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## Original article

## Bioimpedance spectroscopy measurements of phase angle and height for age are predictive of outcome in children following surgery for congenital heart disease

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## SUMMARY

**Objective:** Children with congenital heart disease (CHD) are often growth restricted (low weight- and/or height-for-age) which may increase risk of poor post operative resilience. Bioelectrical impedance spectroscopy (BIS) has been used to determine body composition in different clinical settings and has been shown to mark differences in nutritional state and clinical outcome. In disease conditions where fluid is not normally distributed it is proposed that raw impedance values and BIS derived phase-angle may serve as prognostic indicators of clinical outcome. We sought to describe the relationship between nutritional status, phase-angle and post-operative outcomes in children with congenital heart disease.

**Design:** Single centre prospective cohort study.

**Setting:** Paediatric Intensive Care Unit (PICU), Southampton Children's Hospital.

**Patients:** 122 children with CHD following cardiac surgery (March 2015–April 2016). Outcome variables included growth, mechanical-ventilation, PICU length of stay (PICU-LOS) and phase-angle at 50 Hz.

**Measurements and main results:** BIS measurements were taken before and on the day of surgery (day 0), day 2 post-operatively and on discharge from hospital. Pre-operative moderate malnutrition defined as height-for-age-z-score (HAZ)  $\leq -2$  was observed in 28.5% of infants and 20.6% of children. Regression analysis was used to investigate the relationship between phase-angle, HAZ and clinical outcomes. Moderate-malnutrition (HAZ  $\leq -2$ ) was associated with an increased PICU-LOS (odds ratios (OR) with 95% confidence interval: 1.8; 1.1–2.7,  $p = 0.008$ ) whilst a low phase-angle ( $\leq 2.7^\circ$  on day 2) was associated with longer PICU-LOS (OR 7.8; 2.7–22.45,  $p < 0.001$ ); When the model was adjusted for age, known risk factors and length of surgery, HAZ  $\leq -2$  and phase-angle  $\leq 2.7^\circ$  on day 2 were associated with longer PICU-LOS ( $p = 0.001$  and  $p = 0.04$  respectively) and together explained 81.7% of the variability in PICU-LOS.

**Conclusions:** Moderate malnutrition (HAZ  $\leq -2$ ) in infants and children undergoing cardiac surgery is associated with longer PICU-LOS. Post-operative measures of BIS phase angle may further improve our ability to identify those children with an increased risk of prolonged PICU-LOS compared to using pre-operative anthropometry alone.

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**What we know:**

- A low phase angle is associated with poorer clinical outcomes.
- A low phase angle is associated with poor nutritional status.
- A low phase angle may precede anthropometrical changes.

**What this study adds:**

- A post-operative phase angle of  $<2.7^\circ$  is associated with poorer clinical outcomes in children with congenital heart disease.
- A low phase angle may add a sensitivity and specificity to predicting those children who may have poor post operative resilience.

**1. Introduction**

At present there are few reliable surrogate measures for identifying those children at risk of poorer clinical outcomes following surgery for congenital heart disease (CHD). Recent work suggests undernourished children are at risk of prolonged paediatric intensive care length of stay (PICU-LOS) [1,2], however, the use of pre-operative anthropometrical measures to predict those at risk of prolonged PICU-LOS may not be sensitive enough to adequately identify all children at risk [3].

Bioelectrical impedance spectroscopy (BIS) has been used to estimate body composition in a variety of clinical settings and more recently to measure alterations in cell membrane integrity and total body water in order to predict clinical risk [4,5]. Phase angle depends on the opposition to the flow of electrical current (resistance) and the effect of the capacitive ability of cell membranes to impede the current (reactance). Phase angle is negatively associated with resistance and positively associated with reactance and has been used to quantify cell membrane integrity (reactance) and the extent of fluid redistribution between intra- and extracellular fluid compartments (resistance). Changes in phase angle have also been shown to precede anthropometrical changes such as weight loss and as such may be an early marker of change in an individual's overall resilience [4,6,7].

Phase angle is usually lower than normal in disease states as a result of the influence of infection, inflammation or disease. As BIS is non-expensive, portable, easy to use and non-invasive there has been growing interest in the use of BIS-derived measures of phase angle in an ICU setting [8]. In adults undergoing cardiac surgery a low pre-operative phase angle ( $<5.37^\circ$ ) was associated with undernutrition and an increased risk of prolonged post-operative intensive care and hospital stay [9]. Shime and colleagues [7] found that a greater than 20% reduction in impedance after surgery in children with CHD was associated with poorer outcomes [10] and Azavedo and colleagues [8] found that lower measures of reactance (Xc) and resistance (R) were found in critically ill children who did not survive their stay on PICU compared to those who were discharged [11].

Low phase angle values have been shown to be predictive of functional reserves [4,6,7] and resilience in a variety of other clinical conditions [12–14] and have been shown to be related to nutritional status in children [15]. A low phase angle may be indicative of i) changes to cellular permeability and tissue

hydration, with an increased extracellular fluid component or, ii) lower cell mass e.g. muscle mass and total body cell mass seen in malnutrition [4,6].

The aim was to determine whether there was a relationship between malnutrition, BIS-phase angle and early post-operative outcomes relating to PICU-LOS, in children following cardiac surgery.

**2. Methods and materials***2.1. Study design and patient population*

This study was approved and NHS ethics committee (West Midlands, reference 15/WM/0020). Children (0–16 years) with CHD undergoing cardiac surgery were prospectively enrolled (March 2015–April 2016) at a single tertiary centre. Infants were defined as those  $\leq 12$  months age and children  $\geq 1$  year–16 years of age. BIS measurements were collected at baseline (day before surgery), on post-operative days 0 and 2, and at discharge from hospital. Exclusion criteria included children with a permanent pacemaker and those receiving corticosteroids.

*2.2. Definitions of moderate malnutrition*

We are not aware of any other literature defining malnutrition in infants/ children with cardiac disease so chose to use Z scores to classify growth and as such chose to use WHO classification of moderate malnutrition  $<-2$  z scores. *A priori* we did not exclude those children with known growth perturbations such as trisomy 21 or Di-George syndrome (22q.11), as we were primarily interested in the relationship of impedance and phase angle and post-operative clinical outcomes in all children undergoing cardiac surgery. However, there are limitations to this approach as growth in children with CHD may be different to that of a healthy population.

Z-scores were calculated using WHO Anthro software version 3.3.3 2011 [16] for participants  $\leq 5$  years and WHO AnthroPlus 3.2 [17] for those  $\geq 5$  years. WHO growth reference interpretation of cut offs for malnutrition were used. Moderate malnutrition was defined as a height-for-age or weight for height  $\leq -2$  z-scores below the mean of the WHO child growth standards [18]. In this study, we chose to use height for age  $<-2$  as a cut off value for moderate malnutrition as it represented persistently poor or chronic state of malnutrition.

*2.3. BIS measurements and anthropometry*

BIS is validated for use in a wide range of paediatric patients particularly with respect to body composition [19] Lower phase angles have been associated with poorer outcomes [4,15].

BIS measurements were made using ImpediMedSFB7 (Pinkenba, QLD 4008 Australia), a single-channel tetra-polar device able to measure resistance and reactance across 256 frequencies. The machine was calibrated before use with a circuit of known impedance provided by the manufacturer. Measurements were taken in triplicate, with the mean used in the analysis. Measurements were conducted using a standard tetrapolar electrodes distribution, on palms of hands and soles of feet, supine with arms and legs apart (Fig. 1). BIS measurements were completed in unfasted subjects. BIS data files were processed using specialist software (Bioimp, ImpediMed), with data points rejected if they met any of the following criteria; i) positive X centre (Xc) values, ii) negative resistance values. Phase angle at a current frequency of 50 Hz was used for analysis [11].

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