Reconstruction of Congenital Microtia and Anotia: Analysis of Practitioner Epidemiology and Postoperative Outcomes

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Background: Microtia refers to a congenital malformation of the external ear that is associated with a range of functional, psychosocial, aesthetic, and financial burdens. The aim of this study was to analyze the epidemiology and postoperative complication profile of microtia reconstruction.

Methods: A retrospective review was conducted using data from the 2012–2017 the American College of Surgeons National Quality Improvement Program Pediatric databases. Patients with a diagnosis of microtia or anotia were identified using International Classification of Diseases codes. Demographics and postoperative complications were analyzed using Chi-square and t tests for categorical and continuous variables, respectively. Multivariable regression was performed to control for confounding variables.

Results: A total of 466 cases were analyzed, of which 290 (62.2%) were performed by plastic surgeons and 176 (37.8%) by otolaryngologists (ear, nose, and throat physicians [ENT]). Autologous reconstruction was the predominant approach [76.2% of cases (n = 355)] in this cohort. ENT physicians operated on a significantly younger patient population (mean age 8.4 ± 3.2 years versus 10.0 ± 3.2 years, $P < 0.001$) and had higher rates of concurrent atresia/middle ear repair [21.0% (n = 37) versus 3.7% (n = 17)] compared with plastic surgeons. The rate of all-cause complications was 5.9% (n = 17) in the plastic surgery cohort and 4.0% (n = 7) in the ENT cohort ($P = 0.372$). Multivariable regression did not reveal any statistically significant predictors for all-cause complications.

Conclusions: Reconstruction of the external ear for patients with microtia/anotia is a safe procedure, with low rates of postoperative complications, readmissions, and reoperations. Autologous reconstruction remains the preferred modality for repair of the external ear and simultaneous atresiaplasty/middle ear repair does not increase the risk of complications. *(Plast Reconstr Surg Glob Open 2019;7:e2318; doi: 10.1097/GOX.0000000000002318; Published online 19 June 2019.)*

INTRODUCTION

Microtia is a congenital anomaly of the external ear, ranging in severity from complete absence (anotia) to mild defects of the external meatus.[1] The estimated incidence of microtia is 1 in every 7,000–8,000 live births, with a predilection for individuals of Hispanic, Asian, and Native American descent.[2] Although numerous syndromic presentations have been described, the most common presentation (77%–93%) is an isolated, unilateral defect.[3–5] At present, the etiology of microtia is poorly understood, with current research suggesting a contribution of both genetic and environmental factors.[1,6,7]

Over 90% of individuals with microtia also suffer from varying degrees of ipsilateral conductive hearing loss.[8–10] Additionally, malformations of the external ear can interfere with the ability to wear hearing aids or glasses, which is of particular importance given the high incidence of other concomitant craniofacial or ocular abnormalities.[11–13] Furthermore, the social stigma and psychological burden associated with these auricular defects have been shown to negatively impact quality of life.[14–17] Taken together, adequate management of microtia demands substantial time and resources.

Reconstruction of the external ear, which has been shown to improve psychologic and audiologic functioning,[14,15,18,19] is one of the most challenging procedures encountered by plastic surgeons and otolaryngologists (ENT). Currently, reconstructive options are dichotomized into 2 main categories: autologous repair using costal cartilage and alloplastic, implant-based reconstruction, often composed of porous polyethylene.[4] Moreover, a consensus regarding the optimal surgical technique, number of stages, and timing of repair has not yet been described.[20,21]

Various prior studies have reported on the technical considerations, surgical complications, and aesthetic outcomes following microtia reconstruction.[22–40] However, these studies are predominately single-institution projects involving highly trained surgeons with many years of experience, thereby precluding a nationwide assessment of microtia reconstruction outcomes. Likewise, the existing epidemiologic data are limited by similar regional and institutional factors.

The objective of this study is to analyze the postoperative complication profile and epidemiologic characteristics related to auricular reconstruction for microtia using the American College of Surgeons National Quality Improvement Program Pediatric (ACS NSQIP-P) database.

METHODS

Datasets

We conducted a retrospective cohort study using the ACS NSQIP-P database from 2012 to 2017. The ACS NSQIP-P is a nationally validated, multi-institutional surgical outcomes program that collects data on approximately 240 variables, including demographics, preoperative comorbidities, and 30-day postoperative outcomes from over 400 institutions nationwide.[41] The data contained in this cohort are deidentified and available to all institutions adhering to the ACS NSQIP data use agreement. Methods of data collection have been previously described.[41,42]

Cohort Selection

Patients with a primary diagnosis of microtia or anotia at the time of surgery were selected using codes from the International Classification of Diseases, Ninth Revision (ICD-9) or corresponding Tenth Revision (ICD-10; Table 1). Current Procedural Terminology codes were reviewed to assess reconstructive modality (Table 2) and to exclude patients undergoing concurrent operations unrelated to the ear reconstruction. The operative team was then divided into 2 cohorts: plastic surgery (PS) and otolaryngology (ENT).

Variables

We collected and analyzed demographic information, including age, sex, race, and ethnicity. Baselines health characteristics, medical and surgical history, and diagnosis of additional congenital malformations were collected and analyzed. A complete list of variables used in this analysis, along with their corresponding definitions, can be found on the National Surgical Quality Improvement Program website (http://site.acsnsqip.org/).

Table 1. ICD-9 and ICD-10 Codes

Description	ICD-9 Code	ICD-10 Code
Congenital absence of external ear (anotia)	744.01	Q16.0
Congenital hypoplasia of external ear (microtia)	744.23	Q17.2

ICD-9, International Classification of Diseases, Ninth Revision; ICD-10, International Classification of Diseases, Tenth Revision.

Table 2. CPT Codes Corresponding to Reconstructive Modality and Concurrent Auditory Procedure

Description	CPT Code
Autologous reconstruction	
Rib cartilage graft	21230
Ear cartilage graft	21235
Alloplastic reconstruction	
Insertion, non-biodegradable implant	11981
Implantation of auricular prosthesis	21086
Local tissue rearrangement	
Complex tissue repair	13120, 13151, 13152
Adjacent tissue transfer	14040, 14060, 14061
Split thickness skin graft	15120, 15121
Full thickness skin graft	15200, 15220, 15240
Muscle, myocutaneous, or fasciocutaneous flap	15576, 15732
Concurrent auditory procedure	
Reconstruction of atresia	69310, 69320
Tympanoplasty	
Without mastoidectomy	69631, 69632, 69633
With antrotomy	69635, 69637
With mastoidectomy	69641, 69643, 69645
Placement of bone-anchored hearing aid	69714, 69717
Cochlear implant placement	69930

CPT, Current Procedural Terminology.

There are also more than 20 variables related to 30-day postoperative outcomes contained within the NSQIP databases. These variables were used in univariate analysis between cohorts and were aggregated to define several additional outcomes measures. Wound complications include superficial surgical-site infection, deep surgical-site infection, and wound dehiscence. Surgical complications include graft/prosthesis/flap failure, unplanned readmission, and unplanned reoperation. Of note, reoperation as defined as a complication in this study includes only those that were unplanned, and therefore excludes planned, and staged microtia repairs. Medical complications were defined as sepsis, venous thromboembolism, urinary tract infection, and pneumonia. Finally, the aggregate variable "all-cause complications" represents all of those variables included in wound, surgical, and medical complications.

Statistical Analysis

All statistical analyses were performed using IBM SPSS version 24 for Windows (IBM Corp, Armonk, N.Y.). A univariate analysis was performed to assess for unadjusted differences between our 2 cohorts in relation to demographic features, clinical characteristics, perioperative comorbidities, and risk factors, and individual and aggregate postoperative outcomes measures. The Chi-square test was used to assess differences in categorical variables, whereas the 2-sided unpaired t test was used to assess the difference in

means of continuous variables. Statistical significance was defined as $P < 0.05$. A multivariable binary logistic regression was performed to identify independent predictors of all-cause complications and included variables with unadjusted $P < 0.05$ on univariate analysis, and predetermined, clinically relevant variables. An adjusted odds ratio and its corresponding 95% confidence interval were derived for each independent risk factor.

The patient information in this study is deidentified and available to all institutions complying with the ACS NSQIP Data Use Agreement.

RESULTS

General

From 2012 to 2017, a total of 476 cases of interest were initially identified (Fig. 1). There were 10 cases that involved other or con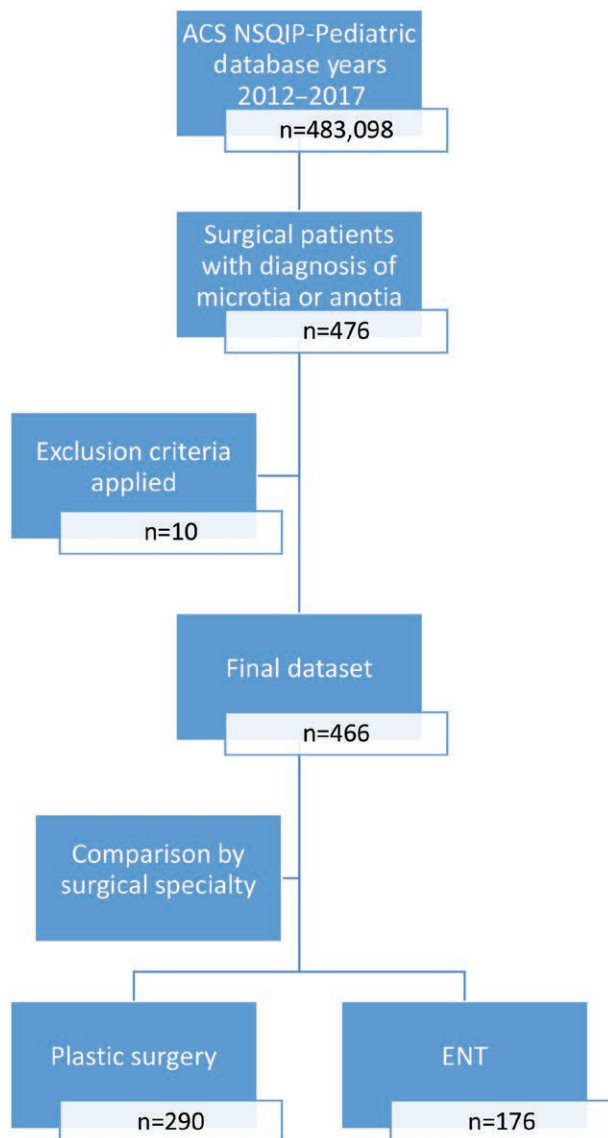current procedures unrelated to auricular reconstruction and, thus, were excluded from analysis. The final cohort contained 466 cases, of which 62.2% (n = 290) were performed by plastic surgeons and 37.8% (n = 176) by otolaryngologists (ENT). Increasing number of external ear reconstruction cases were noted each year (Table 3), which is typically attributed to increased institutional enrollment.[43]

Patient Demographics

The average age of the entire study population was 9.4 ± 3.3 years (Fig. 2), with ENT physicians operating on significantly younger patients compared with plastic surgeons (mean age 8.4 ± 3.2 years versus 10.0 ± 3.2 years, $P < 0.001$; Table 3). Similarly, subjects in the ENT cohort had lower average weight (70.4 ± 36.3 pounds versus 81.0 ± 37.7 pounds, $P = 0.003$) and shorter height (50.0 ± 7.6 inches versus 53.2 ± 7.1 inches, $P < 0.001$) compared with those in the PS cohort. Overall, the study cohort was predominantly male [60.3% (n = 281)] and

Fig. 1. Data extraction strategy.

Table 3. Patient Demographics and Reconstructive Modality

	Plastic Surgery	Otolaryngology	P
No. patients	290	176	
Mean age ± SD, y	10.0±3.2	8.4±3.2	**<0.001**
Sex, n (%)			0.450
Female	119 (41.0)	66 (37.5)	
Male	171 (59.0)	110 (62.5)	
Race, n (%)			0.511
White	162 (55.9)	103 (58.5)	
Black	17 (5.9)	8 (4.5)	
Asian	17 (5.9)	13 (7.4)	
AI or AN	2 (0.7)	3 (1.7)	
NH or PI	7 (2.4)	1 (0.6)	
Unknown/unreported	85 (29.3)	48 (27.3)	
Ethnicity,* n (%)			**0.036**
Hispanic	134 (51.3)	64 (40.8)	
Not Hispanic	127 (48.7)	93 (59.2)	
Mean height ± SD, inches	53.2±7.1	50.0±7.6	**<0.001**
Mean weight ± SD, pounds	81.0±37.7	70.4±36.3	**0.003**
Admission year, n (%)			0.800
2017	65 (22.4)	37 (21.0)	
2016	53 (18.3)	32 (18.2)	
2015	47 (16.2)	21 (11.9)	
2014	43 (14.8)	29 (16.5)	
2013	40 (13.8)	29 (16.5)	
2012	42 (14.5)	28 (15.9)	
Reconstructive modality, n (%)			**<0.001**
Autologous reconstruction	241 (83.1)	114 (64.8)	
Alloplastic reconstruction	4 (1.4)	0 (0)	
Local tissue rearrangement	45 (15.5)	62 (35.2)	
Concurrent auditory procedure, n (%)			**<0.001**
Reconstruction of atresia	11 (3.8)	20 (11.4)	
Repair of middle or inner ear malformation	6 (2.1)	17 (9.7)	

*Some variables have less numbers than the total population because of omitted data.

AI, American Indian; AN, Alaska Native; NH, Native Hawaiian; PI, Pacific Islander. Bold values indicate statistically significant values (p<0.05).
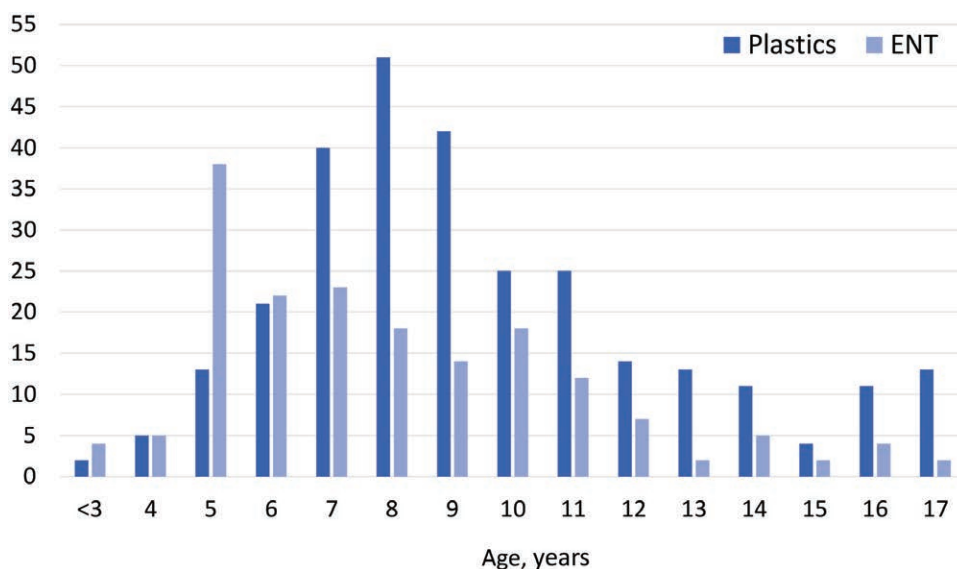
Fig. 2. Distribution of age and time of surgery for ENT and plastic surgery.

Table 4. Comorbidities and Perioperative Risk Factors

	Plastic Surgery	Otolaryngology	P
No. patients	290	176	
ASA classification, n (%)			0.502
1 – No disturbance	119 (41.3)	84 (47.7%)	
2 – Mild disturbance	142 (49.3)	78 (44.3%)	
3 – Severe disturbance	26 (9.0)	14 (8.0%)	
4 – Life threatening	1 (0.3)	0 (0%)	
Presence of additional congenital anomalies*, n (%)	62 (21.4)	23 (13.1)	**0.024**
Premature birth, n (%)	66 (22.8)	37 (21.0)	0.662
Cardiac risk factors, n (%)			**0.017**
None	274 (94.5)	162 (92.0)	
Minor risk factors	11 (3.8)	3 (1.7)	
Major or severe risk factors	5 (1.7)	11 (6.3)	
Asthma, n (%)	14 (4.8)	4 (2.3)	0.165
Developmental delay, n (%)	79 (27.2)	26 (14.8)	**0.002**
Steroid use, n (%)	1 (0.3)	2 (1.1)	0.300
Nutritional support, n (%)	2 (0.7)	2 (1.1)	0.612
Location of procedure, n (%)			**0.016**
Inpatient	135 (46.6)	62 (35.2)	
Outpatient	155 (53.4)	114 (64.8)	
Operative time, min	235.2±142.9	205.8±129.2	**0.026**
Length of stay, d	0.31±1.4	0.11±4.5	0.093

*Excluding congenital anomalies of the external ear.
ASA, American Society of Anesthesiologists.

Table 5. Summary of Concomitant Congenital Anomalies

Classification	No. Diagnoses
No.	127
Craniofacial*, n (%)	83 (65.4)
Other musculoskeletal, n (%)	9 (7.1)
GI/GU, n (%)	9 (7.1)
Auditory, n (%)	8 (6.3)
Metabolic, n (%)	8 (6.3)
Central nervous system, n (%)	5 (3.9)
Unspecified congenital anomaly, n (%)	4 (3.1)

*Excluding congenital anomalies of the external ear.
GI, gastrointestinal; GU, genitourinary.

white [56.9% (n = 265)]. However, the PS cohort had a significantly greater proportion of Hispanic patients [51.3% (n = 134) versus 40.8% (n = 64), $P = 0.036$] compared with the ENT cohort.

Comorbidities and Intraoperative Characteristics

Eighty-five patients (18.2%) in the study cohort had 1 or more concomitant congenital anomaly, in addition to the microtia/anotia (Table 4). Overall, there were 127 diagnoses corresponding to concurrent congenital anomalies, the majority of which were craniofacial malformations [65.4% (n = 83); Table 5]. Patients in the PS cohort had higher rates of additional congenital malformations [21.4% (n = 62) versus 13.1% (n = 23), $P = 0.024$]

and developmental delay [27.2% (n = 79) versus 14.8% (n = 26), $P = 0.002$] compared with the ENT cohort.

Autologous reconstruction was the predominant approach [76.2% of cases (n = 355)] in this cohort, followed by local tissue rearrangement [23.0% (n = 107)] and alloplastic reconstruction [0.9% (n = 4)]. Of note, local tissue rearrangement likely represents a later stage of microtia reconstruction. There were 54 (11.6%) cases of simultaneous external ear reconstruction and atresia/middle ear repair, of which 68.5% (n = 37) were performed by ENT physicians and 31.5% (n = 17) by plastic surgeons ($P < 0.001$). ENT physicians also performed a greater proportion of cases in the outpatient setting [64.8% (n = 114) versus 53.4% (n = 155), $P = 0.016$]. Operative time was significantly longer in the PS cohort (235.2±142.9 minutes versus 205.8±129.2 minutes, $P = 0.026$).

Postoperative Complications and Multivariable Regression

The rate of all-cause complications was 4.0% (n = 7) in the ENT cohort and 5.9% (n = 17) in the PS cohort ($P = 0.372$). No significant differences were noted for any of the postoperative complication variables ($P > 0.05$ for all comparisons; Table 6). Rates of reoperation were also similar between the 2 groups [2.8% (n = 8) in the PS cohort versus 2.3% (n = 4) in the ENT cohort, $P = 0.241$].

Table 6. Postoperative Outcomes

	Plastic Surgery	Otolaryngology	P
No. patients	290	176	
All-cause complications, n (%)	17 (5.9)	7 (4.0)	0.372
Wound complications, n (%)	6 (2.1)	4 (2.3)	0.883
Superficial surgical-site infection, n (%)	5 (1.7)	3 (1.7)	0.987
Deep surgical-site infection, n (%)	0 (0)	1 (0.6)	0.199
Wound dehiscence, n (%)	1 (0.3)	1 (0.6)	0.721
Surgical complications, n (%)	14 (4.8)	5 (2.8)	0.293
Graft/prosthesis/flap failure, n (%)	1 (0.3)	0 (0)	0.435
Unplanned reoperation, n (%)	8 (2.8)	4 (2.3)	0.748
Unplanned readmission, n (%)	8 (2.8)	2 (1.1)	0.241
Medical complications, n (%)	0 (0)	0 (0)	
Sepsis, n (%)	0 (0)	0 (0)	
Deep vein thrombosis, n (%)	0 (0)	0 (0)	
Urinary tract infection, n (%)	0 (0)	0 (0)	

To identify independent risk factors, a multivariate binary regression analysis was performed for all-cause complications (Table 7) and included the following variables: age, sex, surgical specialty, diagnosis of 1 or more additional congenital anomalies, and concurrent repair of auditory defect. The regression analysis did not identify any statistically significant predictors for all-cause complications.

DISCUSSION

Congenital auricular deformities are associated with significant psychosocial, functional, aesthetic, and financial burdens.[9–15,44–48] The treatment of microtia and the concomitant health issues is costly, with reconstruction alone estimated at $17,000 per ear.[33,44] Further, there is substantial psychological morbidity in both children and adults with microtia, including low self-esteem, difficulty with social integration, and high rates of depression and anxiety.[11,12,15,17] Improvement in psychological functioning following successful ear reconstruction is well documented,[14,49–52] thus highlighting the importance of continued investigation into the safety, efficacy, and epidemiology of this procedure.

Prior epidemiologic research into microtia has been predominantly focused on the condition itself,[1,45–47] with little published regarding the demographics of reconstruction specifically. Furthermore, the majority of outcomes research in this arena pertains to aesthetics,[2,23,35–40,53,54] thus creating a dearth of information on the overall safety of this operation. This study employed the ACS NSQIP-P

Table 7. Multivariable Regression Analysis for All-Cause Complications

	OR	95% CI	P
Age, y	1.026	0.905–1.164	0.687
Sex (male)	1.068	0.452–2.525	0.881
Surgical specialty, plastic surgery	1.514	0.600–3.823	0.380
One or more concomitant congenital anomaly	0.597	0.172–2.068	0.416
Simultaneous auditory defect repair*	0.000	–	1.000

*None of the patients undergoing repair of auditory defect experienced any postoperative complications.
OR, odds ratio.

database to provide an assessment of nationally reported demographic characteristics and postoperative complication rates of auricular reconstruction for microtia and anotia.

Overall, our study demonstrates that microtia repair is a safe procedure, with low rates of 30-day postoperative complications, readmissions, and reoperations. Plastic surgeons and ENT surgeons had comparable postoperative complication profiles. Rates of postoperative complications reported in the literature are highly variable, ranging from 0% to 72%,[55] a finding that likely reflects differences in experience with the procedure. Wound infections were the most common complications encountered in our analysis, a finding consistent with prior studies.[55,56]

Importantly, the presence of 1 or more co-occurring congenital anomalies was not associated with an increased risk of postoperative complications. Numerous authors have reported on the difficulty of reconstructing the auricle in patients with concomitant facial asymmetry, as in most syndromic presentations.[34,57–59] However, such cases typically involve more extensive preoperative planning and are often postponed until optimal treatment of the skeletal malformations is complete,[60] which may explain the absence of adverse events in this cohort.

There was a preponderance of male subjects in this cohort, with a male-to-female ratio of 1.51:1. This finding is consistent with the literature, which notes a 20%–40% increased risk of microtia in males compared with females.[1] Similarly, Hispanic ethnicity has been identified as an independent risk factor for the development of microtia.[1,61] The proportion of Hispanic individuals in our cohort was 2.5 times greater than that of the United States general population,[62] thus reflecting prior studies.

Autologous reconstruction using costal cartilage was the predominant approach to microtia repair in our study. This technique, pioneered by Radford Tanzer in 1959[54,63–65] and subsequently refined by Brent,[66,67] Nagata,[38,68–71] Firmin,[72] and Park,[73,74] has remained the preferred method since its inception. After harvesting the rib cartilage, the surgeon carves the auricular framework out of the graft, often using the contralateral (if normal) ear as a reference. The majority of surgeons elect to perform this procedure in 3 stages, although anywhere from 1 to 3 has been reported.[21] Importantly, autologous reconstruction necessitates that patients have an adequate bulk of costochondral cartilage. This anatomical requirement ultimately limits the age at which this operation can be performed, with the majority of surgeons opting to wait until the patient is at least 8 years old.[20] Our analysis is consistent with the literature, as the mean age of subjects was 9.4 years. ENT surgeons, however, operated on a significantly younger patient population. The discrepancy in age between the 2 surgical specialties is possibly explained by the high rate of coexisting auditory abnormalities[8–10,13] and the improved outcomes seen with earlier atresiaplasty.[75] This is also consistent with our analysis, as ENT surgeons performed the majority of the cases involving concurrent atresia or middle ear repair.

Families of patients affected by microtia often request that reconstruction be completed as early as possible, pref-

erably before school begins.[4] The psychosocial impact of auricular deformity has been well documented[12,15] and, importantly, it has been suggested that this may worsen with age.[76,77] Further, as Rutter[78] proposes, psychological morbidity becomes less amenable to external influences as children age, thus increasing the likelihood that certain maladaptive behaviors will become fixed.

Driven in part by the dynamic psychosocial impact of microtia and the steep learning curve associated with autologous reconstruction, there has been a rise in the frequency of alloplastic repair.[20,21] As described by Romo,[79–81] Reinisch,[82,83] Berghaus,[84] Yang,[85] and others, this technique involves a porous polyethylene framework along with a temporoparietal fascial flap. Implant-based reconstruction requires, on average, less stages and shorter operating times than its autologous counterpart and is generally considered to have a gentler learning curve.[21] Additionally, this approach obviates the need for costal cartilage, thereby reducing donor-site morbidity, and, importantly, permitting reconstruction at as early as 3 years of age. Horlock et al.[15] reported improvements in psychosocial outcomes in children following ear reconstruction, with no difference between autologous and alloplastic techniques.

However, alloplastic techniques were initially plagued by high rates of implant exposure and poor long-term outcomes.[86] Although the use of a temporoparietal fascial flap significantly reduced these complications,[2,83] it is likely that the early failures have prevented a major paradigm shift in auricular reconstruction. This is apparent in our analysis with alloplastic techniques accounting for only 0.9% of all reconstructions. As technical refinements continue to yield improved outcomes, rates of alloplastic reconstruction are expected to rise.

Another important consideration in this population is the timing of microtia reconstruction relative to the restoration of auditory function, if needed. Some surgeons, like Tanzer,[65] believed that early efforts to improve hearing would complicate auricular reconstruction at a later point, whereas other surgeons believed just the opposite.[87] Recently, there has been a growing interest in simultaneous repair of the external ear along with atresiaplasty[88,89] or placement of bone-anchored hearing aids.[25] Of the 54 patients in our study, who underwent simultaneous auricular reconstruction and either atresiaplasty, middle ear reconstruction, or placement of bone-anchored hearing aids, there were no postoperative complications.

Limitations to this study are inherent to all analyses using large databases. First, postoperative outcomes are limited to 30 days and, thus, fail to capture potential long-term complications. With respect to auricular reconstruction, outcomes such as graft failure or prosthesis extrusion may arise outside of this 30-day window. Second, the data recorded in the ACS NSQIP-P preclude an assessment of the functional, aesthetic, or patient-reported outcomes of auricular reconstruction, all of which are important aspects of this procedure. Finally, case selection within the ACS NSQIP-P relies on ICD and/or Current Procedural Terminology codes, which may explain the low number of alloplastic reconstructions within our patient population.

Thus, the ability to identify and analyze a subset of this database depends on the precision with which these codes are defined. For example, atresia repair on the contralateral side could not be extrapolated. For this reason, we were unable to assess differences in outcomes between first and later stage ear reconstructions. Furthermore, the decision to undergo reconstruction is partially based on confounders that are not accounted for in NSQIP. This bias could be due to referral patterns, surgeon experience, or case complexity and could impact the number of cases included in this study. Additionally, the rigor with which ICD codes are defined inherently limits an assessment of preoperative illness severity, such as the specific type or classification of the ear deformity. Similarly, the accuracy of data entry and interinstitutional variability in reporting are also important limitations to consider. Although the ACS NSQIP offers a robust dataset from over 400 institutions, all studies utilizing this database are subject to sampling bias; thus, results should not be extrapolated onto a population level.

Nonetheless, this is the first study to use a national database to conduct an analysis of the epidemiologic characteristics and postoperative complication rates for auricular reconstruction. Important future directions of this study include assessment of the socioeconomic characteristics of this patient population and a further cost analysis for microtia reconstruction.

CONCLUSIONS

Auricular reconstruction is a critical component in the management of microtia. Our findings suggest that this is a safe procedure exemplified by low rates of postoperative complications. Autologous reconstruction remains the preferred modality for repair of the external ear. A nationwide epidemiologic analysis informs the demographic composition of this patient population. Overall, these results have implications in the context of resource utilization and patient selection.

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