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# Efficacy and Safety in Combining Primary Palatoplasty and Myringotomy in Patients with Cleft Palate

Esperanza Mantilla-Rivas, MD*
Ishwarya Mamidi, BS*
Alex Rokni, BS*
Ashleigh Brennan, BS*
Md Sohel Rana, MBBS, MPH†
Agnes Goldrich, BS*
Monica Manrique, MD*
Monica Shah, MD‡
Brian K. Reilly, MD§
Gary F. Rogers, MD, JD, LLM, MBA, MPH*
Albert K. Oh, MD*

**Background:** Patients born with a cleft lip and palate undergo multiple surgical procedures, increasing the infants' exposure to anesthesia and potential risk of neurocognitive delays. In addition, these numerous procedures lead to greater use of hospital resources. This study analyzes the differences in anesthetic exposure and perioperative characteristics between performing combined versus separate primary palatoplasty (PP) and placement of bilateral myringotomy tubes (BMT).
**Methods:** We reviewed patients younger than 2 years who underwent PP and BMT at our institution from June 2014 to January 2019. Patients who underwent PP and BMT during the same admission (combined group = 74) and during separate admissions (separate group = 26) were studied. Due to the small sample size in the separate group, additional data for this group were gathered by propensity score matching by gender, race, and American Society of Anesthesiology class. Statistical analyses were carried out to identify significant differences between the 2 groups. Linear regression was performed to compare perioperative variables.
**Results:** One hundred patients met the inclusion criteria. There were no significant differences in demographic characteristics or American Society of Anesthesiology class, surgery and anesthesia duration, dosage of intraoperative dexmedetomidine, hospital length of stay, and perioperative complications ($P > 0.05$). Per contra, combined group had significantly lower intraoperative dosages of fentanyl ($P = 0.01$) and shorter postoperative care unit stay ($P = 0.047$).
**Conclusions:** This study documents decreased postoperative care unit time and anesthesia drug exposure without increased length of stay or perioperative complications in patients undergoing combined PP and BMT. These results support combining PP and BMT to reduce exposure to potentially neurotoxic medications and to increase efficient utilization of hospital resources. *(Plast Reconstr Surg Glob Open 2020;8:e2824; doi: 10.1097/GOX.0000000000002824; Published online 27 May 2020.)*

## INTRODUCTION

Cleft lip and palate (CLP) are among the most common congenital malformations.[1] Patients with CLP have higher rates of health complications such as speech delays, behavioral disorders, failure to thrive, otitis, hearing loss, and dental anomalies, for which they undergo numerous surgical procedures.[2–4] Although operative treatment has been proven to be beneficial for these patients, there are increasing concerns about higher exposure to general anesthesia and its association with abnormal neurocognitive development.[5]

A common comorbidity seen in children with CLP is recurrent otitis media, with a reported prevalence of 97%, primarily due to concomitant eustachian tube dysfunction.[6–8] When left untreated, chronic ear dysfunction often causes atrophy and scarring of the tympanic membrane, resulting in conductive hearing loss.[9] Thus, in an effort to improve speech and audiologic outcomes, patients with CLP are often treated with bilateral myringotomy and tube (BMT) insertion. Previous literature has described the benefits of an early intervention. Specifically, Hubbard et al[10] found that children with cleft palate who underwent early BMT at the age of 3 months, in comparison to children with cleft palate who underwent BMT at the age of 30.8 months, performed better on hearing examinations.

*From the *Division of Plastic and Reconstructive Surgery, Children's National Hospital, Washington, D.C.; †Joseph E. Robert, Jr., Center for Surgical Care, Children's National Hospital, Washington, D.C.; ‡Division of Anesthesiology, Children's National Hospital, Washington, D.C.; and §Division of Anesthesiology, Department of Otolaryngology, Children's National Hospital, Washington, D.C.*

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Additionally, children in the early intervention cohort were found to have greater consonant articulation.[10]

Previous studies have shown that combining common procedures results in decreased length of surgery, anesthesia exposure, and hospital costs. Recent literature in the cardiac field has reported shorter anesthesia, shorter procedure duration, and shorter length of stay (LOS).[11,12] In patients born with CLP, BMT and palatoplasty (PP) can be performed concomitantly, theoretically decreasing exposure to anesthesia. There is a paucity of plastic surgery literature objectively assessing the efficacy of performing concomitant surgeries with regards to such factors as surgical outcomes, morbidity, total operative time, LOS in the post-anesthetic care unit, and anesthesia dosages administered. Thus, the objective of this study was to analyze differences between operative and postoperative parameters, as well as outcomes in patients who underwent combined or separated BMT and PP procedures at a single tertiary care institution in hopes of understanding the risks or benefits associated with combining surgeries.

## METHODS

Following institutional review board approval, we retrospectively reviewed the charts of all patients who underwent primary PP and placement of BMT at Children's National Medical Center from June 2014 to January 2019. The information recorded from all cases included demographic characteristics, indications for PP and BMT, American Society of Anesthesiology (ASA) classification, surgical technique for PP, surgical time, total anesthesia time, type of anesthetic agent(s) and dosages used, time in the postanesthetic care unit (PACU), length of hospital stay, and surgical complications within 30 days (eg, infection, fistula, bleeding). This information was documented in a standardized database using Microsoft Excel (2016; Microsoft Corp, Redmond, Wash.) for Windows.

We included patients who underwent PP with BMT before the age of 2 years. Patients were excluded if they had revision or secondary PP, if they underwent unilateral myringotomy and ear tube insertion, or if they had another procedure done simultaneously. The procedures were performed by either 1 of 2 plastic surgeons (A.K.O. or M.J.B.) for PP and 1 otolaryngologist (B.R.) for BMT.

Patient data were queried and classified into 2 groups: combined group (CG), with patients who underwent combined PP and BMT placement, and separate group (SG), which comprised patients who had both procedures in separate settings. Due to the small sample size in the SG, additional data for this group were gathered by propensity score matching 22 patients (11 paired patients) who had undergone BMT or PP matching by gender, race, and ASA risk.

### Statistical Methods

Summary statistics for continuous variables were presented as medians with interquartile ranges (IQR), and categorical variables were presented as frequencies with percentages. The baseline characteristics between separate and combined surgery groups were compared using Wilcoxon–Mann-Whitney test for continuous data and chi-square test or Fisher's exact test (if any of the expected cell counts were less than 5). We compared total anesthesia duration, PACU duration, and anesthetic drugs doses separately between 2 surgical groups using multivariable linear regression, adjusting for the potential confounder age, gender, weight, type of PP, and dose of anesthetic drugs. Confounders were included in the regression model if they were significant at the 0.05 level or if they altered the coefficient of the primary predictor variable, type of surgery, by more than 10%.[13] LOS and incidence of complication were compared using Wilcoxon–Mann-Whitney test and binomial proportion test, respectively. Shapiro-Wilks test and graphical assessments (histogram and qq plot) were used to check the normality assumption. Reported *P* values were 2-sided.

Our study had a statistical power of 80% to detect a large effect size (0.8) between the 2 groups of surgery at the level of $\alpha = 0.05$. Power analysis was done using GPower 3.1 software,[14] and all other statistical analyses were performed with Stata software, version 15.1 MP (Stata Corporation, College Station, Tex.).

## RESULTS

A total of 100 patients met the inclusion criteria. There were 74 patients in the CG, while the SG comprised 26 patients (4 who had both surgeries in separate setting and 11 paired patients whose data were gathered using propensity score matching, counted as a total of 15 sets). The majority of patients were men (53.9%). All patients underwent PP at a median (IQR) age of 10.6 (10.06–12.16) and 12.8 (9.7–14.8) months for CG and SG, respectively ($P = 0.19$). A portion of patients (56.1%) had isolated cleft palate (complete = 15; incomplete = 35), 39 (43.8%) patients had CLP for which 13 (33.3%) were bilateral and 26 (66.7%) unilateral. Fifteen patients had a syndromic diagnosis including Stickler syndrome (n = 4), Van der Woude syndrome (n= 2), 22q11.2 deletion syndrome (n = 1), Culler-Jones syndrome (n = 1), SATB2-associated syndrome (n = 1), Kabuki syndrome (n = 1), caudal regression syndrome (n = 1), 1q22 micro duplication (n = 1), and unknown cause or other chromosomal abnormality (n = 3). The demographic variables between the 2 groups were not significantly different. A summary of patients' demographics and ASA classification between the 2 groups is presented in Table 1.

The type of PP was performed upon the surgeons' discretion. The majority of patients underwent a modified 2-flap PP with V-Y pushback and intravelar veloplasty (n = 79), and the remaining underwent Furlow PP (n = 10). Fisher's test suggested statistically significant difference (*P* value, 0.008) in regards to type of PP between CG (2 flap PP n = 69, Furlow n = 5) and SG (2 flap PP n = 10, Furlow n = 5).

Intraoperative dosage of fentanyl was statistically significantly different for CG and SG. Mean dosage of fentanyl for CG was 2.9 μg/kg (IQR 2.6–3.2) versus 4.0 μg/kg (IQR 3.3–4.7) for SG ($P = 0.01$). Mean dosage of propofol was lower in the CG versus the SG groups, with 3.1 mg/kg

(IQR 2.7–3.5) versus 4.2 mg/kg, though this difference did not reach statistical significance (IQR 3.2–5.2) ($P$ = 0.057). No statistically significant differences were found regarding the intraoperative dosage of dexmedetomidine; mean 1.4 µg/kg (IQR 1.1–1.6) versus 1.5 mg/kg (IQR 0.9–2.0) for CG and SG, respectively ($P$ = 0.68).

Mean LOS in PACU was 184.3 ± 20.8 minutes for CG and 237.4 ± 46.4 minutes for SG ($P$ = 0.04). Five patients (CG, n = 5 versus SG, n=0; $P$ = 0.58) were admitted directly to the pediatric intensive care unit as a precautionary measure for known comorbidities or for airway monitoring. Mean total LOS was 1.0 days (1.0–1.0 days) for CG and 1.0 days (1.0–2.0 days) for SG ($P$ = 0.82); all BMT procedures done separately from PP were performed on an outpatient basis. Perioperative variables are summarized in Table 2.

Patient follow-up ranged from 30 days to 5.57 years, with a mean of 1.62 years for CG, and 91 days to 4.88 years, with a mean of 1.88 years for SG ($P$ = 0.49). Eight patients had a postoperative complication. Complication rate was 8.1% for CG and 20% for SG ($P$ = 0.173.). Patients with an underlying syndromic diagnosis had higher complications, though this did not reach statistical significance (20% versus 8.1%; $P$ = 0.173). One patient with a history of syndromic cleft palate and intraventricular hemorrhage was admitted to the pediatric intensive care unit for postoperative monitoring. During his stay, the patient presented with urinary tract infection and phlebitis secondary to an intravenous peripheral catheter placement. The patient was admitted for 12 days and completed 14 days of antibiotic therapy (ceftazidime and clindamycin) at home via peripherally inserted central catheter line. Two patients were admitted to the emergency department. One patient with a history of Robin sequence was admitted at postoperative day (POD) 3 for poor postoperative (PO) intake and urinary output and respiratory distress. The patient was diagnosed with a viral infection and was discharged the same day. The other patient had a history of Stickler syndrome. He was readmitted to the hospital on POD 2 for decreased PO intake and dehydration, which required pain management and fluid resuscitation. Three additional patients presented at plastic surgery follow-up with postoperative palatal fistula. The remaining complications (n = 2) had ear tube blockage due to otorrhea. Out of the 89 patient who underwent BMT, 20 patients in CG and 5 patients on the SG required a second trip to the operating room for a second set of tubes ($P$ = 0.753).

## DISCUSSION

The results from this study supported a strong initiative to implement and continue multidisciplinary approaches to treat patients with CLP, as patients with CLP have higher risk for undergoing multiple surgical procedures within the first years of life.[15,16] The patients in the CG were exposed to significantly less intraoperative fentanyl and required a shorter stay in the PACU. The potential neurotoxicity of general anesthesia on early cerebral development is controversial, with numerous studies both supporting and refuting any clinically significant effect on later cognitive function. Nevertheless,

**Table 1. Baseline Patient Characteristics Stratified by Type of Surgical Procedures**

| Variable | Combined Group (n = 74) | Separate Group (n = 15)* | P† |
|---|---|---|---|
| Palatoplasty | | | |
| Age, mo, median (IQR) | 10.6 (10.6–12.16) | 12.8 (9.7–14.8) | 0.19 |
| Weight, kg, median (IQR) | 8.5 (7.7–9.7) | 9.4 (8.2–9.9) | 0.12 |
| BMT | | | |
| Age, mo, median (IQR) | 10.6 (10.6–12.19) | 13.36 (10.3–16.13) | 0.40 |
| Weight, kg, median (IQR) | 8.5 (7.7–9.7) | 9 (8.6–10.1) | 0.16 |
| Gender, n (%) | | | 0.78 |
| Male | 38 (51%) | 10 (67%) | |
| Female | 36 (49%) | 5 (33%) | |
| Race, n (%) | | | 0.25 |
| African American | 13 (18%) | 1 (7%) | |
| Asian | 11 (15%) | 0 (0%) | |
| Caucasian | 28 (38%) | 6 (40%) | |
| Hispanic/Latino | 13 (18%) | 4 (27%) | |
| Others | 9 (12%) | 4 (27%) | |
| ASA classification, n (%) | | | 0.39 |
| 1 | 13 (18%) | 2 (13%) | |
| 2 | 55 (74%) | 10 (67%) | |
| 3 | 5 (7%) | 3 (20%) | |
| 4 | 1 (1%) | 0 (0%) | |
| Veau classification, n (%) | | | 0.028 |
| 1 | 31 (42%) | 3 (20%) | |
| 2 | 12 (16%) | 6 (40%) | |
| 3 | 18 (24%) | 6 (40%) | |
| 4 | 13 (18%) | 0 | |
| Palatoplasty | | | 0.008 |
| Two flap palatoplasty with intravelar veloplasty | 69 (93%) | 10 (66.6%) | |
| Furlow palatoplasty | 5 (7%) | 5 (33.3%) | |
| Syndromic | | | 0.27 |
| No | 63 (85%) | 11 (73%) | |
| Yes | 11 (15%) | 4 (27%) | |

Wilcoxon–Mann-Whitney test, $t$ test, and Fisher's exact test were performed between combined group and separate group.
*A total of 26 patients were analyzed: 4 patients had both surgeries in separate setting, while the remaining 22 (11 paired) patients were paired using propensity score matching. Counting as a total of 15 sets.
†$P$ < 0.05 was consider statistically significant.

**Table 2. Comparison of Perioperative and Anesthetic Characteristics by Surgery Procedure**

| Variable | Mean (95% CI) Combined (n = 74) | Mean (95% CI) Separate (n = 15)* | Difference (95% CI) | P† |
|---|---|---|---|---|
| Surgery duration, min | | | | |
| Palatoplasty | 92.5 (87.7–97.3) | 91.7 (80.2–103.2) | −0.8 (−13.4 to 11.8) | 0.90 |
| BMT | 6.0 (5.4–6.5) | 6.3 (5.1–7.6) | 0.3 (−1.0 to 1.7) | 0.61 |
| Anesthesia duration, min | 164.6 (157.8–171.5) | 178.0 (160.8–195.0) | 13.3 (−5.7 to 32.3) | 0.17 |
| PACU duration, min | 184.3 (163.5–205.0) | 237.4 (191.1–283.8) | 53.2 (1.5–104.8) | 0.04 |
| Anesthetic dosage | | | | |
| Propofol, mg/kg | 3.1 (2.7–3.5) | 4.2 (3.2–5.2) | 1.1 (−0.03 to 2.2) | 0.057 |
| Fentanyl, µg/kg | 2.9 (2.6–3.2) | 4.0 (3.3–4.7) | 1.1 (0.26 to 1.8) | 0.01 |
| Dexmedetomidine, µg/kg | 1.4 (1.1–1.6) | 1.5 (0.9–2.0) | 0.1 (−0.5 to 0.7) | 0.68 |
| Length of stay, d, median (IQR) | 1.0 (1.0–1.0) | 1.0 (1.0–2.0) | | 0.82 |
| Complications, % | 8.1 | 20 | | 0.17 |

*A total of 26 patients were studied: 4 had both surgeries in separate setting, and data were gathered for 22 (11 paired) patients using propensity score matching, counted as a total of 15 sets.

†$P < 0.05$ was considered statistically significant. *P* values were obtained from multivariable linear regression, Wilcoxon–Mann-Whitney test, and binomial proportion test.

recurrent procedures and exposure to general anesthesia have been shown to potentially pose deleterious effects on the proper neurocognitive development of children.[17,18]

The American Academy of Pediatrics has recently heralded the potential for impaired development from repetitive or prolonged use of anesthetics in children under the age of 3 years.[19] This directly addresses patients with CLP because most of them undergo cheiloplasty and/or PP between 6 and 12 months after birth in an effort to optimize feeding and speech outcomes.[20] Conrad et al[21] found that recurrent exposure to anesthesia can result in impaired cognitive growth and frontal lobe development. Additionally, they observed that pediatric patients with an isolated cleft lip who underwent several procedures were more likely to present with decreased verbal intelligence quotient (IQ). These patients with isolated cleft lip and a low verbal IQ were found to have a higher frontal lobe volume. Interestingly, no significant relation between regional brain volume and anesthesia exposure was found in patients with CLP.[21] Likewise, other groups have reported impaired brain development, manifesting as deficits in language development, cognitive abilities, and brain volume.[5,17,18,22] The results from these studies further emphasized the importance of minimizing anesthesia time, as well as the dosage of administered medications. In 2009, Wilder et al[23] performed a large-scale retrospective analysis studying the incidence of behavioral, learning, or developmental problems in children with prolonged or repeated exposure to anesthesia. Data demonstrated that there was a 2-fold increase in the rate of these problems when compared to children without anesthesia administration.[23] There has also been increasingly new evidence that shows the effect of anesthesia on neonatal neurotoxicity in rodents. In a review of 55 rodent studies and 7 primate studies, apoptosis in the nervous system was found after exposure to anesthesia.[24]

On the other hand, a number of studies, most notably the Pediatric Anesthesia Neurodevelopment Assessment (PANDA) study in 2016, demonstrated that healthy children under the age of 3 years with a single anesthesia exposure, in comparison to their healthy sibling with no exposure to anesthesia, did not have any statistically significant difference in IQ when assessed later in childhood.[25] Additionally, the general anesthesia and awake-regional anesthesia in infancy (GAS) study found compelling evidence that less than 1 hour exposure to sevoflurane anesthesia during infancy has no risk of neurodevelopmental outcomes at the age of 2 years.[26] However, there are limited data on neurocognitive impacts of anesthesia on patients with repeated or prolonged exposure.[25]

In an effort to reduce exposure to anesthesia, as well as reap other potential benefits, combining surgical procedures across multiple specialties may prove to increase efficiency, decrease anesthesia administration, and improve cohesiveness of care.[27–30] Combining procedures may prove to be more cost-effective and may decrease the burden on families. Additional benefits with regards to cost-effectiveness and financial burdens may further be studied for its efficacy in long-term health and financial implications for a holistic review of the potential benefits to this approach. As reported by Balraj et al,[27] additional benefits such as reduced hospital resource utilization, missed school and workdays, and overall financial burden for both the institution and the patient may be encountered when combining surgeries. Syed et al[28] reported greater efficiency when combining dental procedures and tonsillectomies under one anesthetic encounter. Though the study lacked specifics on exact anesthetic dosages that were administered to these patients, they found that combining the 2 procedures resulted in reduced costs, no differences in complications or outcomes, and similar time under anesthesia in comparison to separately performed procedures.[28] The decrease in health care cost of concurrent procedures compared to consecutive procedures was also determined in a retrospective study conducted by Stapleton et al[29] that focused on the financial and temporal differences between separate and combined dental and medical procedures. Bansal et al[11] studied the cost-effectiveness of combining cardiac catheterization with electrophysiology in pediatric patients and reported a shorter recovery time, shorter LOS, and an average reduction in costs in combined procedures. In adults with congenital heart disease, Lindsay et al[12] noted shorter anesthesia usage, shorter hospital stays, and a 37% reduction in hospital charges among other decreased outcome measures when comparing combined and consecutive electrophysiologic and structural interventions.

While there have been studies supporting the potential benefits of combined procedures across different specialties,[11,12,27–31] the current study is the first, to our knowledge, that specifically examines the safety and efficacy of combining PP and BMT. Our study demonstrated statistically significant decreased time spent in the PACU and decreased dose administration of fentanyl in comparison to cases of separate procedures. Interestingly, our analyses did not show significant differences in the total length of hospital stay or perioperative complication rates, suggesting that both approaches are equally safe.

Although combined procedures may have many benefits, there are logistical difficulties that surgeons encounter. This approach requires precise coordination across different specialty teams to organize 2 procedures concurrently. Due to logistical challenges associated with combining procedures and the limited availability of surgeons, unwanted delays in scheduling the procedures may be unavoidable. In addition, inefficiencies in operating room turnover and inherent challenges to a surgeon who may be needed in 2 separate cases may actually result in increased total surgical and anesthesia time. In light of the results presented in this study, surgeons must carefully plan and work out the logistics of performing simultaneous procedures to avoid unforeseen delays that could ironically result in longer exposure to anesthesia and operative times and to reduce long-term health risks in these children.

The current study presents with some methodological limitations. Due to its retrospective nature, selection bias may be present between the 2 groups. In addition, follow-up may be inherently different after combined versus separate procedures, as patients may only have postoperative evaluation with the plastic surgeon or otorhinolaryngologist, and not both surgeons. Another limitation was the difficulty of gathering enough cases in both groups, which led the authors to use propensity matching to increase statistical power while reducing selection bias. Patients who had PP or BMT were matched based on patient demographics and ASA class. Though this statistical method may not present the exact same results as a patient cohort that had actually undergone these procedures separately, other studies have successfully used propensity matching to generate matched cohorts to reduce potential selection biases and confounding effects of patient characteristics between the 2 procedures.[32] Final limitations included the possibility of longer PACU time in the separate group due to higher administrative time associated with outpatient procedures (ie, discharge paperwork, providing follow-up information, and waiting until stable progression). Nevertheless, the decreased absolute time in PACU, regardless of reason should result in lower costs associated with PACU.

## CONCLUSIONS

This analysis of anesthetic and surgical efficacy and safety in combined PP and BMT placement documented decreased anesthetic time and drug exposure without increasing LOS or perioperative complications. Overall, our study's findings implicate a significant impact on the management of patients with cleft palate anomalies and chronic otitis media and effusion. The data suggest that performing PP and BMT under a single operative encounter mitigates the effects of anesthesia by decreasing intraoperative dosages of fentanyl, while also reducing utilization of hospital resources. With increasing awareness and concern regarding the potential negative impact of anesthetic agents during infancy on neurocognitive development, plus increasing financial pressure to reduce associated costs, our results support combining PP and BMT when feasible.

***Albert K. Oh, MD***
Division of Plastic and Reconstructive Surgery
Children's National Hospital
111 Michigan Avenue NW
West Wing, 4th Floor, Suite 100
Washington, DC 20010
E-mail: aoh@childrensnational.org

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