	16	0.04 (0.02–0.06)
Q731. Phocomelia, unspecified limb(s)*	7	0.02 (0.01–0.03)
Q738. Other reduction of unspecified limb(s)*	9	0.02 (0.01–0.04)
Other anomalies	4,507	9.91 (9.62–10.20)

Q681. Congenital deformity of hand	1,741	3.83 (3.65–4.01)
Q688. Other specified congenital musculoskeletal deformities of U/E	1,592	3.50 (3.33–3.68)
Q740. Other congenital malformations of upper limb(s), including shoulder girdle	980	2.15 (2.02–2.29)
Q743. Arthrogryposis multiplex congenita*	121	0.27 (0.22–0.32)
Q748. Other specified congenital malformations of limb(s)*	114	0.25 (0.21–0.30)
Q749. Unspecified congenital malformation of limb(s)*	160	0.35 (0.30–0.41)

example, if one patient was registered with three different codes (e.g., accessory finger(s) (Q690.), accessory thumb(s) (Q691.), and other congenital malformations of upper limb(s) including shoulder girdle (Q740.)), he or she was counted separately for each code incidence, but as a single case for the annual incidence of CULA. For some diagnostic codes, upper and lower extremities were not discriminated. For example, polydactyly unspecified (Q699.), polysyndactly (Q704.), and congenital absence of unspecified limb(s) (Q730.) were considered as CULA codes when they were registered with the procedure codes for radiographs of the upper extremity from clavicle to finger (clavicle: G3101–3105; scapula: G3201–3205; shoulder: G33013305; acromioclavicular joint: G3901–3905; forearm: G6101–6105; elbow: G6201–6205; humerus: G6301–6305; wrist: G6401–6405; hand: G6501–6505; carpal bone: G6601–6605; finger: G8101–8105). The annual incidence of CULA was defined as the proportion of the population who were newly diagnosed with CULA at age < 1 year among the live births during that year. Annual live birth data, including numbers and sex, were acquired from the Korean Statistical Information Service (Statistics Korea, 2020). In addition, other demographic information including sex and insurance type (whether a patient had health insurance or medical aid, which indirectly reflect the social economic status) of each patient were acquired.

Second, other accompanying congenital anomalies were analyzed for CULA patients. Patients who were diagnosed and registered as having other anomalies within one year of birth, were considered to have other congenital anomalies, classified by the major classification level of ICD-10 codes (Table 2). For congenital anomalies of the musculoskeletal system, patients with anomalies other

Table 2. Other accompanying congenital anomalies in total and for each category of congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016: number (incidence (%)).

	Nervus system (Q00–07)	Eye, ear, face and neck (Q10–18)	Circulatory system (Q20–28)	Respiratory system (Q30–34)	Cleft lip and cleft palate (Q35–37)	Digestive system (Q38–45)	Genital organs (Q50–56)	Urinary system (Q60–64)	Musculoskeletal system (Q65–79)*	Other malformations (Q80–89)	Chromosomal abnormalities (Q90–99)	Total
All patients with CULA	835 (7.8)	1,213 (11.3)	2,670 (24.9)	607 (5.7)	663 (6.2)	2,103 (19.6)	962 (9.0)	1,396 (13.0)	2,130 (19.9)	889 (8.3)	548 (5.1)	4,149 (38.8)
Polydactyly	401 (7.6)	639 (12.1)	1,366 (25.9)	312 (5.9)	336 (6.4)	1,120 (21.3)	510 (9.7)	740 (14.1)	841 (16.0)	414 (7.9)	286 (5.4)	1,843 (35.0)
Syndactyly	133 (9.5)	192 (13.7)	392 (27.9)	77 (5.5)	101 (7.2)	324 (23.1)	139 (9.9)	237 (16.9)	337 (24.0)	145 (10.3)	93 (6.6)	614 (43.7)
Limb	57	79	197	43	48 (9.8)	144	68	84 (17.1)	170	65	32 (6.5)	302

deficiency	(11.6)	(16.1)	(40.2)	(8.8)		(29.4)	(13.9)		(34.7)	(13.3)		(61.6)
Other	370	477	1,060	260	281	813	376	539 (12.0)	1,083	387	218 (4.8)	1,884
anomalies	(8.2)	(10.6)	(23.5)	(5.8)	(6.2)	(18.0)	(8.3)		(24.0)	(8.6)		(41.8)

*For congenital anomalies of the musculoskeletal system, patients with anomalies other than CULA were assessed.

than CULA were included. The number of patients with other anomalies were evaluated for each type of CULA. If one patient had multiple other anomalies, each anomaly was counted separately according to the major classification level of ICD-10 codes for initial analysis, but when calculating the incidence of other accompanying anomalies in patients with CULA, and each category of CULA, it was considered as a single case. For example, if one patient with thumb polydactyly was registered with two different anomalies including the circulatory system (Q20–28) and the digestive system (Q38–45) within one year after birth, he or she was counted separately for the incidence of each anomaly, but counted as a single case for the incidence of accompanying other anomalies in patients with all CULA and polydactyly.

Third, the surgical treatment status for CULA patients was analyzed. Since the data were collected until the end of 2019, surgical treatments conducted within minimum three years of the initial diagnosis of CULA were included. Patients registered with operation codes under the CULA codes were defined as having surgery for CULA. In the HIRA operation codes, only three codes were disease specified codes for CULA including operation of polydactyly required reconstruction of tendon and bone (N0251), operation of polydactyly required other procedures (N0252), and operation of syndactyly (N0260). The remaining codes were for general bone and soft tissue procedures. Therefore, we identified all operation codes which were possible for surgical treatment of CULA (Table 3). The incidence of surgical treatment, the time to initial operation from diagnosis, and the number of operations were analyzed for each type of CULA.

Table 3. Available operation codes of Health Insurance Review and Assessment Service of South Korean for congenital upper limb anomalies (CULA).

	Description	Codes
Disease specified codes	Operation for polydactyly	N0251 (construction of tendon or bone), N0252 (others)
	Operation for syndactyly	N0260
General bone and soft tissue procedures	Release of scar contracture	N0241
	Release of scar contracture and skin graft	Full thickness: N0242 (<25 cm^2), N0243 (≥25 cm^2) Split thickness (face or joint): N0244 (<25 cm^2), N0245 (≥ 25 cm2) Split thickness (others): N0246 (<25 cm^2), N0247 (25–99 cm^2), NA241 (100–399 cm^2), NA242 (400–899 cm^2), NA243 (≥900 cm^2)
	Release of scar contracture and flap operation	N0249
	Osteotomy	N0302 (upper or lower extremity), N0316 (carpal or tarsal), N0317 (metacarpal, metatarsal, finger, or toe)
	Osteotomy and internal fixation	N0304 (radius or ulna), N0306 (humerus), N0307 (radius and ulna), N0318

		(carpal or tarsal), N0319 (metacarpal, metatarsal, finger, or toe)
	Ostectomy	N0311
	Bone graft	N0312
	Disarticulation of extremities	N0563 (shoulder), N0565 (elbow, wrist, or ankle), N0566 (finger or toe)
	Amputation of extremities	N0573 (upper arm, forearm, or lower leg), N0574 (hand or foot), N0575 (finger or toe)
	Excision of carpal or tarsal bone	N0610
	Resection arthroplasty	N0722 (shoulder, knee, elbow, wrist, or ankle), N0723 (finger or toe)
	Arthrodesis	N0733 (elbow, wrist, or ankle), N0734 (finger or toe), N0738 (shoulder),
	Open reduction of dislocation	N0752 (shoulder), N0753 (elbow), N0755 (wrist or ankle), N0756 (finger or toe)
	Closed reduction of dislocation	N0762 (shoulder), N0763 (elbow or knee), N0764 (wrist, ankle, finger, or toe), N0765 (radial head subluxation)
	Mechanical correction for deformity	N0792 (deformity of extremity)

	Manipulative correction for deformity	N0804
	Reconstruction of tendon and ligament	N0931 (simple: resection, suture, or release), N0932 (complex: graft, transfer, or reconstruction with allograft)
	Tenolysis	N0941
	Vascularized osteocutaneous free flap	N1583 (vascularized bone graft), N1584 (vascularized osteocutaneous graft), N1585 (pedicled vascularized bone graft)
	Autogenous fat graft or dermofat graft	NX021

Statistical analysis

Continuous data were presented as mean ± standard deviation (SD) or median and interquartile range (IQR), and categorical data are presented as numbers and percentages. We calculated the annual incidence of CULA (per 10,000 live births) in boys and girls assuming a Poisson distribution. Poisson regression analysis was used to analyze the trends in annual incidence of overall CULA, CULA in each sex, and in the four categories of CULA. The chi-square test was used to compare the proportion of patients in each category who had other accompanying congenital anomalies and those who underwent operative treatment and multiple operations with the rest of CULA patients. $P < 0.05$ was interpreted as statistically significant. All statistical analyses were performed using the SAS Enterprise Guide software version 7.1 (SAS Institute, Inc., Cary, NC, USA).

Results

Annual incidence of CULA

A total of 10,704 patients were registered with CULA from 2007 to 2016, including 6,174 boys (57.7%) and 4,530 girls (42.3%), and a total of 4,550,102 live births were registered in the same period (Table 4). The mean annual incidence of CULA was 23.5 per 10,000 live births, and it was significantly higher in boys (26.3 per 10,000 live births) than girls (20.5 per 10,000 live births) ($p < 0.001$) (Table 5). Among the total 10,704 patients, 10,561 patients (98.7%) had health insurance and 143 patients (1.3%) had medical aid. The Poisson regression analysis showed that the annual incidence of CULA increased during the study period (incidence rate ratio (IRR), 1.017; 95% CI, 1.009–1.025; $p < 0.001$). This increase was observed in both boys (IRR, 1.016; 95% CI, 1.006–1.026; $p = 0.021$) and girls (IRR, 1.018; 95% CI, 1.006–1.031; $p = 0.036$) (Fig 1A and 1B).

Table 4. Annual number of total and each category of congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016.

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Total
All patients with CULA	1,045	1,067	983	1,082	1,166	1,096	1,083	1,101	1,070	1,011	10,704
Polydactyly	585	552	485	517	573	529	556	489	527	451	5,264
Syndactyly	148	135	130	132	137	152	159	140	142	130	1,405
Limb deficiency	54	54	39	44	56	62	47	38	52	44	490
Other anomalies	375	426	413	487	495	466	416	521	447	461	4,507

Table 5. Annual incidence of congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016.

	Total			Boy			Girl		
Year	No. of patients	No. of population	Incidence per 10,000 live births (95% CI)	No. of patients	No. of population	Incidence per 10,000 live births (95% CI)	No. of patients	No. of population	Incidence per 10,000 live births (95% CI)
2007	1,045	496,822	21.0 (19.78–22.35)	622	255,872	24.31 (22.44–26.30)	423	240,950	17.56 (15.92–19.31)
2008	1,067	465,892	22.9 (21.55–24.32)	589	240,119	24.53 (22.59–26.59)	478	225,773	21.17 (19.32–23.16)
2009	983	444,849	22.1 (20.74–23.52)	568	229,351	24.77 (22.77–26.89)	415	215,498	19.26 (17.45–21.20)
2010	1,082	470,171	23.0 (21.66–24.43)	621	242,901	25.57 (23.59–27.66)	461	227,270	20.28 (18.47–22.22)
2011	1,166	471,265	24.7 (23.34–26.20)	695	242,121	28.70 (26.61–30.92)	471	229,144	20.55 (18.74–22.50)
2012	1,096	484,550	22.6 (21.30–24.00)	640	248,958	25.71 (23.75–27.78)	456	235,592	19.36 (17.62–21.22)
2013	1,083	436,455	24.8 (23.36–26.34)	612	223,883	27.34 (25.21–29.59)	471	212,572	22.16 (20.20–24.25)
2014	1,101	435,435	25.3 (23.81–26.82)	645	223,356	28.88 (26.69–31.19)	456	212,079	21.50 (19.57–23.57)
2015	1,070	438,420	24.4 (22.97–25.91)	625	224,906	27.79 (25.65–30.06)	445	213,514	20.84 (18.95–22.87)
2016	1,011	406,243	24.9 (23.38–26.47)	557	208,064	26.77 (24.59–29.09)	454	198,179	22.91 (20.85–25.12)

No. (Number), CI (Confidence intervals)

Fig. 1A. Annual number of congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016.

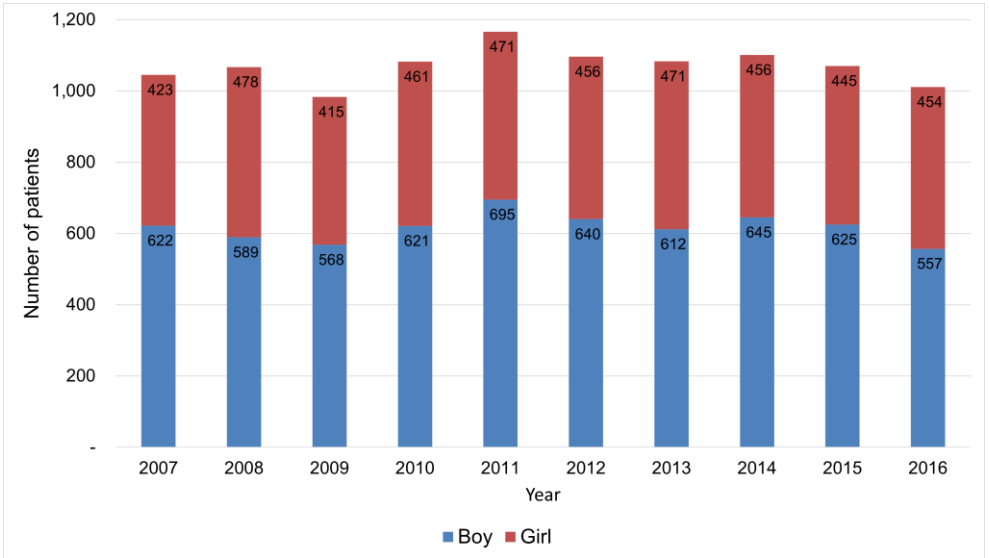
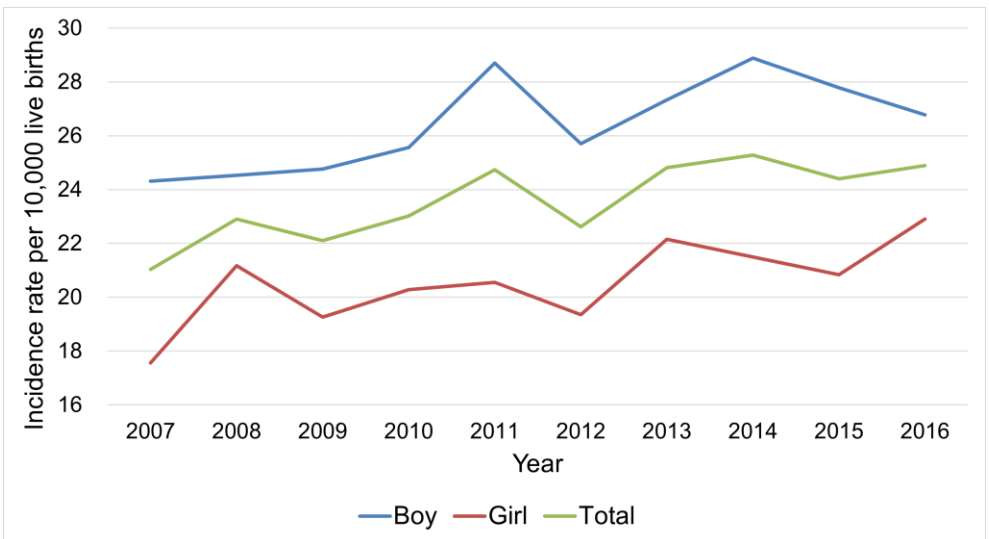
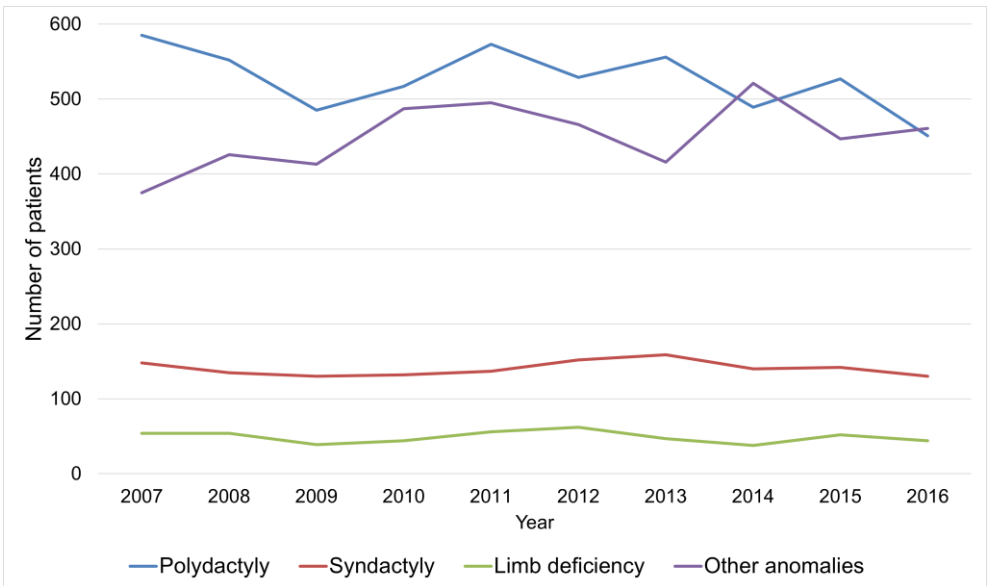


Fig. 1B. Annual incidence of congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016.



Among the four ICD-10 codes categories, polydactyly (5,264 patients, 49.2%) was most common and followed by other anomalies (4,507 patients, 42.1%), syndactyly (1,405 patients, 13.1%), and limb deficiency (490 patients, 4.6%). The Poisson regression analyses showed that the annual incidence of polydactyly (IRR, 1.000; 95% CI, 0.988–1.013; p = 0.951) and limb deficiency (IRR, 1.004; 95% CI, 0.974–1.034; p = 0.810) were not significantly changed during the study period. However, the annual incidence of syndactyly (IRR, 1.017; 95% CI 1.003–1.031; p = 0.018) and other anomalies (IRR, 1.033; 95% CI, 1.013–1.052; p = 0.001) were significantly increased during the study period (Fig 2).

Fig. 2. Annual number of patients with congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016 according to the categories.



Other accompanying congenital anomalies in patients with CULA

Among the 10,704 patients with newly diagnosed CULA, 4149 patients (38.8%) had other congenital anomalies. Congenital anomalies in the circulatory system were the most common (2670 patients, 24.9%), followed by congenital anomalies in the musculoskeletal system other than CULA (2130 patients, 19.9%) and congenital anomalies in the digestive system (2103 patients, 19.6%) (Table 2). The proportion of patients with other accompanying congenital anomalies was described in Fig. 3A, 3B, 3C, and 3D. Among the four categories, other congenital anomalies was significantly higher in limb deficiency (61.6% vs. 37.7%, $p < 0.001$), syndactyly (43.7% vs. 38.0%, $p < 0.001$), and other anomalies (41.8% vs. 36.5%, $p < 0.001$), but significantly lower in polydactyly (35.0% vs. 42.4%, $p < 0.001$) than rest of CULA patients.

Fig. 3A. Other accompanying congenital anomalies which accompanied with congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016: polydactyly

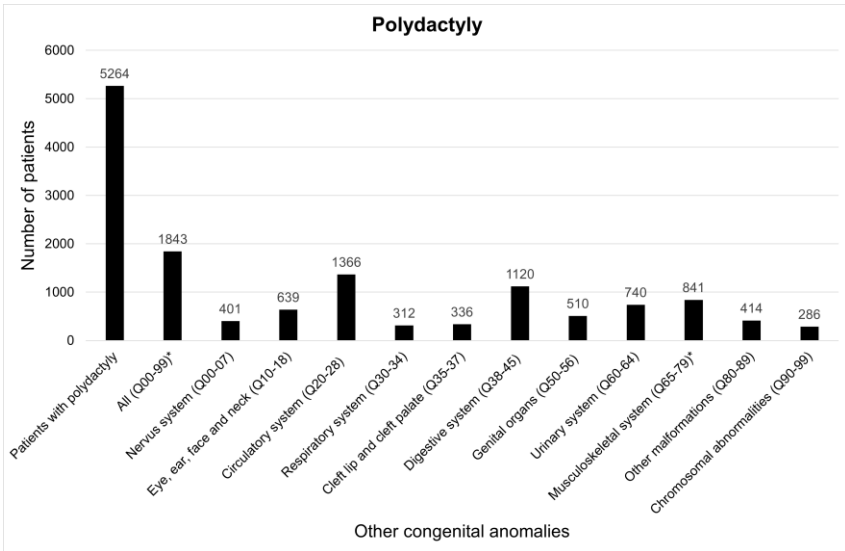


Fig. 3B. Other accompanying congenital anomalies which accompanied with congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016: syndactyly

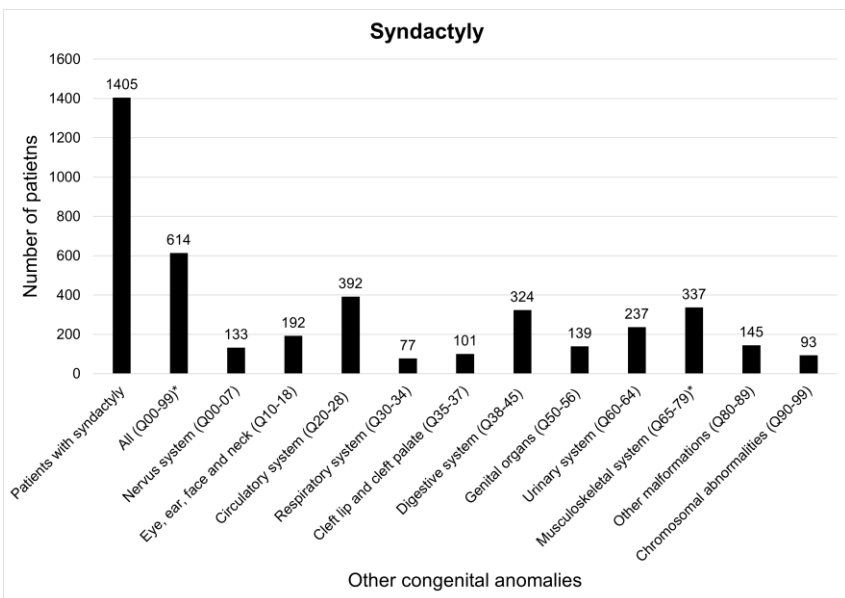


Fig. 3C. Other accompanying congenital anomalies which accompanied with congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016: limb deficiency

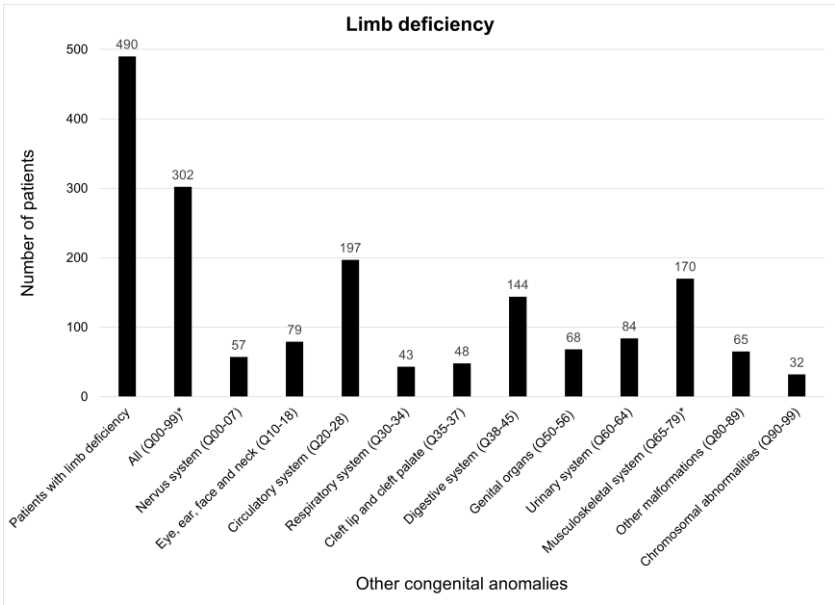
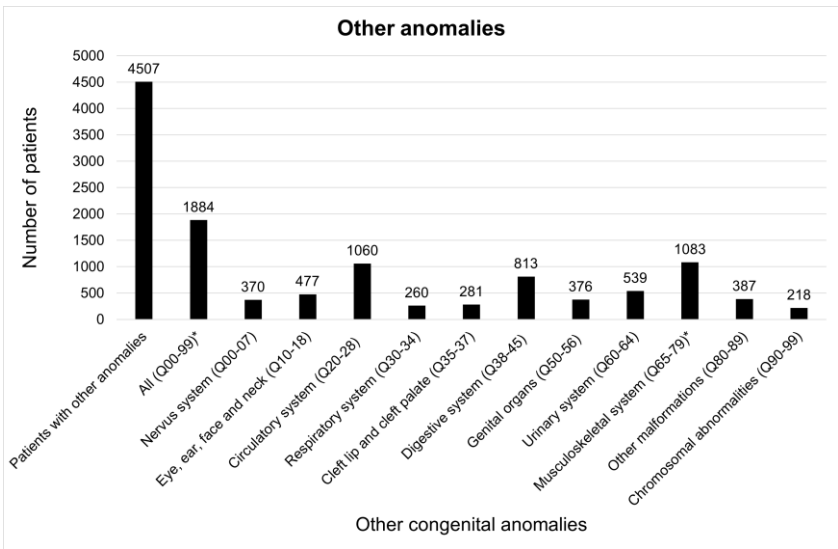


Fig. 3D. Other accompanying congenital anomalies which accompanied with congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016: other anomalies



Surgical treatment status for CULA

Among the 10,704 patients with newly diagnosed CULA, 4,776 patients (44.6%) underwent operative treatment for CULA within minimum three years of the diagnosis. The proportion of patients who had surgical treatments was described in Table 6 and the details of applied surgical treatments were described in Table 7. Among the four categories, surgical treatment rate was significantly higher in polydactyly (73.4% vs. 16.8%, $p < 0.001$), and syndactyly (65.3% vs. 41.5%, $p < 0.001$), but significantly lower in limb deficiency (27.6% vs. 45.4%, $p < 0.001$), and other anomalies (10.0% vs. 69.8%, $p < 0.001$) than rest of CULA patients.

Table 6. The proportion of patients who underwent operative treatment for congenital hand and upper extremity anomaly (CULA) in South Korea from 2007 to 2016 within minimum three years of diagnosis.

Diagnostic code	**Proportion (%)**
Total	44.6
Polydactyly	73.4
Q690. Accessory finger(s)	77.5
Q691. Accessory thumb(s)	79.6
Q699. Polydactyly unspecified*	72.4
Syndactyly	65.3
Q700. Fused fingers	70.2
Q701. Webbed fingers	61.0
Q704. Polysyndactyly*	80.7

Q709. Syndactyly, unspecified*	63.0
Limb deficiency	27.6
Q710. Congenital complete absence of upper limb(s)	16.7
Q711. Congenital absence of upper arm and forearm with hand present	20.0
Q712. Congenital absence of both forearm and hand	12.5
Q713. Congenital absence of hand and finger(s)	26.7
Q714. Longitudinal reduction defect of radius	32.5
Q715. Longitudinal reduction defect of ulna	20.0
Q716. Lobster–claw hand	47.8
Q718. Other reduction defects of upper limb(s)	32.2
Q719. Reduction defect of upper limb, unspecified	44.4
Q730. Congenital absence of unspecified limb(s)*	0.0
Q731. Phocomelia, unspecified limb(s)*	0.0
Q738. Other reduction of unspecified limb(s)*	22.2
Other anomalies	10.0
Q681. Congenital deformity of hand	15.6
Q688. Other specified congenital musculoskeletal deformities of U/E	4.0
Q740. Other congenital malformations of upper limb(s), including shoulder girdle	9.0
Q743. Arthrogryposis multiplex congenita*	14.0
Q748. Other specified congenital malformations of limb(s)*	12.3
Q749. Unspecified congenital malformation of limb(s)*	18.8

Table 7. Applied operation codes of Health Insurance Review and Assessment Service for the first operative treatment of congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016.

	Operation of polydactyly		Pollicization	Operation of syndactyly		Osteotomy	Excision of carpal bone	Amputation or disarticulation
	N0251	N0252	N1581	N1582	N1582 + S0173-4 & N0173-9	N0302, N0304, N0306-7, N0316-9	N0610	N0573-5, N0563, N0565-6
Total	2661	1475	18	640	467	27	4	41
Polydactyly	2478	1417	1	94	57	7	2	32
Syndactyly	329	132	1	543	418	6	1	3
Limb deficiency	20	9	17	57	39	8	1	4
Other anomalies	144	52	6	115	85	14	1	10

	Resection arthroplasty	Arthrodesis	Open reduction of dislocation	Closed reduction of dislocation	Operation for tendon and ligament	Contracture release	Bone graft	Others
	N0722-3	N0733-4, N0738	N0752-3, N0755-6	N0762-5	N0931-4, N0941-2	N0241-7, N0249, NA241-3, NX021	N0312, N1583-5	N0792, N0804
Total	26	7	9	24	260	207	1	5
Polydactyly	9	2	0	2	145	81	0	0
Syndactyly	1	1	2	0	36	67	0	0
Limb deficiency	4	1	3	0	39	37	1	0
Other anomalies	15	4	7	23	113	97	0	5

For the 4,776 patients who had surgical treatments, the median time to the initial operation from diagnosis was 5.1 months (IQR, 0.9–9.4 months). Among the four categories, it was longest in limb deficiency, median value 11.7 months (IQR, 6.4–19.1 months) and shortest in polydactyly, median value 4.4 months (IQR, 0.7–8.4 months) (Fig 4). Among the 4,776 patients who underwent operations, 3750 patients (78.5%) underwent a single operation, but 1026 patients (21.5%) underwent multiple operations for CULA. Among the four categories, the portion of patients who had multiple operations was significantly higher in syndactyly (35.6% vs. 18.1%, $p < 0.001$), but significantly lower in polydactyly (4.0% vs. 95.5%, $p < 0.001$) and other anomalies (17.9% vs. 21.9%, $p < 0.001$) than rest of CULA patients (Fig 5A and 5B). The details of applied surgical treatments for multiple operations for CULA were described in Table 8.

Fig. 4. The median time from diagnosis to initial operation from the diagnosis for patients who had surgical treatment for congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016 according to the categories; empty blue circle: mean time.

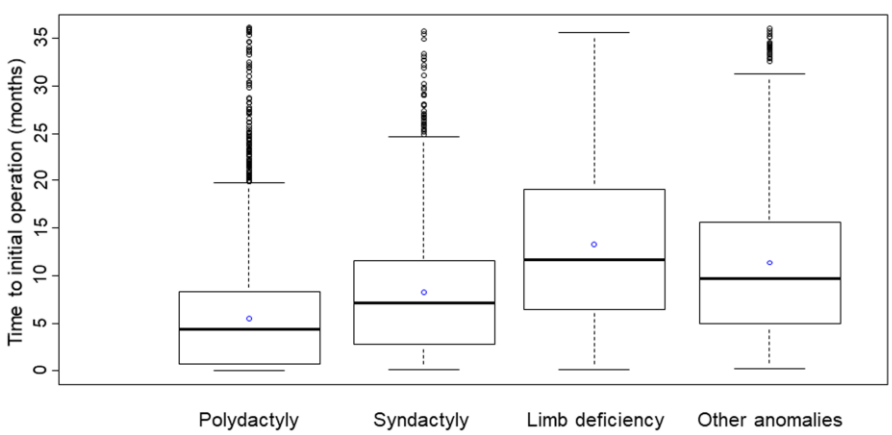


Fig. 5A. The number of operations for patients who had surgical treatment for congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016 according to the categories: number of patients and (B) proportion of patients according to the operation numbers.

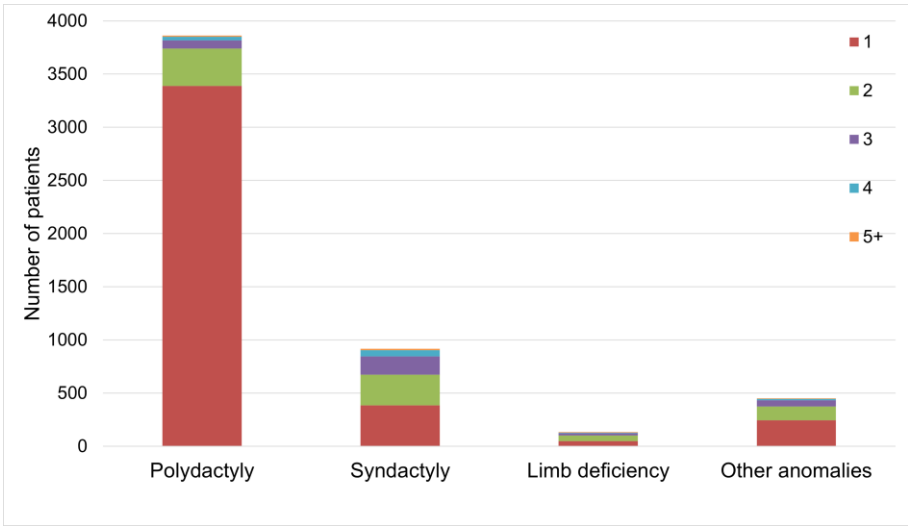


Fig. 5B. The number of operations for patients who had surgical treatment for congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016 according to the categories: proportion of patients according to the operation numbers.

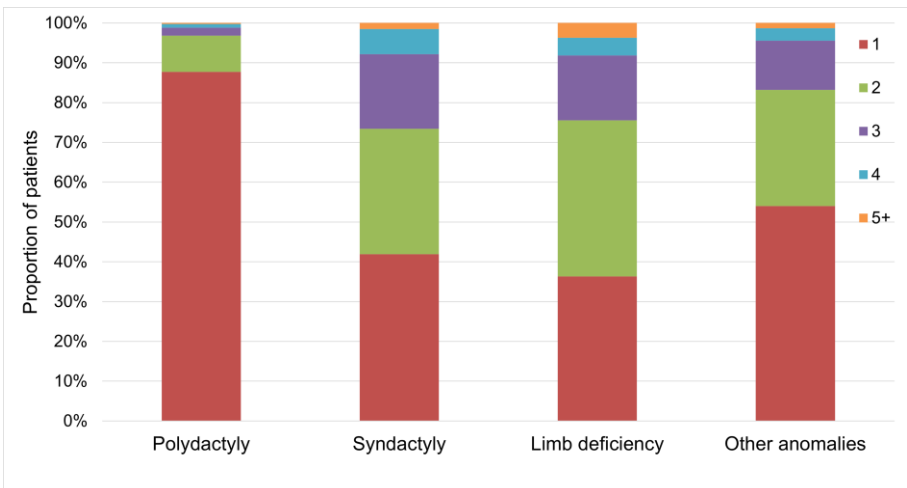


Table 8. Applied operation codes of Health Insurance Review and Assessment Service for the multiple operations of congenital upper limb anomalies (CULA) in South Korea from 2007 to 2016.

	Operation of polydactyly		Pollicization	Operation of syndactyly		Osteotomy	Excision of carpal bone	Amputation or disarticulation
	N0251	N0252	N1581	N1582	N1582 + S0173-4 & N0173-9	N0302, N0304, N0306-7, N0316-9	N0610	N0573-5, N0563, N0565-6
Total	110	34	3	269	221	52	1	2
Polydactyly	84	24	1	32	24	18	1	0
Syndactyly	43	16	0	252	208	19	0	2
Limb deficiency	2	1	3	11	9	6	0	0
Other anomalies	4	3	0	29	25	13	0	0

	Resection arthroplasty	Arthrodesis	Open reduction of dislocation	Closed reduction of dislocation	Operation for tendon and ligament	Contracture release	Bone graft	Others
	N0722-3	N0733-4, N0738	N0752-3, N0755-6	N0762-5	N0931-4, N0941-2	N0241-7, N0249, NA241-3, NX021	N0312, N1583-5	N0792, N0804
Total	12	11	5	3	83	237	7	1
Polydactyly	1	4	0	1	23	36	2	0
Syndactyly	4	5	0	1	27	180	1	0
Limb deficiency	1	2	1	0	12	9	2	1
Other anomalies	7	2	4	1	39	40	3	1

Discussion

Incidence of CULA

The overall incidence of CULA in our study (23.5 per 10,000 live births) was similar to that reported in previous studies. In a total population study of Western Australia spanning 11 years, Giele et al. reported the prevalence of CULA as 19.8 per 10,000 live births (Giele et al., 2001). In a total population study of Stockholm, Sweden over 11 years, Ekblom et al. reported the incidence of CULA as 21.5 in 10,000 live births (Ekblom et al., 2014). In a study of the New York Congenital Malformations Registry spanning 18 years, Goldfarb et al. reported the prevalence as 27.2 per 10,000 live births (Goldfarb et al., 2017). These differences could originate from the differences in data sources, racial compositions of the populations studied, and whether incidence or prevalence was measured. In two previous studies (Ekblom et al., 2014; Giele et al., 2001), more boys than girls had CULA, however a statistical significant difference was revealed for the first time in our study. The annual live birth rates for Korea slightly decreased, but the annual numbers of CULA was constant or slightly increased during the study period. This resulted in the statistically significant increase in the annual incidence of CULA regardless of sex. The increased mean maternal age (30.6 years in 2007 and 32.4 years in 2016) and decreased mortality rate of newborns (34 per 10,000 live births in 2007 and 28 per 10,000 live births in 2016) (Statistics Korea, 2020) which mean higher survival rate of babies with multiple anomalies could attribute to the rise in incidence of CULA (Giele et al., 2001). In addition, this increasing trend may reflect improved detection and reporting of CULA, or an increase of exogenous teratogens in our environment (Koskimies et al., 2011).

Proportion of each category of CULA

Polydactyly was the most common category of CULA, but the data did not allow for identification of the anomaly location. Although the ‘other anomalies’ category was the second most common category which included unspecified various anomalies, syndactyly was the second most common as a single anomaly entity. This finding is the generally accepted ranking of CULA incidence (Goldfarb et al., 2017; Percival and Sykes, 1989). The incidence of upper limb deficiency was lower than the incidence in Northern Europe cohorts (Ekblom et al., 2014; Klungsøyr et al., 2019; Koskimies et al., 2011), with half of the patients having an absence of hand and finger(s). We think that these differences in CULA compositions originates from the ethnic differences of each cohort.

Other accompanying congenital anomalies in patients with CULA

Among the patients with newly diagnosed CULA, 38.8% had other congenital anomalies in our cohort. This portion is lower than the 46% in the Western Australian cohort (Giele et al., 2001), but higher than the 23.1% in the Swedish cohort (Ekblom et al., 2014). Regarding the type of accompanying congenital anomalies, syndromic anomalies were the commonest or second commonest cause in previous studies (Ekblom et al., 2014; Giele et al., 2001); however, it was less common in our cohort. We think that these discrepancies originate from data collection methods. In previous studies, all available medical records and radiographs were reviewed by specialists and in cases where the CULA was a part of syndromic anomalies it was classified as ‘accompanying a syndromic anomaly’

and not ‘other specific organ anomalies’. However, in our cohort, only the registered data were analyzed, and we could not review the detailed medical records or diagnosis for CULA patients. As all healthcare providers could submit the patients` data in our cohort, there is the possibility that specific organ anomalies were registered simultaneously with a syndromic anomaly. Among the four categories, a higher portion of limb deficiency patients had other congenital anomalies than other CULA categories. Therefore, when we treat patients with limb deficiency, we should consider the possibility of other anomalies and their general medical condition.

Surgical treatment status for CULA

As most surgical treatments for CULA are initiated within two or three years after birth (Kozin and Zlotolow, 2015; Waters and Bae, 2012), we think that the observation period of this study (minimum three years after the diagnosis) would include most of the surgically treated CULA patients. Although the portion of surgically treated patients were higher in polydactyly and syndactyly than the rest of CULA patients, it was not over 90% in both categories. This may relate to the underreporting of rudimentary type polydactyly, which could be removed with ligation or simple excision at an outpatient clinic or neonatal nursery instead of official surgery under anesthesia (Abzug and Kozin, 2013). In addition, some cases of partial syndactyly which do not show functional disability could be observed without operation, while in some complex syndactyly cases surgery could be contraindicated if there was a risk of further functional impairment (Braun et al., 2016; Goldfarb et al., 2017). For limb deficiency and other anomalies, the portion

of surgically treated patients were lower than for the rest of the CULA patients. This phenomena could be explained by the limited role of surgical treatment in limb deficiency patients (Klungsøyr et al., 2019; Koskimies et al., 2011) and ‘other anomalies’ include anomalies which do not impair the function and thus do not require surgical treatment, such as clinodactyly, brachydactyly, minor type clasped or hypoplastic thumb (Waters and Bae, 2012). The portion of patients who had multiple operations was significantly higher in syndactyly than for the rest of the CULA patients. This may relate to the higher reoperation rate of syndactyly due to web creep and deviation of the divided digit (Ferrari and Werker, 2019), and the multiple operations required for multiple webs or for operations on both hands (Wang and Hutchinson, 2019).

Limitations

Our study has several limitations similar to those found in any registry study. First, this is an imperfect registry for identifying all CULA correctly as confirmation of CULA often requires clinical and radiological assessment by specialists such as congenital hand surgeons (Goldfarb et al., 2017). Therefore, some patients could be registered with different codes at different times. We believe that the polydactyly, syndactyly, and limb deficiency data are reliable as these cases were easy to identify. In addition, we are confident total CULA incidence data is accurate as we removed repetitive data for the same patient. In contrast, patients with ‘other anomalies’ are the least reliable data due to various and less straightforward diagnoses. Second, most studies stratified their cases with known CULA classification systems such as the International Federation of Societies for Surgery

of the Hand (IFSSH) classification (Ekblom et al., 2010; Giele et al., 2001) or the Oberg, Manske, and Tonkin (OMT) classification (Ekblom et al., 2014; Goldfarb et al., 2015). We could not apply these classification systems to our cohort because the information required was not captured in our database. This limits the direct comparison of results between epidemiological studies. However, because this study covered the whole national population and most of the CULA diagnoses would be registered by non-specialists, registration and analysis of ICD-10 data is suitable for this type of study, as these are familiar to all healthcare providers. Third, the time limitations of this study could under-estimate the incidence of CULA and their surgical treatments. Some CULA such as clinodactyly, brachymesophalangy, and the Sprengel deformity could be detected after one year of age. Limiting the time for surgery to be performed to three years from diagnosis may be too short to include all multiple operations.

Conclusion

The incidence of CULA to be 23.5 per 10,000 for 10 years and the incidence increased slightly over a 10-year period. Among the four categories, polydactyly was the most common type of CULA. A total of 38.8% of patients with CULA had other congenital anomalies with anomalies of the circulatory system being the most associated. A total of 44.6% of patients with CULA underwent operative treatment for CULA and the proportion was significantly higher in polydactyly and syndactyly. Among the patients who underwent operations, 21.5% of the patients underwent multiple operations. The portion of patients who had multiple operations was significantly higher in syndactyly. These results could facilitate an understanding of the epidemiology of CULA in an Asian population and provide a basis for estimating the national healthcare costs for CULA and the number of specialists needed to treat CULA.

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국문 초록

연구 배경: 선천성 기형의 역학에 대한 이해는 공공 의료 기반 확립 및 의료 인력 양성 계획 수립 측면에서 중요하다. 이러한 이유로 선천성 상지 기형 (congenital upper limb anomalies, CULA)의 역학 또한 여러 연구를 통해 밝혀졌으나, 기존의 연구 결과들을 정설로 받아들이기에는 여러 단점들이 있었다. 이번 연구에서는 대한민국 전인구의 선천성 상지 기형의 역학에 대해 알아보고자 하였다. 구체적으로 선천성 상지 기형의 유형별 빈도, 선천성 상지 기형 환자에서 동반된 다른 선천 기형의 유형 및 빈도, 선천성 상지 기형의 수술적 치료 현황 등을 분석하고자 하였다.

대상 및 방법: 2007 년부터 2016 년까지 선천성 상지 기형으로 진단받은 후 대한민국 건강보험심사평가원에 등록된 1 세 미만의 환자 정보를 후향적으로 분석하였다. 첫번째로, 선천성 상지 기형 환자는 1 세 미만 시기에 선천성 상지 기형에 해당하는 건강 문제의 국제 통계 분류 10 차 개정판 (International Classification of Diseases, 10th revision, ICD-10) 진단 코드를 부여 받은 환자를 검색하여 확인하였다. 두번째로, 이 선천성 상지 기형 환자에서 동반된 다른 선천성 기형의 유무 및 현황을 확인하였다. 구체적으로, 생후 1 년 이내 다른 선천성 기형으로 진단 후 진단 코드를 부여 받은 환자를 확인하였다. 세번째로, 선천성 상지 기형 환자의 수술적 치료 현황을 분석하였다. 이번 연구에서는 2019 년 말까지의 자료를 분석하였기 때문에, 처음 선천성 상지 기형 진단 후

최소 3 년 이내에 수술적 치료를 시행 후 수술 코드가 등록된 환자만을 분석에 포함하였다.

결 과: 해당 기간 동안 총 10,704 명의 환자가 선천성 상지 기형으로 진단 받았고, 남아가 6,174 명 (57.7%), 여아가 4,530 명 (42.3%) 이었다. 선천성 상지 기형의 평균 연간 발생율은 10,000 생태아 중 23.5 명이었고, 남아가 여아보다 유의미하게 높았다 (26.3 명 vs. 20.5 명, p<0.001). 선천성 상지 기형의 4 개의 대분류 (다지증, 합지증, 사지 결손, 그 밖의 선천성 기형) 중에 다지증이 가장 흔하였다. 선천성 상지 기형을 가진 환자 중 총 4,149 명 (38.8%)에서 동반된 다른 선천성 기형을 가지고 있었고, 순환기계 기형 (24.9%)이 가장 흔하였다. 선천성 상지 기형을 가진 환자 중 총 4,776 명 (44.6%)의 환자가 진단 후 최소 3 년 이내에 수술적 치료를 받았다. 수술적 치료를 시행 받은 환자의 비율은 다지증 (73.4% vs. 16.8%, p<0.001), 합지증 (65.3% vs. 41.5%, p<0.001)이 다른 기형에 비해 유의미하게 높았고, 사지 결손 (27.6% vs. 45.4%, p<0.001), 그 밖의 선천성 기형 (10.0% vs. 69.8%, p<0.001)에서는 유의미하게 낮았다. 수술적 치료를 시행 받은 환자의 21.5%에서 2 회 이상 수술을 시행 받았다. 2 회 이상 수술적 치료를 시행 받은 환자의 비율은 합지증 (35.6% vs. 18.1%, p<0.001)이 다른 기형에 비해 유의미하게 높았고, 다지증 (4.0% vs. 95.5%, p<0.001)과 그 밖의 선천성 기형 (17.9% vs. 21.9%, p<0.001)에서는 유의미하게 낮았다.

결 론: 2007 년부터 2016 년까지 10 년 동안 선천성 상지 기형의 평균 연간 발생율은 10,000 생태아 중 23.5 명이었고, 10 년 동안 연간 발생율은 유의미하게 증가하였다. 4 개의 대분류 중 다지증이 가장 흔하였다. 총 38.8% 환자에서 다른 선천성 기형을 가지고 있었고, 순환기계 기형이 가장 흔하였다. 총 44.6% 환자들이 진단 후 3 년 이내에 수술적 치료를 받았고, 그 비율은 다지증, 합지증에서 높았다. 수술적 치료를 시행 받은 환자의 21.5%에서 2 회 이상 수술을 시행 받았고, 그 비율은 합지증에서 높았다. 이번 연구 결과는 아시아인에서 선천성 상지 기형의 역학을 이해하는데 도움이 되고, 선천성 상지 기형 치료에 필요한 비용 및 의료 인력을 추정하는데 기초 자료로 활용될 수 있을 것이다.

색인 단어: 선천성 기형; 사지 결손; 다지증; 합지증

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