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# Hand Function in Apert Syndrome

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**Background:** The Michigan Hand Questionnaire is widely used to assess hand outcomes in congenital hand deformities. The purpose of the present study is to compare Apert syndrome hand outcomes according to Upton hand type and age stratification with age-matched unaffected controls.
**Methods:** The Brief Michigan Hand Questionnaire was administered to 39 Apert patients after completion of the digit separation surgical regimen, and 140 age-matched unaffected controls. Patients were divided into 3 groups according to age. In group 1 (from 4 months to 7 years of age), responses were provided by parents of Apert patients, and in group 2 (from 8 to 17 years of age), patients responded with assistance from their parents, and in group 3 (18 years of age or older), responses were provided by the patients themselves. Groups were substratified according to Upton hand type (type I, II, and III). Comparisons were made among groups, subgroups, and controls.
**Results:** Comparisons of hand types for intragroups 1, 2, and 3, did not demonstrate any statistically significant differences ($P > 0.05$) between hand outcomes according to Upton hand type, regardless of patient age. Comparisons between Apert patients and their age-matched controls demonstrated statistically significant differences ($P < 0.05$), as the control group had higher outcome scores.
**Conclusions:** Similar hand outcomes scores were achieved by all Apert patients regardless of hand type. Following completion of the digit separation regimen, Apert patients presented hand outcome scores that were lower than those of the patients in the normative control group. *(Plast Reconstr Surg Glob Open 2019;7:e2230; doi: 10.1097/GOX.0000000000002230; Published online 3 May 2019.)*

## INTRODUCTION

The Michigan Hand Questionnaire (MHQ) is one of the most important and comprehensive instruments used to assess patient outcomes and quality of care. As the MHQ has been translated and validated into 9 languages, including Brazilian Portuguese, it can be used worldwide to assess a variety of hand conditions.[1–3]

The brief format MHQ (bMHQ), which includes 12 items from the standard version MHQ, despite its abbreviated format, is nevertheless able to assess psychometric properties, and can be used to holistically address hand surgery outcomes by providing some of the same data obtained by means of Michigan Hand Outcome (MHO) scores.[4] Apert patients generally experience a wide range of developmental delay issues that may prevent them from appropriately responding to all of the questions that would be present in a long questionnaire. Longer questionnaires are known to result in lower response rates and insufficient data.[5] Usage of the bMHQ, which has a superior rate of responsiveness and feasibility, results in reduced data loss, more complete responses, and decreased patient fatigue while responding.[3,6–8]

Comprehensive assessment of Apert children is necessary to facilitate further discussion with families, improve overall therapeutic planning, and support decision-making regarding the type of surgical regimen that will be adopted in cases of complex congenital hand deformities.[9] Thus, final decisions regarding hand surgery for these young patients need to also be based on parent-reported outcomes, to ensure consideration of important data that young patients may be unable to adequately communicate independently.[9] This is vital in the case of Apert patients.

Upton[10] created a comprehensive clinical classification system that stratifies Apert hand severity according to its clinical features. It should be noted that the MHQ to date has not been used to assess and compare surgical outcomes for the 3 different Upton hand types. According to

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studies involving the MHQ, patients with a greater severity of hand type, generally tend to present lower hand outcome scores than those patients who have a lower severity of hand type.[11]

The purpose of the present study is to describe Apert syndrome hand outcomes according to Upton hand type and age stratification and compare those outcomes with age-matched controls. We hypothesized that Apert patients treated under our surgical regimen would present similar outcome scores, regardless of the severity of Upton hand type.

## PATIENTS AND METHODS

An observational retrospective study was performed by our craniofacial multidisciplinary team on consecutive Apert patients who were treated between 2007 and 2017. Patients were divided into 3 groups according to age: (1) from 4 months of age to 7 years of age, (2) from 8 to 17 years of age, and (3) 18 years of age or older.[12] The 3 groups were substratified into 3 subgroups (for each group) according to Upton classification of hand severity (type I, type II, and type III).

The bMHQ was administered (handed out in paper format) to our 3 groups, to determine the effect of the surgical regimen on hand outcome.[8] In group 1, only the parents of patients responded to the questionnaire; in group 2, patients responded to the questionnaire with the aid of parents located nearby, who assisted them in understanding the meaning of each question; and in group 3, patients responded to the questionnaire, without any outside assistance.

The bMHQ was administered during a 6-month timeframe to all Apert patients whose digit separation and secondary surgeries for deepening the commissures were performed under a specific surgical regimen (no questionnaires were administered until the passage of at least 1 year following completion of the entire surgical protocol for each particular patient).[13] Patients in the 3 groups who responded to the bMHQ were not compensated at any time for their participation in this study.

Patients were excluded if they were unable to respond to the questionnaire due to significant cognitive impairment (groups 2 and 3), for refusing to further participate in the study (groups 1, 2, or 3), or if there was a complete lack of response during the 6-month timeframe referenced above (groups 1, 2, and 3).

An age-matched control group of patients with cleft lip and palate, and unaffected hands, also responded to the questionnaire during the same timeframe.

Demographic (patient gender and age at the time of the operation) and outcome (perioperative and long-term complications) data were verified through medical records and clinical photographs. Data related to the socioeconomic status of both Apert syndrome patients and patients in the control group were also collected and stratified in accordance with the Brazilian Association of Research Companies.

All subjects were enrolled after patient consent (at least 18 years of age) or parental consent (less than 18 years of age) was obtained, in accordance with the Helsinki Declaration of 1975 as amended in 1983. Local institutional research ethics board approval was obtained for this study. Permission to use the bMHQ was granted as per MHQ IR #3372.[14,15]

### Surgical Regimen

Patients with Upton type I and II hands were similarly treated with a 2-stage release using a straight incision with quadrangular dorsal and volar flaps of equal length to create a web space, starting with separation of the second and fourth web spaces as early as possible (ideally at 4 months of age). A second stage was performed to separate the third web space in type I hands, and the third and first web spaces in type II hands. A skin graft was harvested from the lower abdomen. Fourth–fifth metacarpal release was performed as needed to improve thumb opposition and grasp.

Surgical procedures for patients with Upton type III hands were performed in 2 or 3 stages depending on metacarpal and phalanx fusion magnitude and phalanx width, using skin graft tissue from a similar donor region. The first stage was performed to release the first and fourth web spaces, allowing border digits to be released first. After the first operation, we were able to determine whether a 4- or 5-digit hand could be achieved. In stage 2, we released the second or third web space, depending on the phalanx bone fusion magnitude and phalanx width. If the phalanx width was insufficient to provide a 5-digit hand (when compared with the other digits), then we released the third web space and left the second and third digits fused together. Otherwise, we obtained a 5-digit hand after 2 additional operations.[13]

### Statistical Analysis

In the descriptive analysis, the mean and SD were used for metric variables, and percentages were given for categorical variables. Statistical intragroup comparisons were made among the subgroups of hand types of groups 1, 2 and 3, with the aid of the Kruskal–Wallis test (comparison of types I–III in groups 1 and 2), and the Mann-Whitney test for group 3 (comparison of types I and III). Each subgroup and age-matched control group was compared with the aid of the Mann-Whitney test. In addition, outcomes of 4- and 5-digit hands on all patients with Upton type III hands were also compared using the Mann-Whitney test. All analyses were performed using IBM SPSS Version 20.0 (IBM Corp., Armonk, N.Y.). Statistical significance for all analyses was set at $P < 0.05$.

## RESULTS

A total of 39 Apert patients out of 51 patients and 140 unaffected controls responded to the bMHO questionnaire (Table 1).

Intragroup 1–3 comparisons of hand types did not demonstrate statistically significant differences ($P > 0.05$) between hand outcomes according to Upton hand type, regardless of patient age (Table 2).

Comparison between Apert patients and their age-matched controls demonstrated statistically significant

**Table 1. Characteristics of Apert Patients and Control Groups**

| Characteristics | Group 1 (<8 y) | Group 2 (8–17 y) | Group 3 (≥18 y) | Control |
|---|---|---|---|---|
| No. individual n (%) | 23 (59) | 13 (33.3) | 3 (7.7) | 140 (100)* |
| Age at first hand surgery (Mean ± SD) | 15.3±14.4 | 23.5±11.4 | 69.9±86.1 | — |
| Age at questionnaire response (Mean ± SD) | 56.1±24.6 | 134.7±30.9 | 252±31.8 | 249.2±199.0 |
| Gender (%) | | | | |
| Male/female | 33.3/66.6 | 38.4/61.5 | 65.2/34.7 | 36.4/63.5 |
| Upton classification n (%) | | | | |
| Type 1 | 12 (52.1) | 7 (53.8) | 1 (33.3) | — |
| Type 2 | 5 (21.7) | 2 (15.3) | — | — |
| Type 3 | 6 (26) | 4 (30.7) | 2 (66.7) | — |

*Less than 8 y (36 patients); 8–17 y (38 patients); and ≥18 y (66 patients).

**Table 2. Michigan Hand Outcomes Questionnaires Scores for Apert Patients Distributed According to Upton Classification**

| Groups | bMHO (Mean ± SD) | *P* |
|---|---|---|
| Group 1 (<8 y)* | | |
| Type I | 79.34 (62.5–95.83) | 0.144 |
| Type II | 82.08 (75–91.67) | |
| Type III | 86.46 (81.25–91.67) | |
| Group 2 (≥8 and <18 y) | | |
| Type I | 85.12 (79.17–93.75) | 0.396 |
| Type II | 78.13 (70.83–85.42) | |
| Type III | 84.38 (70.83–85.45) | |
| Group 3 (≥18 y) | | |
| Type I | 81.25 | 0.221 |
| Type II | — | |
| Type III | 87.50 (85.42–89.58) | |

*Questionnaire responded by parents.
bMHO, brief format Michigan Hand Outcomes questionnaires.

**Table 3. Michigan Hand Outcomes Questionnaires Scores Comparisons for Apert Patients and Age-matched Controls**

| Groups | bMHO (Mean ± SD) | *P** | *P*† |
|---|---|---|---|
| Group 1 (<8 y) | | | |
| Apert patients | 81.79 (62.5–95.83) | <0.001 | |
| Age-matched controls | 92.77 (66.67–100) | | |
| Group 2 (≥8 and <18 y) | | | |
| Apert patient | 83.81 (70.83–93.75) | <0.001 | |
| Age-matched controls | 95.44 (70.83–100) | | |
| Group 3 (≥18 y) | | | |
| Apert patients | 85.42 (81.25–89.58) | 0.02 | |
| Age-matched controls | 95.08 (64.58–100) | | >0.05 |

*Intragroup.
†Intergroup ($P > 0.05$ for all comparisons).

differences ($P < 0.05$), as the patients in the control group had higher outcome scores (Table 3).

A 5-digit hand was achieved in all 27 patients (100%) with type I and II hands, and in 9 patients (75%) with type III hands. A 4-digit hand was obtained in 3 out of 12 patients (25%) with type III hands. Further comparison between type III hand patients having 4-digit hands, and those with 5-digit hands, resulted in scores of 83.3 for 4-digit hand patients, and 86.8 for 5-digit hand patients; thus, there were no significant statistical differences (Figs. 1–4).

There were no major complications. There were, however, 2 minor complications at the donor sites, in which dehiscence occurred after removal of the sutures. Patients and controls were classified as socioeconomic class C1 as seen in this video (previously published video link) (average family and/or adult patient monthly income of $399 USD).

## DISCUSSION

Acrocephalosyndactyly includes a unique set of craniofacial and hand conditions with a broad clinical spectrum.[16] Studies that address parent- and patient-reported outcomes specifically related to the Apert hand syndrome are limited in number, likely because of the rarity of the syndrome, and the complexity and number of surgeries required to achieve stable and long-lasting separation of the digits. The selection of an established set of metrics to comprehensively assess hand function in a wide variety of hand presentations and neurocognitive status in Apert syndrome patients remains challenging. As we recommend a surgical regimen for Apert syndrome patients that incorporates complex multistaged early reconstruction,[13] it is essential to be able to demonstrate the functional and aesthetic benefits of each of these interventions, to encourage parents to fully commit to a lengthy course of treatment.

Upton[10,17] in his seminal study described not only significant clinical differences among the hand types with regard to the magnitude of bone fusion, but also with the tightness of the soft tissue envelope.

The bMHQ has psychometric properties that enable surgeons to understand the role of varying levels of Apert hand severity on hand outcomes and detect subtle differences between these outcomes according to each hand type. As we previously hypothesized, our data showed that different hand types within the 3 groups did not result in significantly different bMHQ scores after completion of the digit separation surgical regimen. Nevertheless, differences in the scores between the control group and the Apert groups suggest that both patients with Apert syndrome and their parents are able to recognize the existence of continuing functional limitations, such as limited interphalangeal digit movement, which remained following digit separation.

Although symphalangism may function as a protection against secondary healing contractures after surgery, it nevertheless interferes with childrens' daily activities such as buttoning shirts or tying shoelaces. The inability to make a fist and perform free movement in

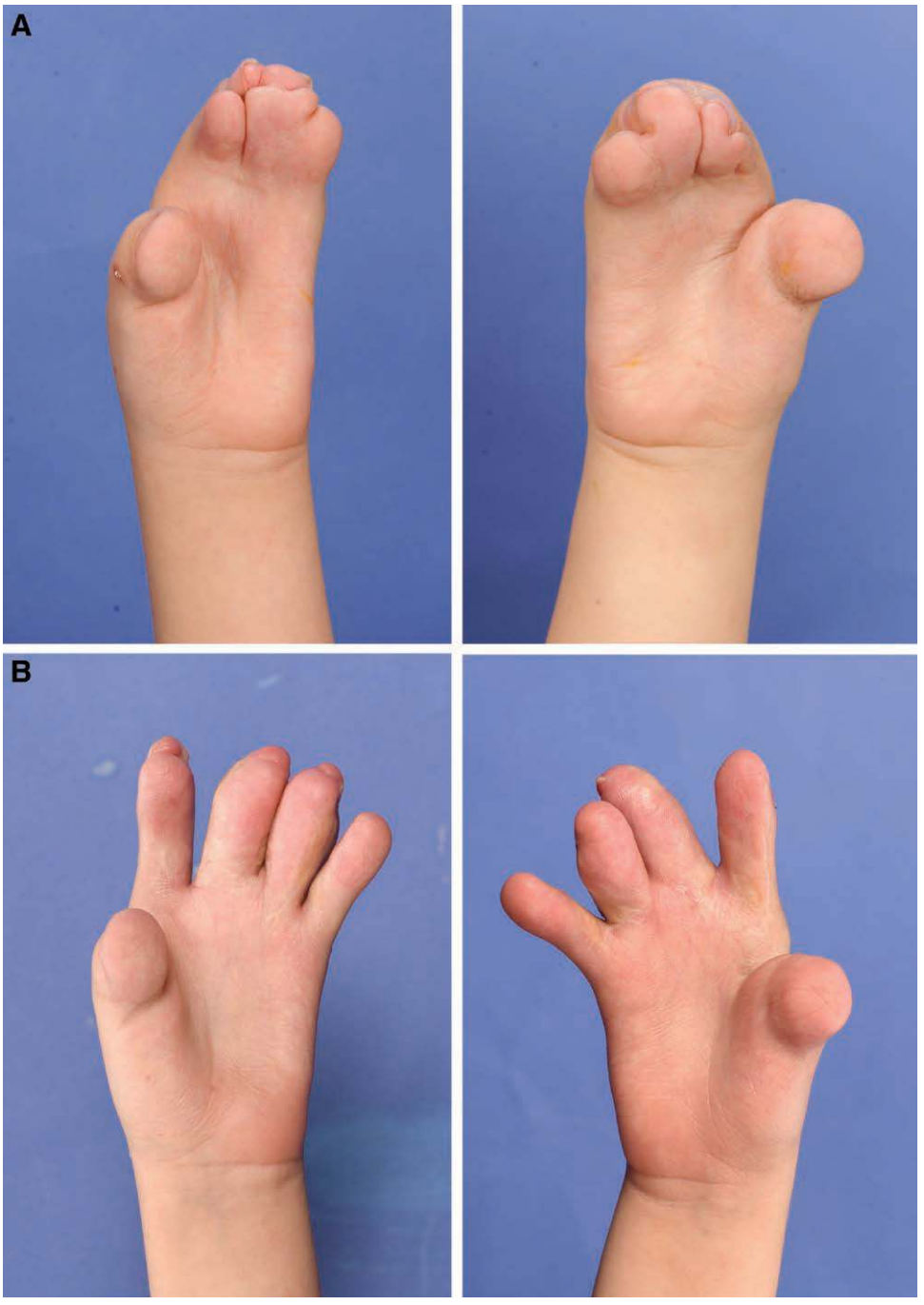


**Fig. 1.** A, Preoperative photographs of a 4-year-old Apert patient with Upton type I hands. B, Postoperative photographs of the same patient at 6 years of age, following completion of a 5-digit release.

the interphalangeal joints are common concerns among patients and their families. Multiple hand scars may also interfere with hand aesthetics, potentially leading to stigma, distress, and social withdrawal by patients and their families. Our Hospital provides cognitive behavioral treatment and support to all craniofacial patients to assist them in improving their coping skills.[18,19] Thus, in our study, both Apert patients and those of the control group with unaffected hands and cleft lip and palate underwent the same cognitive behavior longitudinal approach, which might have positively influenced their hand outcome scores.[20,21]

Contrary to studies suggesting that psychological comorbidities may contribute to lower reported health outcome measures,[22,23] it is our belief that patients in our control group with cleft lip and palate and unaffected hands tend to present higher overall MHO scores than healthy individuals without cleft and/or craniofacial deformities, possibly because these patients are focused on craniofacial appearance, and tend to overlook any minor hand problems. At

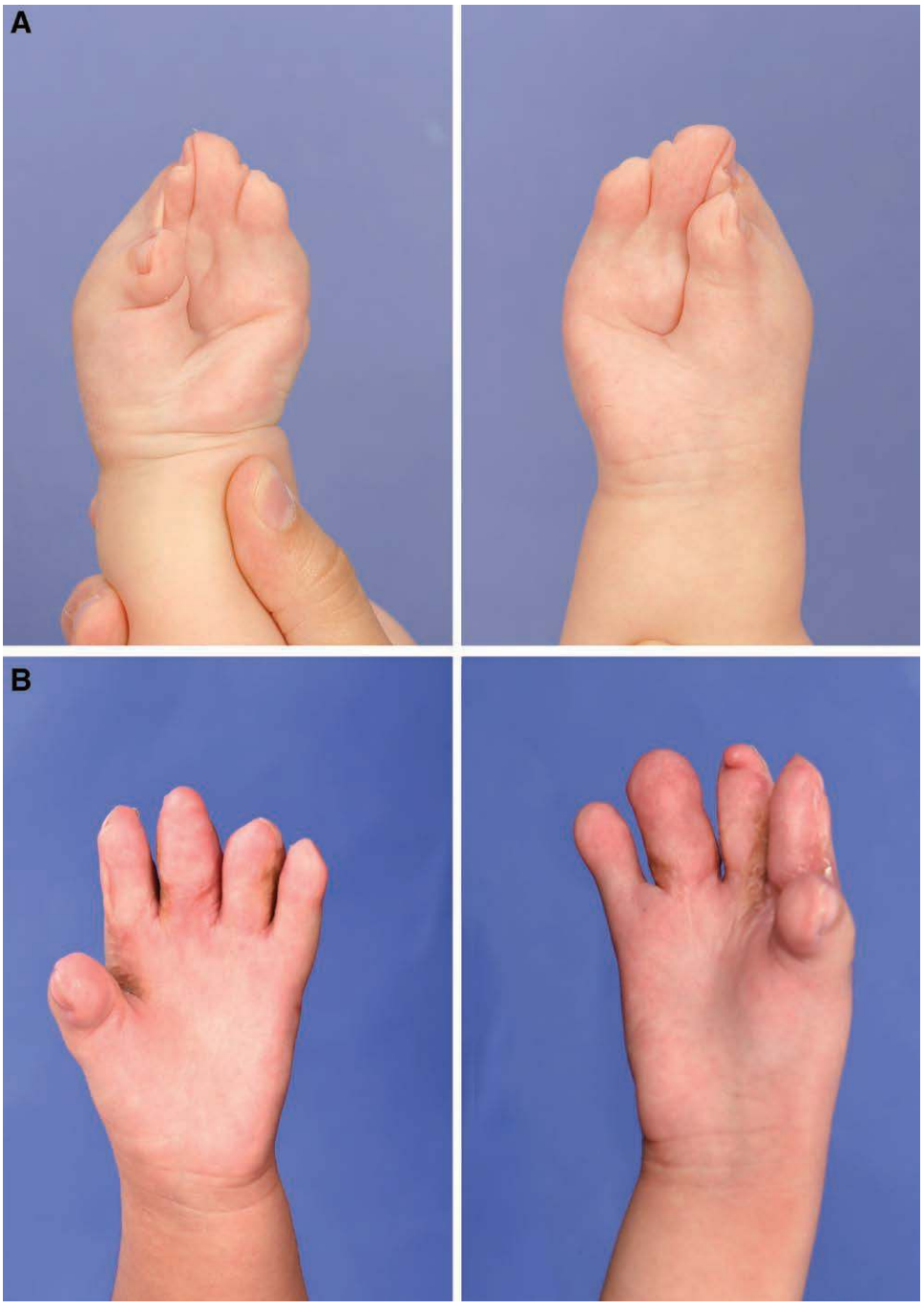


**Fig. 2.** A, Preoperative photographs of a 1-year-old Apert patient with Upton type II hands. B, Postoperative photographs of the same patient at 2 years of age.

our Hospital, patients under our longitudinal and comprehensive multidisciplinary care are carefully monitored for depression and anxiety behaviors; the presence of which can also lower the overall bMHO scores.[23] Having normative data regarding patients with craniofacial deformity and unaffected hands who have acquired similar coping skills may mitigate any of the psychological factors that can lower the bMHO scores[24] and skew the comparative results between Apert patients and the controls.

All of our patients in this study presented congenital craniofacial conditions, and were treated at the same hospital, by the same team, under the Brazilian public health care system, thus our study was performed under conditions of limited diversity. As our study was focused on hand outcomes in Apert syndrome patients whose digit separation regimen had been completed, this resulted in a well-defined target population to be studied, along with their age-matched controls.

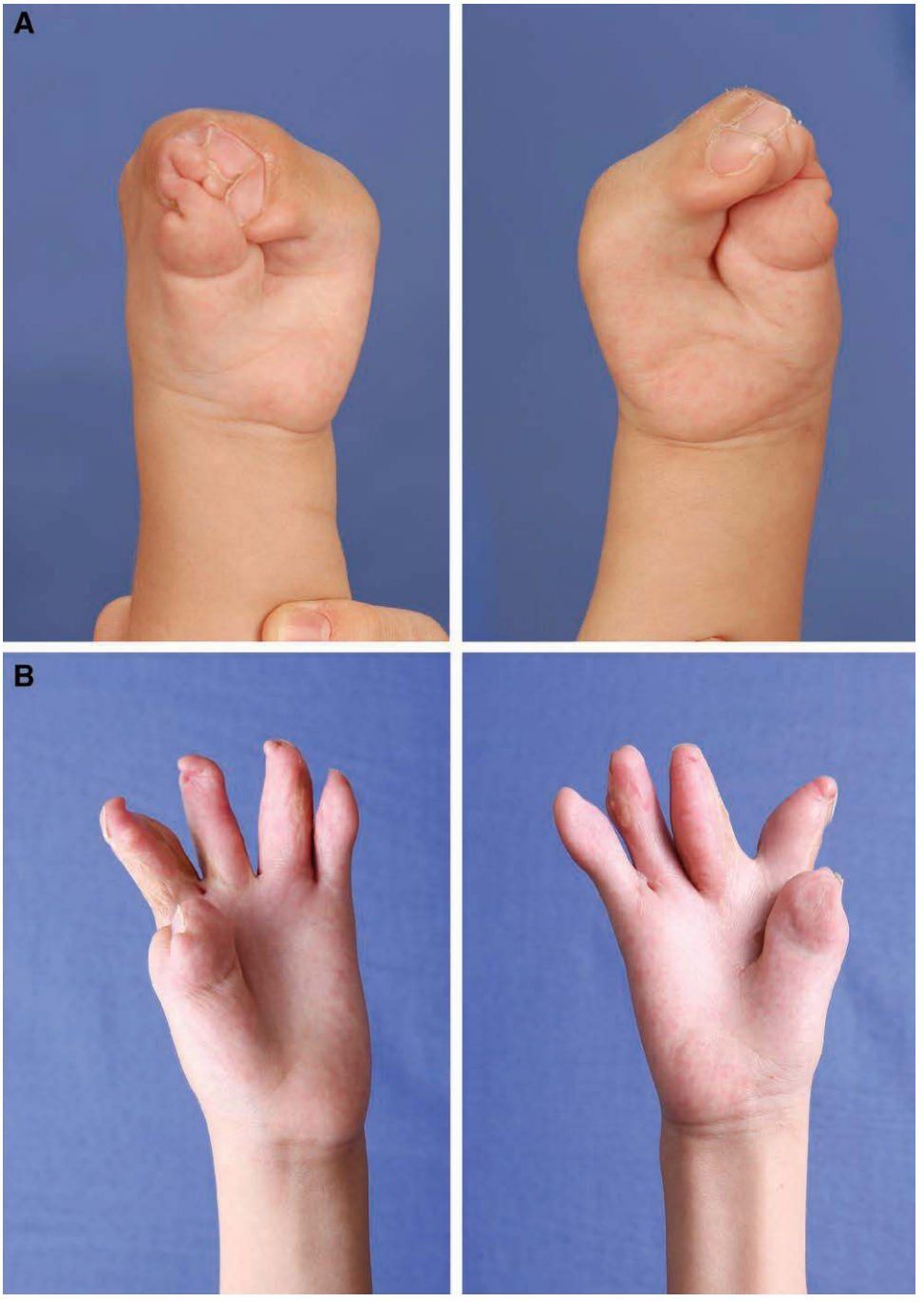


**Fig. 3.** A, Preoperative photographs of a 3-year-old Apert patient with Upton type III hands. B, Postoperative photographs of the same patient at 8 years of age.

In Brazil, children do not begin to become literate until 7 years of age, and for this reason, group 1 was limited to children 7 years of age or younger. Questionnaires provided to children younger than 8 years of age do not result in accurate and meaningful information, because of the limited cognitive and linguistic ability of children within this age group.[12] Thus, information regarding outcomes for this age group should be based on parent-reported outcomes.

The vast majority of our patients' parents want their children to have two 5-digit hands, and this is the major reason that these parents are willing to come to our Hospital from all over the country. As our surgical regimen consistently results in a 5-digit hand for all patients with Upton type I and II hands, and for the majority of patients with type III hands, along with free digit movement and the ability to pinch and grasp objects, parents in our study tended to present high bMHQ scores. These positive re-

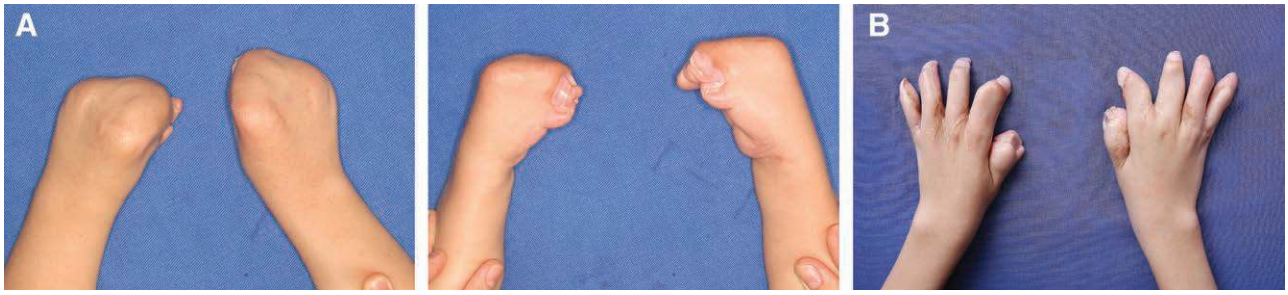


**Fig. 4.** A, Preoperative dorsal and lateral views of the same patient. B, Postoperative dorsal view of the same patient at 8 years of age.

sults can encourage other parents to adhere to a digit separation treatment regimen, and also create awareness of the remaining limitations with which these patients may have to cope during their entire lives.

Our study showed that patients with type III hands presented similar outcome scores to patients with type I and II hands, regardless of whether 4- or 5-digit hands were achieved. Further comparison of hand outcome scores between Upton type III hands with 4 digits and with 5 digits, after the end of the digit separation regimen, showed no significant statistical differences. It is noteworthy that Upton type III hands with 4 digits were the most severe hands in our series due to the magnitude of bone fusion and tightness of the soft-tissue envelope. In this particular group of patients, a 5-digit hand could not be achieved, despite our best efforts. Preoperatively, patients with Upton type III hands cannot pinch or grasp objects with one hand, and need to use both hands to grasp an object. After completing a surgical regimen, patients and parents tend to deeply appreciate any functional gain, resulting in high MHO scores.

Our study is not without limitation. We only evaluated the hand outcomes at one period of time, and patients and their parents were not given the questionnaire preoperatively. As we operated on patients at an early age, limited hand function is to be expected, due to an immature brain cortex.

We did not use objective measurements to assess hand function impairment, nor did we use other hand outcome questionnaires. We anecdotally observed that a patient's hand deformity did not directly correlate with that patient's overall hand mobility, as Apert patients had varying levels of manual dexterity despite physically observable deficits. We used only the bMHQ as it has unique properties that can assess and detect differences between treated Apert patients and the control group. In addition, it has been translated and validated for Brazilian Portuguese.[2,3] Standard objective measurements are limited in this patient population, as these patients were not able to freely move and flex their digits preoperatively. Another limitation of our study is the small sample size used to support conclusions regarding hand function among the groups of different Apert hand types. Even though the sample size of the control group was large enough to detect statistical differences between Apert hands and the control group, when we substratified our Apert cohort among the 3 different Upton hand types, only a small number of each type was available for comparison. It is possible that with a larger cohort, differences in hand dexterity among the Upton subtypes may be shown, especially in those patients with severe type III hands.

Despite the aforementioned caveats, this is the first study in the literature to offer specific data regarding hand outcomes for Apert patients, and it utilizes one of the largest Apert patient cohort groups that have completed a surgical regimen.

## CONCLUSIONS

Similar bMHQ outcome scores were achieved by all Apert patients who completed our digit separation surgical regimen, regardless of hand type. Additionally, these Apert patients presented lower hand outcome scores than the normative control group.

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