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Oral Clefting in China Over the Last Decade: 205,679 Patients

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Background: China is the most populated country and has one of the highest prevalences of oral clefting. The present study reports the epidemiology and surgical procedures performed on the largest reported cohort of individuals with clefting in China.
Methods: A retrospective review of patients who received cleft repair through Smile Train in China from 2000 to 2011 was conducted. Data on demographics, cleft characteristics, associated malformations, pregnancy and family history, and surgical technique were analyzed using SPSS (IBM, Chicago, Ill.).
Results: A total of 205,679 patients underwent 209,169 cleft procedures. Cleft lip and palate (42.7%) was most common followed by isolated cleft palate (32.4%) and isolated cleft lip (24.9%). Males accounted for 63.5% of cases. The average age at initial surgery was 6.12 years. By 2011, this decreased to 1.8 years of age for lip repair and to 5.9 years of age for palate repair. The preferred techniques were rotation-advancement (55%) for unilateral lip repair and Von-Langenbeck (38%) and pushback (39%) for palate repair. The percentages of cases with associated anomalies and surgical complications were 12.8% and 0.36%, respectively.
Conclusions: This study provides insight into cleft care in China as it reports the largest cohort of cleft patients treated by surgeons to date. Our results generally follow trends previously reported in China and developed countries. The male:female ratio for cleft palate patients was higher than expected. The average age at primary repair is higher than recommended, but seems to be decreasing. *(Plast Reconstr Surg Glob Open 2014;2:e236; doi: 10.1097/GOX.0000000000000186; Published online 23 October 2014.)*

Oral clefting is the most common congenital malformation of the head and neck. Over a quarter of a million babies with a cleft were born in 2009, and more than 70% of these were born in the developing world.[1–3] The epidemiology of oral clefts has been studied in many populations, and differences around the world have been recognized. The estimated incidence of clefting is highest in Asians with a rate of 1 in 500, followed by whites (1 in 1000) and African-Americans (1 in 2500).[4–8] In China, the reported incidence of clefting varies from 1.2 per 1000 to 30.7 per 10,000.[9,10] The wide variation in incidence is partially due to a paucity of standard criteria for data collection and the absence of a universal classification system. Although information is available in many countries, differences in sample source (hospital versus birth

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registry) and inclusion/exclusion criteria lead to inconsistent findings.

The epidemiology of clefting has been studied extensively in white populations; however, only a few studies have been conducted in China (Table 1).[9–24] China is home to a quarter of the world's population with over 1.3 billion people. There are more than 20 million births per year in China. Based on an estimated incidence of 1 in 500 cases of oral clefting in China, there are more than 40,000 new cases of oral clefts each year. Although this incidence rate is frequently cited, it is based on reports with relatively small sample sizes, widely varying incidence rates, and incomplete population ascertainment. The true birth prevalence of clefting in China is unknown.

Similarly, there are no exact statistics on how many individuals with cleft deformity have been treated in China.[25] Chinese health-related information is inconsistent and underreporting has been documented.[26] The birth defect rate in China has increased from 87.7 per 10,000 in 1996 to 149.9 per 10,000 in 2010, which may reflect true rise in congenital malformations and/or improved reporting.[27] Limited access to surgical care in rural areas, financial constraints, and rise in the prevalence of birth defects have all contributed to a backlog of an estimated 421,000 to 2.8 million with unrepaired clefts.[28,29] With a growing population and old data, there is a need to better define the epidemiology of clefting in China.

Smile Train is the largest cleft charity based on numbers treated.[2] Rather than sending medical

Table 1. Epidemiologic Studies of Clefting in China

			Cleft Type				Male:Female Ratio						
Study	Period	Study Design	Total	CLP (%)	CP (%)	CL (%)	Total	CLP	CP	CL	Associated Anomalies (%)	Reported Incidence	Family History
Hu et al[9]	1972–1982	Livebirth data	60	—	—	—	—	—	—	—	—	1.33/1000	4.47% for first degree; 0.97% for second degree
Wang et al[10]	—	Hospital records	1755	43.9	30.9	25.2	1.1	1.6	0.6	1.1	—	1.45–1.92/1000	—
Shi[22]	1985–1987	Livebirth data	116	56.9	9.5	33.6	1.1	1.4	0.2	1.1		4.478/1000	2.83% for first degree; 7.76% for consanguinity; 5.17% for twin cases
Xiao[11]	1986–1987	Livebirth data	2265	61.3	8.2	30.5	1.2	—	—	—	—	18.20/10,000	—
Wu et al[12]	1988–1991	Livebirth data	4548	84.7	15.3	—	1.3	1.5	0.8	1.5	—	16.50/10,000	—
Chen et al[13]	1986–1992	Livebirth data	204	56.4	13.7	29.9	1.3	1.4	0.8	1.7	13.7	1.46/1000	7.35% for positive family history; 2.54% for consanguinity; 0.57% for twin cases
Cooper et al[14]	1980–1989	Livebirth data	643	65.0	—	35.0	—	—	—	—	—	1.20/1000	—
Liang et al[15]	1988–1992	Birth defect surveillance	3766	67.0	—	32.9	1.6	1.6	—	1.4	0.1	—	—
Meng et al[16]	1996–2005	Hospital records	4268	46.5	28.3	25.2	—	2.3	0.8	1.9	3.6	—	6.68%
Zhou et al[17]	2000–2002	Hospital records	7812	59.6	17.0	23.4	2.0	2.9	0.8	1.9	2.9	—	6.84%
Li et al[18]	2003–2004	Birth defect surveillance	83	62.0	8.2	29.6	1.0	1.5	0.5	1.2	14.5	3.27/1000	—
Wang et al[19]	2000–2007	Birth defect surveillance	634	58.7	15.1	26.2	2.0	2.9	0.7	1.9	—	1.76/1000	—
Dai et al[20]	1996–2005	Birth defect surveillance	8133	53.2	15.4	31.4	1.1	1.3	0.6	1.4	—	16.6/10,000	—
Shu et al[23]	2008	Hospital records	4675	30.7	28.9	40.4	1.6	—	—	—	—	13.5/10,000	
Sun et al[21]	2009–2011	Hospital records	2180	33.9	31.5	34.6	1.3	—	—	—	30.1	—	—
This study	2000–2011	Hospital records	205,679	42.7	32.4	24.9	1.7	2.3	1.2	1.9	12.8	—	0.73% for first degree; 0.64% for second degree

mission teams to developing countries, Smile Train supports local surgeons to perform cleft surgeries at local hospitals. The goal is to provide training and financial support to local surgeons. Smile Train extends cleft care to individuals mostly of lower socioeconomic status. The present study reports data collected by Smile Train that supported 209,675 cleft surgeries in China from 2000 to 2011.[29] Smile Train maintains a database, Smile Train Express, of all cleft surgeries it has supported around the world. This enables the collection of comparable patient data. The following report is based on the largest reported cohort of individuals treated for clefting in China.

METHODS

A retrospective review was conducted of patients who received cleft repair through Smile Train in China from 2000 to 2011. The project was reviewed and approved by the Icahn School of Medicine at Mount Sinai IRB Committee and conforms to the Helsinki Declaration. Information on birth month and year, cleft characteristics, associated malformations, pregnancy history, family history, surgical technique, and postoperative complications were surveyed and entered by surgeons and healthcare workers into the Smile Train Express database at the time of surgery. Deidentified data were entered into Excel (Microsoft, Redmond, Wash.) and analyzed. Patients with missing data on cleft type were excluded from the analysis.

Based on visual inspection, data were entered regarding anatomic location (lip, alveolus, hard palate, and soft palate), laterality (left, right, and bilateral), and completeness of cleft. This information was recoded according to the International Classification of Diseases (ICD-9) for clefting, which contains 3 broad groups: cleft lip and palate (CLP), isolated cleft lip (CL), and cleft palate (CP). CLP and CL were further divided into subcategories based on laterality and completeness. CP was subdivided into incomplete or complete CP. The data were analyzed statistically using SPSS 20.0 (IBM, Chicago, Ill.). Chi-square test was used to compare proportions of 2 groups. Statistical significance level for α was set at 0.05.

RESULTS

During the study period, 212,066 cases were recorded in Smile Train Express. A total of 6387 patients with missing or erroneous information were excluded. Data were available for 205,679 patients who underwent 209,169 cleft repairs that were performed in all 31 provinces of mainland China. Complete geographic data were available for 183,182 patients undergoing repair. The highest numbers of surgeries were performed in the South Central (36.9%), East (21.2%), and Southwest (14.6%) regions with most done in the Henan province (19.1%) and less than 11% in each of the other regions (Table 2). The number of surgeries increased over the study period (Fig. 1).

For the study population, cleft type and distribution by gender, laterality, and completeness are presented in Table 3. Of the 205,679 patients with cleft, 87,745 patients (42.7%) presented with CLP, 66,727 patients (32.4%) with CP, and 51,207 patients (24.9%) with CL (Fig. 2). The number of patients for each cleft type remained relatively constant through the study period (Fig. 3). Male patients were more frequent over the period of data collection; 130,658 patients (63.5%) were male and 75,021 patients

Table 2. Geographic Distribution of Cleft Repairs

Region and Province	Repairs Performed, *n* = 183,182 (%)
Northern region	20,531 (11.2)
Beijing	2205 (1.2)
Hebei	11,704 (6.4)
Inner Mongolia*	1873 (1.0)
Shanxi	4749 (2.6)
Northwest region	15,612 (8.5)
Gansu	6643 (3.6)
Ningxia	1495 (0.9)
Qinghai	635 (0.3)
Shaanxi	3313 (1.8)
Xinjiang	3526 (1.9)
Southwest region	26,761 (14.6)
Chongqing	3290 (1.8)
Guizhou	8001 (4.4)
Sichuan	8534 (4.7)
Tianjin	628 (0.3)
Tibet	245 (0.1)
Yunnan†	6063 (3.3)
Northeast region	13,996 (7.6)
Heilongjiang	5533 (3.0)
Jilin	3373 (1.8)
Liaoning	5090 (2.8)
Eastern region	38,720 (21.2)
Anhui	6733 (3.7)
Fujian	3804 (2.1)
Jiangsu	6048 (3.3)
Jiangxi	10,705 (5.8)
Shandong	10,389 (5.7)
Shanghai	106 (0.1)
Zhejiang	935 (0.5)
South Central Region	67,562 (36.9)
Guangdong	5551 (3.0)
Guangxi‡	6820 (3.7)
Hainan	731 (0.4)
Henan	35,048 (19.2)
Hubei	7516 (4.1)
Hunan	11,896 (6.5)

Percentages are calculated based on 183,182 patients with complete geographic data available.
There are 56 ethnic groups in China. The Han Chinese is the largest ethnic group (92% of population) and a majority in every province.
*Mongols comprise 17.1% of Inner Mongolia.
†Yunnan has the most ethnic minorities.
‡Zhuang is the largest ethnic minority and over 90% live in Guangxi.

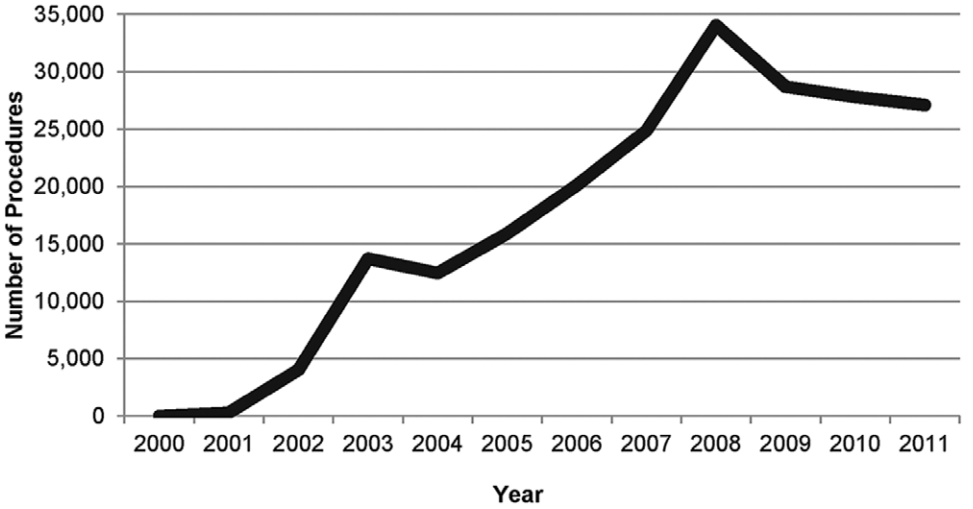

Fig. 1. The number of cleft repairs performed per year.

(36.5%) were female (Fig. 4). Unilateral clefts were more common than bilateral clefts, the left side was involved about twice as often as the right side, and incomplete clefts were more than twice as common as complete clefts ($P < 0.01$). Bilateral complete CL and CLP were infrequent in this population (7.13%). The ratios for gender, laterality, and completeness by cleft type are presented in Table 4.

At least one associated anomaly was found in 26,285 patients (12.8%) (Table 5). Anomalies were seen in 19.4% of CLP, 16.2% of CP, and 3.7% of CL patients. The most commonly noted anomalies affected the mandible (79.8%; no details about the type of mandibular anomalies were requested by the questionnaire). Only 2% of patients reported pregnancy or birth-related complications. A small percentage reported prenatal use of tobacco (0.09%) or alcohol (0.09%). A family history of clefting was reported in 1.37% of patients, and patients with CLP have the strongest association with a positive family history. A total of 73,681 patients (35.8%) reported a prior cleft-related surgery of which 75.6% had a previous lip repair.

Among all patients, 42.3% were younger than 2 years. Chinese patients presenting older than 15 years were not uncommon (19%). The overall average age at surgery was 6.12 years. The average age was 7.22 years for primary palate repair, 2.23 years for primary lip repair, and 13.41 years for alveolar bone grafting. The average age of primary surgery was noted to decrease over the period of data collection (Fig. 5).

The preferred technique for unilateral lip repair was rotation-advancement (55.0%) (Fig. 6). The preferred technique for bilateral lip repair was "other" followed by straight-line repair (Fig. 7; no details were requested about "other" types of repairs by the questionnaire). The rotation-advancement was used more frequently for bilateral incomplete CLs (18% for incomplete versus 5% for complete),

Table 3. Classification and Prevalence of Cleft Types

Cleft Type	No.	%
Total	205,679	—
CL	51,207	24.90
Unilateral complete CL, left	10,619	
Unilateral complete CL, right	5396	
Unilateral incomplete CL, left	19,777	
Unilateral incomplete CL, right	11,681	
Bilateral complete CL	638	
Bilateral incomplete CL	3096	
CLP*	87,745	42.66
Unilateral complete CLP, left	18,212	
Unilateral complete CLP, right	9935	
Unilateral incomplete CLP, left	19,659	
Unilateral incomplete CLP, right	10,715	
Bilateral complete CLP	9269	
Bilateral incomplete CLP	19,955	
CP	66,727	32.44
Complete	5985	
Incomplete†	60,742	

*Cleft lip with alveolar cleft accounts for 1.8% of CLP cases.
†Submucous cleft palate accounts for 1.4% of incomplete CP cases.

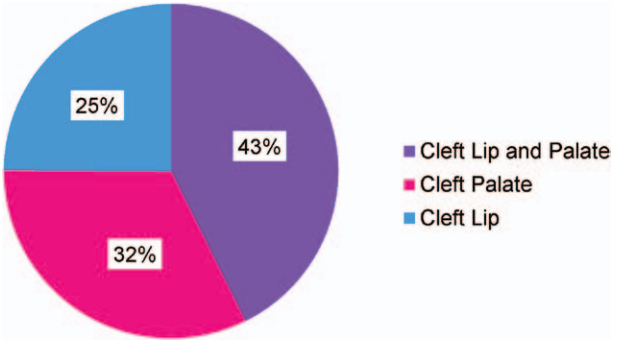

Fig. 2. The overall percentages of cleft types.

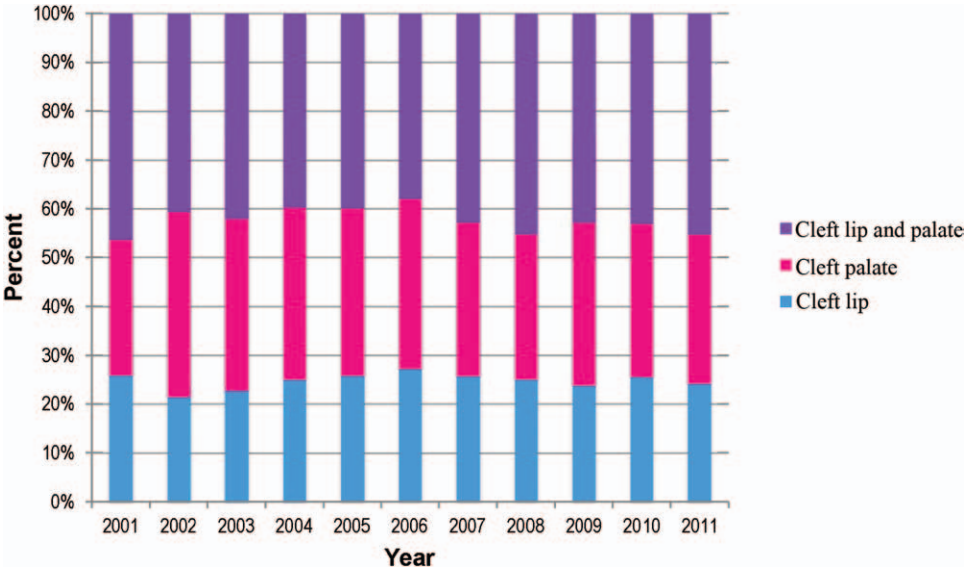

Fig. 3. The percentages of cleft types per year.

whereas the forked flap was used more frequently for bilateral complete CLs (15% for complete versus 10% for incomplete). For CP repair, the most common techniques were pushback (38.5%) and Von-Langenbeck repairs (37.5%) (Fig. 8). The average hospital stay was approximately 11 days for either CL or CP repairs.

A complication rate of 0.36% was calculated based on the total number of reported complications and the total number of repairs over the entire period of data collection. Dehiscence was the most frequently reported complication (44.0% of all complications) followed by fistula (32.0% of all complications). The complication rate of bilateral lip repair (0.45%)

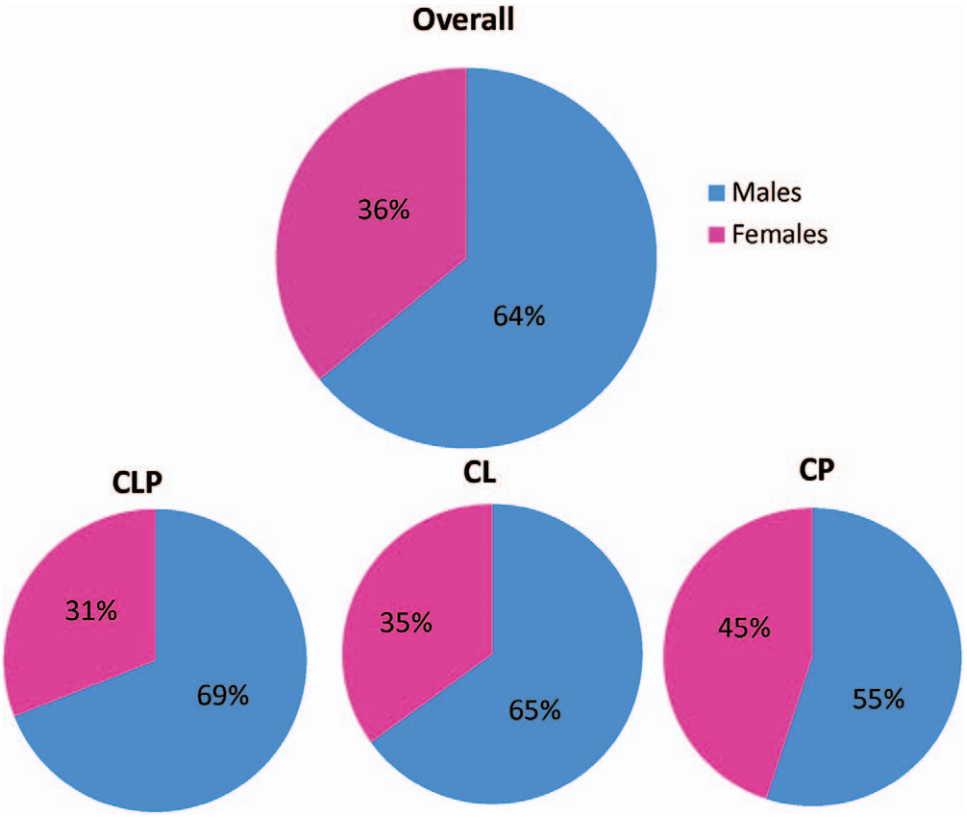

Fig. 4. The percentages of cleft types by gender.

Table 4. Gender, Laterality, and Completeness Ratios by Cleft Type

	Cleft Lip and Palate (*n* = 87,745)	Cleft Palate (*n* = 66,727)	Cleft Lip (*n* = 51,207)	Total (*n* = 205,679)
Male:female ratio	2.22	1.23	1.87	1.74
Unilateral: bilateral ratio	2.00	—	12.71	1.76
Left:right ratio	1.83	—	1.78	1.88
Incomplete: complete ratio	1.35	10.15	1.68	2.29

was twice as high as the rate of unilateral lip repair (0.20%). Among CP repairs, the Von-Langenbeck had the highest complication rate (0.58%), with dehiscence being most commonly reported.

DISCUSSION

The epidemiology of clefting varies with geography and ethnicity. It is widely accepted that China has one of the highest prevalences of clefting, which has remained relatively constant over the study period.[14] Current literature on cleft epidemiology in China has been incomplete as a result of extensive unregistered births, which may be compounded by relatively small sample sizes and limitations of ascertainment methods (Table 1). Data from previous studies were derived from livebirth data, birth defect registries, or hospital records. Although livebirth data are less prone to referral bias than hospital-based data, only 62% of women from rural provinces give birth in a hospital setting.[30] Data derived from birth defect surveillance registries have the advantage of multiple sources of ascertainment; however, the rate of national surveillance coverage in China is less than 40%.[31] A significant portion of the population were excluded from previous studies, thus painting an incomplete picture of the epidemiology of clefting in China. In a previous report by Zhou et al[17] on Smile Train patients treated from 2000 to 2002, a cohort of 7812 patients of which 84.7% were from rural villages were analyzed for demographics, cleft type, associated malformations, and family history. The present study, although also has inherent ascertainment bias and limitations in data collection, is an extension of Zhou's report by 8 more years of data collection and includes at least 25 times more patients than any previous cleft publication. Further, the distribution of patients treated was representative of all provinces in mainland China (excluding Hong Kong, Macau, and Taiwan) (Table 2) and include many rural villages and minority groups.

Table 5. Patient Medical Information

	No.	%
Pregnancy complications		
Yes	3571	1.74
No	197,052	95.81
Do not know	5056	2.46
Birth complications		
Yes	699	0.34
No	200,066	97.27
Do not know	4914	2.39
Mother smoked		
Yes	177	0.09
No	201,141	97.79
Do not know	4361	2.12
Mother consumed alcohol		
Yes	179	0.09
No	201,267	97.85
Do not know	4233	2.06
Family history		
First-degree relative	1504	0.73
Second-degree relative	1319	0.64
Prior cleft-related surgery	73,681	35.82
Associated anomalies	26,285	12.78

One of the challenges of understanding clefting in any region is inconsistent data collection as various classification systems are used, making interpretation and comparison of data difficult. In the present study, surgeons were required to complete information in Smile Train Express, which enabled the collection of consistent and comparable data. We converted anatomic data from Smile Train Express into a more clinically relevant cleft classification of CL, CLP, and CP. There were also limitations in the questionnaire in the range of choices for responses and in gathering detailed information.

The distribution of cleft types in this study population is relatively consistent with other Chinese populations studied. Previous reports, although based on cohorts of less than 10,000, all found CLP as the most common cleft type with a male predominance, which matches the present findings and previous reports in other Asian and white populations.[6,9–24,32–35] Isolated CP was the second most frequent cleft type found in the present study population, which is consistent with 2 previous studies on Chinese populations in which hospital data were analyzed.[8,14] By contrast, previous Chinese studies that used birth defect surveillance systems or livebirth data reported CP as the least common.[9,13,15–17,22] This may reflect underreporting in newborns, as CP is less visible than CL and more likely to go unnoticed for a longer time.

Isolated CP has been shown to have a female predominance in earlier studies including Chinese populations.[6,10,12,13,16–20,22,32–35] In the present study, the male:female ratio for patients with CP was 1.2. Al-

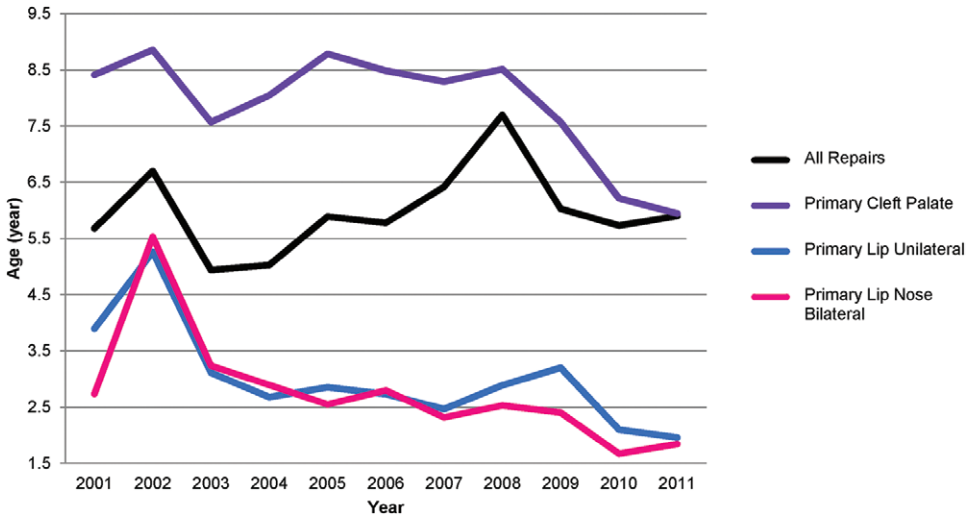

Fig. 5. Average age at primary repair per year.

though lower than the gender ratios of CLP and CL in this study, this is still higher than expected. The higher than expected male:female ratio may be due to female discrimination. Sex-selective abortion has lead to an excess of males in China and less healthcare for females.[36–40] Parents of a female with a cleft are less likely to seek cleft repair than parents of a male with a cleft, and the likelihood is further diminished in cases of CP, which is not visible.

Identifying associated malformations is important for understanding cleft etiology. The reported frequency of associated malformations varies from 1.5% to 63%.[41,42] Few epidemiology studies on clefting in Chinese populations have addressed associated anomalies. The prevalence of malformations of 12.8% in the present study population falls within this range and is much higher than the rates reported by Meng et al[16] (3.6%) and lower than the rates reported by Li et al[18] (14.5%) and Sun et al[21] (30.1%).

It is generally accepted that anomalies occur more frequently in patients with CP than patients with CLP and even less commonly in patients with CL. Some have suggested that more extensive clefts are associated with a higher risk of other congenital defects. In the present study, associated anomalies were most frequent in patients with CLP, followed by CP and then by CL. Although this does not agree with earlier studies, a higher frequency of malformations in patients with CLP has previously been reported in both Chinese and Swedish populations.[16,43] The increased frequency with CLP may be because of increased surveillance with the more visible cleft type. Usually, a small mandible will present with CP, so it is not clear why mandibular anomalies were more prevalent in the present study population who have more associated anomalies with CLP.

Prenatal use of tobacco and alcohol are known teratogens that increase the chances of having a child born with a cleft.[44,45] The majority of patients in this study did not report prenatal use of tobacco (97.8%) or alcohol (97.8%). China is the world's largest consumer of tobacco, with more than 300

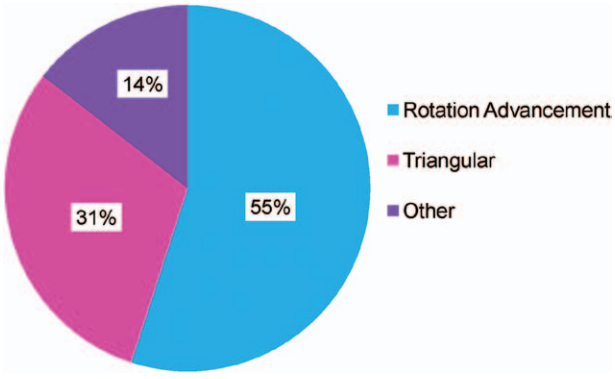

Fig. 6. Techniques preferred by participating surgeons for unilateral lip repair.

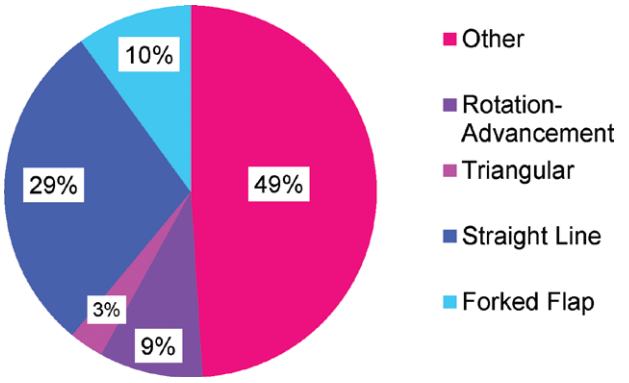

Fig. 7. Techniques preferred by participating surgeons for bilateral cleft lip repair.

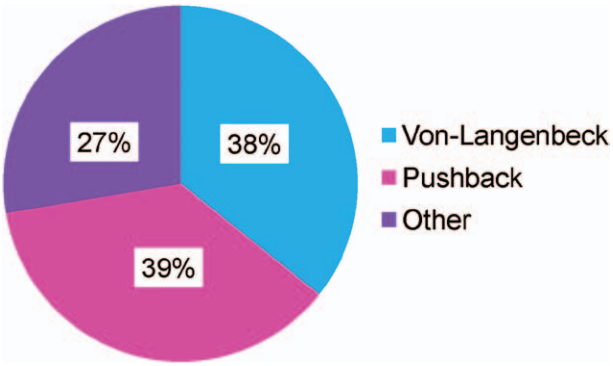

Fig. 8. Techniques preferred by participating surgeons for cleft palate repair.

million smokers; however, only 3.8% of smokers are females. Wang et al[19] also found low prenatal use of tobacco in a Chinese population (2%) and that 28.7% of mothers were exposed to passive cigarette smoke, which has been associated with clefts. Smile Train Express questionnaire did not address secondhand smoking.

Recurrence rates among CLP families range from 3.5% to 5.0% for first-degree relatives and 0.6–0.8% for distant relatives.[46,47] In this study, the recurrence rate was 0.73% among first-degree relatives with little variation among cleft types and 0.64% among distant relatives (Table 5). The low reported recurrence rates may be the result of undetected familial clefts, especially milder cases or a higher environmental contribution.

The average age at primary repair for the present study population is higher than recommended. Possible reasons for later presentation, particularly those living in remote rural provinces, may include lack of medical information, lack of access, long distance to surgical services, and financial constraints. According to a report by UNICEF, 26–60% of Chinese children younger than 5 years are unregistered and, therefore, do not have medical insurance, presenting another barrier to early repair.[48] The age at primary repair has decreased over the study period, suggesting improved access to care or awareness of surgical services.

Numerous surgical procedures for cleft repair have been described. The present study reports commonly used cleft repair techniques by 862 surgeons in China. The preferred technique for unilateral lip repair was rotation-advancement followed by a triangular flap. Advantages of the rotation-advancement technique include flexibility in application, maximal muscle repair, and camouflaged scar.[49] Disadvantages include limited medial element rotation, philtral length, and volume of the advancement flap, which can make closure of wide clefts more difficult. Chinese surgeons surveyed used the same repair techniques for complete and incomplete CL repairs. Although unclear, surgeons in the present study may have used a variation of Millard's rotation-advancement. For bilateral CL repair, "other" was the most frequently reported technique; the Mulliken repair may have contributed to this category.

For CP repair, the most common technique was pushback followed by Von-Langenbeck, and percentages were similar for both complete and incomplete clefts. The pushback has the advantage of lengthening the palate; however, the denuded palatal bone may adversely affect midfacial growth. Also this technique may have a higher rate of fistula formation. Over a quarter of Chinese surgeons surveyed cited "other" as their preferred CP repair technique. The Furlow double-opposing Z-plasty and the Bardach style 2-flap palatoplasty with intravelar veloplasty may have contributed to that category. Future questionnaires should allow better descriptions of the type of repairs so that the results of repair type may be better analyzed.

The described complication rate of 0.36% is significantly low given that the reported incidence of palatal fistulas has been as high as 63%, and respiratory problems are reported to occur up to 45%.[50–52] In the present study, palate repair had the highest rate of complications followed by lip repair, which is consistent with literature on complications of cleft surgery.[53,54] Dehiscence was the most frequent complication among all surgeries (44%) and the most frequent complication of lip repair (57.26%), whereas fistula was most frequent among palate repair (43.53%). The low rate may be explained by the nature of data collection as self-reported complication rates are often underreported. Complications can also occur in the days and weeks following discharge when Smile Train patients return home, and usually, there is little follow-up to assess complications and functional outcome such as velopharyngeal insufficiency.

CONCLUSIONS

To formulate any treatment and management plan, epidemiologic studies are imperative to gauge the impact of oral clefting on the Chinese population and its healthcare system. Much of the epidemiology of clefting in China is based on relatively small sample sizes from incomplete datasets (Table 1). Inherent bias in the present study is that only patients who received repair through Smile Train were included, and therefore, these results may not be truly representative of China. Nevertheless, as the largest reported cohort of Chinese cleft patients, this

study is estimated to represent a notable proportion (6–25%) of the backlog and new oral clefting cases needing treatment in China in the past decade and highlights that clefting is a significant health issue.[29] Furthermore, it fills a gap in the current cleft epidemiology data because many of the low income and rural patients treated by Smile Train were not previously included in reports. It is hoped that this information will aid in the formulation of management plans especially relevant to nongovernmental organizations and serves as a stepping stone for further research investigating the etiology and management of clefting in China.

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