Journal of Cranio-Maxillo-Facial Surgery 43 (2015) 1614–1619

Contents lists available at ScienceDirect

Journal of Cranio-Maxillo-Facial Surgery

journal homepage: www.jcmfs.com

Defining failure and its predictors in mandibular distraction for Robin sequence

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ARTICLE INFO

Article history:
Paper received 23 April 2015
Accepted 29 June 2015
Available online 8 July 2015

Keywords:
Avoidance of tracheostomy
Mandibular distraction osteogenesis
Pierre Robin sequence
Predictors of failure

ABSTRACT

Introduction: Robin sequence (RS) is defined as the triad of micrognathia, glossoptosis and airway obstruction. A popular surgical treatment is mandibular distraction osteogenesis (MDO). In this study, it is demonstrated that the associated variables change, dependent on the manner in which failure is defined. These multiple failure outcomes are used to construct a scoring system to predict MDO failure.
Methods: A retrospective database of neonatal MDO patients was constructed. Failure outcomes studied included tracheostomy; a decrease in the apnea-hypopnea index (AHI) but an AHI >20; and death. A combination of bivariate and regression analysis was used to produce significantly associated variables and a scoring system.
Results: Statistical analysis demonstrated the association of gastroesophageal reflux; age >30 days; neurologic anomaly; airway anomalies, other than laryngomalacia; an intact palate; and pre-operative intubation on the outcome variables studied. Multiple scoring systems were produced with reasonable sensitivity, specificity, and positive and negative predictive value.
Conclusions: When reporting surgical outcomes of MDO in the setting of RS, it is important to consider the AHI as well as avoidance of tracheostomy as an outcome variable. Incomplete amelioration of AHI accounts for half of the patients with a problem after MDO. The predictive scores presented will be used and validated on a larger, prospectively collected dataset.

1. Introduction

Upper airway obstruction caused by micrognathia and subsequent glossoptosis with or without cleft palate defines the triad of Robin sequence (RS) (Robin, 1929, 1934). Affected patients may present with airway obstruction causing detriment to breathing, growth, neurocognitive development and, in advanced cases, life threatening airway stenosis. Indeed mortality associated with Robin sequence is reported to be between 1.7 and 65% (Costa et al., 2014). Surgical intervention has been reserved for patients with severe airway obstruction in which conservative treatment has been unsuccessful. Mandibular distraction osteogenesis (MDO) is the first line of surgical therapy at many craniofacial centers treating Robin sequence. MDO has been demonstrated as a more functional and cost-effective alternative to tracheostomy (Kohan et al., 2010; Hong et al., 2012) and a more effective intervention compared with tongue-lip adhesion in the treatment of isolated Robin sequence (Flores et al., 2014).

Several investigators have reported on the efficacy of MDO in relieving airway obstruction in the RS population (Denny et al., 2001; Denny and Kalantarian, 2002; Monasterio et al., 2002; Denny, 2004; Mandell et al., 2004; Wittenborn et al., 2004; Burstein and Williams, 2005; Dauria and Marsh, 2008; Iatrou et al., 2010; Cascone et al., 2014). Critical appraisal of the literature demonstrates that the definition of successful distraction varies across studies (Denny et al., 2001; Denny and Kalantarian, 2002; Monasterio et al., 2002; Denny, 2004; Mandell et al., 2004; Wittenborn et al., 2004; Burstein and Williams, 2005; Dauria and

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http://dx.doi.org/10.1016/j.jcms.2015.06.039
1010-5182/

Marsh, 2008; Paes et al., 2013; Flores et al., 2014; Lam et al., 2014; Murage et al., 2014; Rachmiel et al., 2014; Runyan et al., 2014; Tahiri et al., 2014) and can include resolution of apnea by clinical exam or polysomnogram (PSG) improvement; avoidance of tracheostomy; changes in airway obstruction patterns; or mortality. Unfortunately, this variation in definitions creates a confounder in determining patient characteristics leading to favorable or unfavorable results and is problematic to formulating definitive treatment protocols of care.

The main hypothesis of this study is that the variables associated with MDO failure depend on the definition of success for this patient population. A total institutional outcomes analysis for the treatment of MDO was performed with regard to the varying dependent definitions of success. These variables were then used to construct a tool with which failure could be predicted. This information will provide greater clarity in the analysis of surgical outcomes of MDO and draws attention to the need for standardized assessment of surgical outcomes in this challenging patient population. It also provides a set of pre-operative variables that can assist the clinician in patient counseling.

2. Material and methods

Institutional Review Board approval was obtained prior to the start of this study. A 10-year retrospective review was conducted of all patients with RS treated with MDO at a single tertiary care children's hospital between 2003 and 2012. RS was defined as micrognathia, glossoptosis, and airway obstruction with or without cleft palate. Study patients required a clinical follow-up of at least one year, pre-operative laryngoscopy/bronchoscopy, and pre-operative and postoperative PSGs, unless precluded by tracheostomy, intubation, or other airway intervention. Patients were not excluded based on secondary diagnosis or age at the time of distraction.

Work up and indication for distraction was based on a previously described, institutionally-derived protocol (Murage et al., 2013, 2014; Flores et al., 2014). A multidisciplinary team with members from plastic surgery, neonatology, genetics, pulmonology, otolaryngology, and nursing participated in patient assessment and surgical indications. Briefly, patients with airway obstruction unresponsive to conservative airway interventions were assessed by PSG. Those patients with an apnea/hypopnea index (AHI) >20 or significant CO_2 retention were considered for MDO unless central sleep apnea was noted. Prior to surgery, non-contrast computed tomography (CT) of the maxillofacial skeleton was obtained to assess mandibular form, bone quality, associated malformations of the condyle, or TMJ ankylosis. A laryngoscopy and bronchoscopy was also obtained prior to distraction to rule out secondary airway anomalies which could preclude successful MDO. Laryngomalacia was not a contraindication to distraction.

Mandibular distraction was performed using a Risdon incision placed 1 cm inferior to the mandibular border. A vertical ramus osteotomy was performed with a sagittal saw in combination with a coronoidectomy. A micro Zurich mandibular distractor (KLS Martin, Jacksonville, FL, USA) was then applied using a horizontal vector. The activation arm exited anteriorly or posteriorly according to each surgeon's preference. After a latency period of 5 days, activation commenced at a rate of 1 mm/day to the maximal allowable length of the distraction device (20–30 mm). Devices were removed in a second operation after 8 weeks of consolidation.

Multiple patient variables were recorded to correlate with the surgical outcomes of MDO. These included: sex, age, low birth weight (LBW, defined as <2500 g), intrauterine growth retardation (IUGR), prematurity (defined as <37 weeks gestation), age at the time of surgery, presurgical intubation, presence of a cleft palate, syndromic or genetic anomaly, cardiac anomaly, central nervous system (CNS) anomaly, respiratory anomaly excluding laryngomalacia, gastrointestinal (GI) anomaly, gastroesophageal reflux (GER), genitourinary (GU) anomaly, or other system anomaly. Outcome variables defining failure were: a decrease in AHI but still above 20, the need for post-intervention tracheostomy, and death. Repeat distraction was considered under the same paradigm but not considered to be a failure unless it led to no further reduction in AHI, tracheostomy, or death.

Statistical analysis was performed using SAS for Windows (SAS Institute, Cary, NC, USA). Changes in AHI in response to surgery were assessed using a paired *t*-test. A chi-square test was used to analyze each dependent variable's effect on the failure of MDO as classified by: an AHI not decreasing below 20; the need for tracheostomy; or death. Statistical significance was defined as $p \leq 0.05$. Identified variables that had a statistically significant association with failure were then used to construct a scoring system that was tested for the best sensitivity, specificity, and positive and negative predictive value. The receiver operating characteristic (ROC) curves for each was then calculated in order to stratify well-performing predictive tests from poorly performing ones.

3. Results

3.1. Study demographics

Eighty-one patients met the inclusion criteria for this study. Patient characteristics included a mean age of 33.5 days at operation, a mean birth weight of 2.92 kg, and a mean operative weight of 3.36 kg. Other systemic anomaly data was collected as per previous studies. All demographic data is represented in Table 1. These variables include: male sex (58.02%); LBW (29.63%); premature (24.69%); GER (41.98%); Nissen (14.81%); gastrostomy tube (67.9%); laryngomalacia (25.93%); syndromic (30.86%); cleft palate (83.75%); isolated RS (20.99%); CNS anomaly (22.22%); cardiac anomaly (24.69%); GI anomaly (2.47%); GU anomaly (14.81%); airway anomaly (other than laryngomalacia) (34.57%); other

Table 1
Pre-operative demographics of mandibular distraction osteogenesis study patients.

	Mean, *n* (%)
Age (days)	33.49
Birth weight (kg)	2.92
Weight (kg)	3.36
Male	47 (58.02)
Female	34 (41.98)
LBW	24 (29.63)
IUGR	24 (29.63)
Premature	20 (24.69)
GER	34 (41.98)
Nissen	12 (14.81)
Gastrostomy tube	55 (67.9)
Laryngomalacia	21 (25.93)
Syndromic	25 (30.86)
Cleft palate	67 (83.75)
Isolated RS	17 (20.99)
CNS anomaly	18 (22.22)
Cardiac anomaly	20 (24.69)
GI anomaly	2 (2.47)
GU anomaly	12 (14.81)
Other airway anomaly	28 (34.57)
Other anomaly	21 (25.93)
Intubated	6 (7.41)

CNS: central nervous system; GER: gastroesophageal reflux; GI: gastrointestinal; GU: genitourinary; IUGR: intrauterine growth restriction; LBW: low birth weight; RS: Robin sequence.