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Can omphalocele ratio predict postnatal outcomes?☆

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ABSTRACT

Background: The clinical course of patients with omphalocele is challenging to predict. There is no standard method to characterize omphalocele size. Previous studies suggest that the ratio of abdominal circumference to omphalocele defect in-utero is indicative of postnatal outcomes. We hypothesize that omphalocele ratio correlates with outcomes of primary closure versus staged closure.

Methods: A retrospective chart review of all neonates diagnosed with omphalocele from 2002 to 2013 with prenatal ultrasounds available (n = 30) was conducted. Omphalocele ratio was defined as omphalocele diameter/abdominal circumference (OD/AC). Data collected included primary versus staged closure, time to full feeds, duration of mechanical ventilation, and length of stay (LOS). Long-term outcomes and quality of life were also reported.

Results: ROC curve analysis generated optimal OD/AC ratio of 0.26. Twenty of 30 patients had a ratio less than this cutoff. Sixty percent (12/20) in the low-ratio group achieved primary closure versus zero (0/10) in the high-ratio group ($p = 0.001$). Time on mechanical ventilation was 15.8 days (low-ratio) versus 79 days (high-ratio) ($p = 0.05$). LOS was 33.8 days (low-ratio) versus 85.6 days (high-ratio) ($p = 0.119$). PedsQL™ mean score was 85.5 ± 11.0 ($n = 20$) at long-term follow-up. Readmission rates yielded no difference.

Conclusions: The omphalocele ratio is a promising predictor of postnatal outcomes.

Patients with an omphalocele have significant associated morbidities including feeding difficulties, respiratory insufficiency, and prolonged hospitalization. Additionally, closure of the defect is not always possible in one stage. Ideally, the defect can be closed primarily with a single operation. However, primary closure is often not technically feasible owing to the large size of the defect and lack of abdominal domain to achieve safe fascial closure. Because of a large spectrum of defect sizes, the clinical course of patients with omphalocele is challenging to predict. Identification of ultrasonographic predictors of postnatal morbidity would be useful in guiding management of the neonate as well as counseling pregnant women with affected fetuses in the prenatal period. Previous studies have demonstrated that the size of the omphalocele has an impact on neonatal morbidities and subsequently postnatal clinical course [1,2]. However, the definition of giant omphalocele is variable across these studies, which limits the ability to make comparisons.

There have been previous studies that suggest the ratio of fetal head or abdominal circumference to size of omphalocele defect in utero is predictive of postnatal outcomes [3–6]. This omphalocele ratio has been found to be predictive of primary closure of the defect and postnatal morbidities, including respiratory insufficiency, feeding intolerance and extended length of stay in the neonatal intensive care unit (NICU) [3–6]. Although these previous studies have similar findings, the low incidence of omphalocele has limited their study populations.

For these reasons, we sought to find support for previous findings that fetal omphalocele ratios can prognosticate postnatal outcomes. We examined the predictability of achieving primary closure versus staged repair with desiccation, the need for mechanical ventilation, delayed enteral feeding and length of stay. Additionally, since previous studies have only evaluated short-term outcomes, we also examined the omphalocele ratio's ability to predict long-term outcomes.

1. Methods

After approval from the institutional review board (IRB), charts of all neonates diagnosed with omphalocele from 2002 to 2013 were retrospectively reviewed. Patients were excluded from the study if they lacked prenatal ultrasounds or if the prenatal ultrasound was of poor quality that precluded accurate calculation of omphalocele ratios. Additionally, patients with cloacal exstrophy were excluded from the study. Omphalocele diameter was compared to abdominal circumference and head circumference to generate omphalocele ratios of omphalocele diameter/abdominal circumference (OD/AC) or omphalocele diameter/head circumference (OD/HC) respectively. The omphalocele diameter was measured in axial views in its greatest dimension from the base of the omphalocele at the level of the abdominal wall fascia, to the apex of the omphalocele (Fig. 1). The AC and HC measurements were

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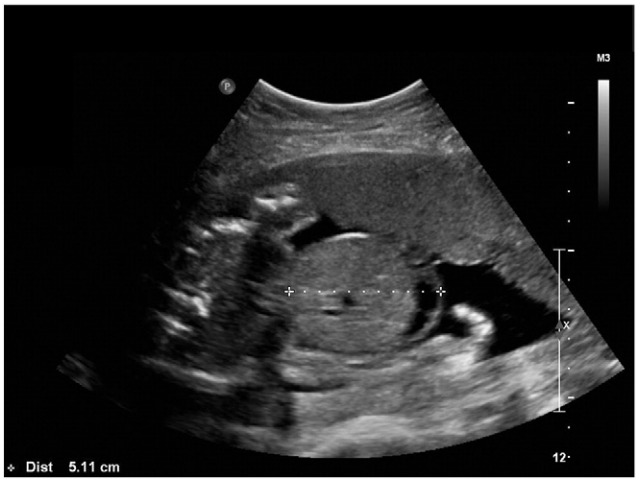

Fig. 1. Fetal omphalocele diameter: The omphalocele diameter was measured from the base of the omphalocele at the level of the abdominal wall fascia, to the apex of the omphalocele in the standard plane.

taken in standard planes. All ultrasound measurements (AC, HC, and OD) were made by one individual (E. L. P.) and the omphalocele ratio was calculated at that time to reduce measurement discrepancies which was from 23.2 to 30.6 weeks gestation. Additionally, the omphalocele ratio was only calculated at one time point during gestation. Receiver operating characteristic (ROC) curves were generated to determine optimal omphalocele ratio cutoffs in prediction of the primary outcome, which was type of closure. The optimal cutoff was chosen as the value which maximizes Youden's index, the sum of sensitivity and specificity [7]. The ROC analysis was conducted using the pROC package for R (v.3.1.0) [8].

Neonatal electronic medical records were reviewed for outcomes. The primary outcome was defined as the ability to achieve primary closure versus staged repair with desiccation using dilute betadine. Primary closure was defined as closure of the defect in a single operation, without the need for a patch, within 24 hours of birth. Secondary outcomes were method of delivery, time to full enteric feeds, need for intubation immediately at birth or upon arrival into the neonatal intensive care unit, length of mechanical ventilation, and length of stay (LOS).

Quality of life (QOL) data were collected utilizing the Clinical Outcomes Registry (COR) at Children's Hospital of Wisconsin [9]. The COR is a prospectively consented, IRB-approved registry that collects both medical and QOL data. The COR collects these variables on select diagnoses, of which omphalocele is one. The pediatric surgery module of the COR conducts annual assessments of QOL using the Pediatric Quality of Life Inventory™ (PedsQL™) [10–13]. A subgroup of our study population was part of the COR. In these patients, the PedsQL™ responses were analyzed to describe QOL in relation to omphalocele ratio.

Patient factors of those who had an omphalocele ratio below the optimal cutoff were compared to those whose omphalocele ratio was above the cutoff using the Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables. Statistical analysis was performed using R version 3.1.0. P values ≤ 0.05 were considered statistically significant.

2. Results

During the defined study period, there were a total of 78 subjects with a diagnosis of omphalocele. Of these, 30 met criteria for study inclusion and were included in data analysis. Of those excluded, 43 were excluded owing to lack of prenatal ultrasound or poor quality ultrasound images and 5 subjects were excluded owing to the diagnosis of cloacal exstrophy. The mean gestational age at prenatal ultrasound was 28.2 weeks. Neonatal characteristics are summarized in Table 1. The mean gestational age at delivery was 36.4 ± 2.3 weeks and the mean birth weight was 2.71 ± 0.57 kg. The low ratio group had a statistically significant greater birth weight than the high ratio group (2.92 kg vs. 2.33 kg, $p = 0.08$). There was an associated anomaly rate of 33.3%. Of these, the most frequent anomaly was cardiac with a rate of 23.3% in the total population. There were a total of 2 mortalities within our study population. One patient was withdrawn from support owing to multiple congenital anomalies and complications including intraventricular hemorrhage. The other patient was born with a ruptured omphalocele sac, which resulted in multiple complications and subsequent withdrawal of care.

ROC curve analysis generated optimal OD/AC ratios of 0.26 (sensitivity – 100; specificity – 88.9; PPV – 85.7; NPV – 100; AUC – 0.979) and an OD/HC ratio of 0.23 (sensitivity – 91.7; specificity – 83.3; PPV – 78.6; NPV – 93.8; AUC – 0.944) (Fig. 2). One of our objectives was to determine if there was any difference in the ability of OD/HC versus OD/AC to predict outcomes. The sensitivity, specificity, and negative predictive value of the OD/AC ratio were all better than that for the OD/HC. Because of this finding, we focused the remainder of our data analysis on this ratio alone.

There were 20 of 30 patients in the study population who had an OD/AC ratio less than 0.26 (low ratio). Of these patients, 60% (12/20) were able to undergo primary closure. This is compared to zero (0/10) in the group whose ratio was above 0.26 (high ratio) ($p = 0.002$). Additionally, the median time to complete fascial closure in the low ratio group was 7.5 days (interquartile range, 465.3) compared to 558.5 days (IQR, 510.2) in the high ratio group ($p = 0.015$) (Table 2). Further, the mean total number of operations to achieve complete fascial closure was 1.65 ± 0.99 (low ratio) versus 4 ± 2.88 (high ratio) ($p = 0.002$). Moreover, of those who achieved primary closure, there were no surgical complications, specifically, no cases of conversion to staged closure owing to abdominal compartment syndrome or dehiscence. Among those who underwent staged repair, there were 4 cases of wound dehiscence (low ratio – 2 patients; high ratio – 2 patients) and one case of abdominal compartment syndrome (high ratio).

The average time on mechanical ventilation in the low ratio group was 15.8 days compared to 79 days in the high-ratio group ($p = 0.05$) with the median time being 0 days (range, 0–152) in the low ratio group and 29 days (range, 0–274) in the high ratio group. Additionally, those in the low ratio group required intubation either at birth or upon arrival to the NICU 25% (5/20) of the time. This number doubled in the high-ratio group to 50% (5/10), however, this was not statistically significant ($p = 0.231$). The low-ratio group was able to achieve full enteric feeds on average 9 days earlier than the high ratio group (14.3 vs 23.3 days; $p = 0.738$). Additionally, the high-ratio group spent a longer amount of time on TPN than the low-ratio group (13.2 vs 47.5 days; $p = 0.212$). However, neither of these findings was statistically significant. The route of delivery was not statistically significantly different between the two groups. In the low ratio group 75% (15/20) underwent a cesarean section, while this number increased to 90% (9/10) in the high ratio group ($p = 0.35$). The length of stay was 33.8 days in the low ratio group compared to 85.6 days in the high ratio group ($p = 0.119$) (Table 3).

There were no differences between groups in emergency room visits or hospital readmissions (intensive care unit or ward). In fact, the rate of any type of readmission was below 1% per 100 days (<0.26 vs >0.26; total readmissions: 0.44% vs 0.17%, $p = 0.25$; ward readmissions: 0.21% vs 0.09%, $p = 0.09$; ICU readmissions: 0.21% vs 0.1%, $p = 1.0$; emergency room visits: 0.42% vs 0.07%, $p = 0.53$). This indicated that the need for readmission after correction of the abdominal wall defect is rare. The median length of follow-up was 806 days (range, 21–3319) in all patients.

A subset of our study population completed a PedsQL™ survey over the course of three years. For comparison purposes, average quality of life scores in pediatric patients with chronic illnesses such as asthma and diabetes mellitus are 71 [10,11]. PedsQL™ scores were similar for both low ratio and high ratio groups. Both groups had scores similar