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Full Length Research Paper

Possible impairment of surgical decision making and confounded outcome in Fontan surgery by Nakata Index

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Since cardiac structuring dimensions inform surgical decisions making, Z-score systematic error impairs surgical decision making and confounds outcome measurement, hence a similar error may affect the Nakata index. In this study, PubMed was searched using the terms: "pulmonary," "artery," "size," "Nakata," "Fontan," and "outcome". Studies that did not describe the outcome of the Fontan procedure and the size of the branch pulmonary arteries were excluded. Outcome measures of interest, in relation to BPA size, included: Operative mortality, Fontan "take-down", length of ICU stay, pleural effusions and functional capacity. The results revealed that of 116 papers retrieved, 9 were included representing 1,042 patients who underwent the Fontan procedure. Six out of 9 papers representing 645 (61.9%) patients reported that BPA size had no relationship with the outcome of the Fontan procedure; while 2 out of 9 papers representing 366 (35.1%) patients found that BPA size did affect the outcome. One paper representing 31 (3%) patients was unable to find any relationship. All the papers that concluded that there was no relationship labelled normal sized BPAs as small because of a systematic error introduced by the Nakata index. Papers that found a relationship did not use the Nakata index. Thus, Nakata index systematic error may impair surgical decision making and confound outcome measurement in Fontan surgery. In addition, continued use of the Fontan index may have similar implications for other congenital heart lesions.

Key words: Nakata Fontan mortality

INTRODUCTION

Fontan and Baudet (1971) described a technique to surgically separate oxygenated blood from deoxygenated blood in patients with a single ventricle. They suggested that normal sized branch pulmonary arteries (BPAs) and the absence of pulmonary hypertension were necessary for success. Nakata et al. (1984) described a technique, the pulmonary artery index (PAI), to measure the size of BPAs; they identified index values for normal BPAs and suggested an index value below which the Fontan procedure was unlikely to be successful. The McGoon index has also been used to examine the relationship between the size of BPAs and outcomes of Fontan surgery (Fontan et al., 1989). Debate continues about the relationship between the size of BPAs and the outcome

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Table 1. Search terms and filters.

Search number	Filter	Search term
1	Title/abstract	Pulmonary
	Title/abstract	Artery
	Title/abstract	Size
	Title/abstract	Fontan
2	Title/abstract	Pulmonary
	Title/abstract	Nakata
	Title/abstract	Fontan
	Title/abstract	Outcome

of the Fontan procedure (Xu et al., 2011). There is evidence that the best long-term outcomes are associated with certain perioperative pulmonary arterial physiological parameters (Pundi et al., 2015) and that branch pulmonary artery (BPA) size contributes to the presence or absence of these parameters (Itatani et al., 2011). Prior work done in relation to the accurate measurement of the size of cardiac structures has shown that the use of poor protocols lead to the introduction of systematic errors in measurement and may contribute to poor surgical decision making (Awori et al., 2017). The objective of the current study was to determine if the ambiguity regarding the relationship between the outcome of Fontan surgery and the size of branch pulmonary artery may have been introduced by a systematic error of pulmonary artery size measurement. This ambiguity could lead to patients receiving the Fontan procedure inappropriately.

PATIENTS AND METHODS

Two searches were made of PubMed using the “advanced” setting. The search terms and filters are shown in Table 1; all filters were combined with the instruction “AND.” Retrieved articles were excluded when it was clear from the abstract that the outcome of the Fontan procedure was not examined in relation to BPA size.

The full text of all the remaining articles was examined to determine the relationship between surgical outcome and BPA size. Outcome measures of interest included: operative mortality, Fontan “take-down”, length of intensive care unit (ICU) stay, pleural effusions and exercise capacity. The actual size of BPAs described in the included articles was appraised by converting them to “equivalent diameter” z-score values as recommended by Awori et al. (2011) This conversion was facilitated using the 50^{th} centile line from World Health Organisation growth charts (www.who.int/childgrowth/standards/en/) to calculate body surface areas. The mean Nakata Index was then calculated for typical patients of various ages as recommended by Awori et al. (2011) for comparison with that reported by Nakata et al. (1984).

RESULTS

Of the 116 papers retrieved, 9 were included representing 1,042 patients who underwent the Fontan procedure. Six out of 9 papers representing 645 (61.9%) patients reported that BPA size had no relationship with the outcome of the Fontan procedure; 2 out of 9 papers representing 366 (35.1%) patients found that BPA size did affect the outcome of the Fontan procedure. One paper representing 31 (3%) patients was unable to determine if any relationship existed. The search results are summarised in Table 2. Table 3 shows the mean Nakata Index for typical patients of various ages calculated for a z score of 0 as recommended by Awori et al. (2011).

DISCUSSION

The Nakata pulmonary artery index was first described in 1984 as a means of quantifying the size of BPAs (Nakata et al., 1984). The diameters of the right and left pulmonary arteries, proximal to the first lobar branches, were measured angiographically and a “correction factor” was applied to correct for angiographic magnification of vessels. An average of the largest and smallest value was taken for each vessel and used to calculate the cross-sectional area (CSA). The CSA was then indexed to the body surface area (BSA) of the patient to obtain the Nakata pulmonary artery index (NPAI). The normal mean NPAI was calculated from 40 “normal controls”, all of which had some form of cardiac or chest wall abnormality; these ‘controls’ were not actually normal. The normal mean NPAI obtained from this group was 330 +/- 30 mm^2/m^2. Patients with NPAI greater than 250 mm^2/m^2 were considered good candidates for the Fontan procedure.

Awori et al. (2011) noted that the use of poorly calibrated tools and protocols to measure cardiac structure size could introduce a systematic error in measurement. This may result in an incorrect assessment of cardiac structure size which could result in the execution of inappropriate surgery (Awori et al., 2017). Awori et al. (2011) proposed an optimal method to measure cardiac structure size and the NPAI calculated

Table 2. Relationship between outcome and BPA size.

Author	Year	RBSAO	n	MT	Outcome	NI-COFC
Lehner et al. (2014)	2014	No	146	NI	IS, E	150
Mendoza et al. (2012)	2012	Yes	32	MR	M	MA
Baek et al. (2011)	2011	No	120	NI	EC.	180
Adachi et al. (2007)	2007	No	121	NI	EC	198
Knott-Craig et al. (1993)	1993	No	139	NI	M, TD	185
Hofbeck et al. (1993)	1993	-	31	NI	M	-
Fontan et al. (1989)	1989	Yes	334	MR	M,TD	MA
Bridges et al. (1989)	1989	No	29	NI	M	233
Girod et al. (1985)	1985	No	90	NI	M	250

E = effusion; EC = exercise capacity; IS = icu stay; M = mortality; MA= multivariate analysis; MT= measurement tool; MR = McGoon ratio; n = number of patients; NI = Nakata pulmonary artery index; NI-COFC = Nakata index cut-off for comparison; RBSAO = relationship between BPA size and outcome; TD = take-down.

Table 3. NPAI in typical patients.

Age	NPAI (mm^2/m^2)*
Neonate	155
6 months	170
1 year	175
2 years	188
3 years	197
4 years	200
5 years	204
10 years	196
18 years.	182

*Calculated from BPA diameter corresponding to Z-score of 0[8].

for typical patients of various ages, using this technique is shown in Table 3. Table 3 demonstrates that the normal NPAI increases as one grows from neonate to adult. Of particular significance is that the normal NPAI for a neonate (155 mm^2/m^2) is less than half of the normal mean (330 mm^2/m^2) quoted by Nakata et al. (1984). In addition, the cut-off NPAI given by Nakata et al. (1984) (250 mm^2/m^2) actually represents normal sized BPAs and not hypoplastic ones when considered in the context of the figures contained in Table 3. This discrepancy may introduce as systematic error when the NPAI is used. It is possible that the source of this error was the use of a small sample size by the Nakata et al. (1984). Additional sources of error may have been the use of a control group with pathology or the use of an inaccurate measurement protocol.

In the current study, 6 out of 9 papers representing 645 (61.9%) patients reported that BPA size had no relationship with the outcome of the Fontan procedure. All these papers reported the use of the normal mean NPAI and NPAI Fontan “cut-off” described by Nakata et al. (1984) to define BPA size. There is a possibility that a significant number of BPAs described as small (NPAI less than 330 mm^2/m^2) in these papers would actually be described as normal using the optimal technique demonstrated in Table 3. This may have confounded attempts to search for a relationship between BPA size and Fontan outcome in these studies. By contrast, 2 out of 9 papers representing 366 (35.1%) patients found that BPA size did affect the outcome of the Fontan procedure. These two papers used the McGoon ratio (MR) to describe the size of BPAs. Table 2 highlights the fact that NPAI cut-off values for comparisons between small and large pulmonary arteries essentially fall within the normal range for most studies included. This implies that it is likely that most studies that showed no relationship between BPA size and surgical outcome actually had significant numbers of patients with normal sized BPA in both groups. The studies that used multivariate analysis did report a relationship between BPA size and outcome. This is reasonable as the multivariate analysis technique negates the confounding effect of NPAI comparison cut-offs that fall within the normal range.

The largest study (Fontan et al., 1989) noted that the predicted 30 day risk of death or Fontan take-down was 55% when the MR was 1.2. A MR of 1.2 corresponds to a BPA diameter z-score of -1.4 when measured as recommended (Awori et al., 2011). This suggests that even mild hypoplasia of the BPAs could significantly compromise the surgical outcome. Work done on Fontan haemodynamics by Itatani et al. (2011) suggests that the lowest acceptable NPAI for a successful Fontan is 110 mm^2/m^2. This corresponds to a BPA diameter z-score of -1.8 in a typical 4-year old child (Pettersen et al., 2008) and is consistent with what was predicted using the MR in the largest study.

When the outcomes of the largest study (Fontan et al., 1989) and the findings of the haemodynamic study (Xu et al., 2011) are considered in the context of the typical mean NPAI values shown in Table 3, they reinforce the idea that size does affect surgical outcome. In particular, smaller BPAs are associated with an increased operative mortality and incidence of Fontan "Take-down". Although available evidence is ambiguous, our findings suggest that the ambiguity regarding the relationship between BPA size and the outcome of the Fontan procedure may be as a result of the introduction of a systematic error through the use of the NPAI. Once this error is accounted for, the ambiguity disappears and the available evidence suggests that BPA size may affect Fontan surgery outcome. We appreciate that the studies included in our work span four decades and that contemporary outcomes of Fontan surgery have improved; however, a recent review suggests that most proponents of Fontan surgery have adhered to the original recommendation by Fontan et al. (1989) and Kverneland et al. (2018). Although we did not have access to other variables that are known to be associated with Fontan surgery outcome, the confounding effects of this are likely to have been mitigated by the fact that most contemporary Fontan proponents, appear to have adhered to Fontan et al. (1989) original recommendations for the selection of Fontan candidates. We would have liked to perform a meta-analysis to better determine the relationship between BPA size and Fontan outcome; however, most of the studies did not include the actual size of the BPAs for each patient and were too heterogeneous to perform as sensible meta-analysis. Although there are myriad of studies on Fontan patients, we were particularly interested in those relating to the relationship between BPA size and Fontan outcome. This informed our search strategy.

Conclusion

The Nakata index may introduce a systematic error in the assessment of BPA size. Correction for this error appears to suggest that there is a relationship between BPA size and Fontan outcome. It was not our intent to address sources of confounding or bias in this study. Rather, we attempted to show how a systematic error introduced by the use of the Nakata Index, could play a role in confounding surgical decision making in Fontan surgery; this could have negative consequences on outcomes. This systematic error in the Nakata Index could have similar implications for other lesions such as Tetralogy of Fallot. As far as Fontan outcomes in relation to pulmonary artery size are concerned, we suggest that a meta-analysis be conducted in future to better elucidate the relationship between BPA size and Fontan outcome. To facilitate this, we recommend that the age appropriate mean NPAI be adopted as opposed to the original normal mean NPAI proposed by Nakata et al. (1984). Better still, the use of the NPAI should be replaced by z-score assessment as recommended in our earlier work (Awori et al., 2011). We do appreciate that a physiological assessment of the pulmonary arterial system (cardiac catheterisation) should also be performed preoperatively to facilitate appropriate surgical decision-making in Fontan candidates.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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