SHORT COMMUNICATION

Cardiac magnetic resonance imaging–derived cardiac index is associated with adverse outcomes in patients with single-ventricle Fontan circulation: a preliminary study

Małgorzata Kowalczyk[1], Piotr Zieliński[1], Magdalena Marczak[2], Katarzyna Kożuch[1], Magdalena Lipczyńska[1], Mirosław Kowalski[1], Piotr Hoffman[1]

1 Department of Congenital Heart Diseases, National Institute of Cardiology, Warsaw, Poland
2 Magnetic Resonance Imaging Unit, Department of Radiology, National Institute of Cardiology, Warsaw, Poland

Introduction Single ventricle (SV) refers to a group of heart defects with only one ventricle properly developed. The term describes a spectrum of cardiovascular malformations that are not feasible for surgical partitioning of ventricular mass.[1] Fontan surgery (currently most often involving total cavopulmonary connection [TCPC]) is a palliative procedure that connects systemic and pulmonary vascular beds in series.[2] This procedure creates a "neoportal system," in which the venous return flows directly to pulmonary capillaries, bypassing the heart. An SV is the only pump that generates energy for blood flow, but its role in determining cardiac output (CO) is limited. Lack of the subpulmonary ventricle, along with a surgically created connection, leads to high central venous pressure and results in decreased CO. Patients undergoing Fontan surgery are exposed to multiorgan dysfunction (Fontan-associated liver disease, chronic kidney disease, protein-losing enteropathy, among others)[3,4] and low exercise capacity.[5] Those patients also have a reduced heart rate reserve.[6] We hypothesized that a cardiac index (CI) derived from cardiac magnetic resonance (CMR) imaging may prove to be an effective tool for the overall assessment of Fontan circulation function. The aim of the study was to determine the usefulness of a CMR-derived CI as a multiorgan dysfunction marker and an adverse-outcome predictor in patients after Fontan palliation.

Methods Thirty-four patients undergoing the Fontan procedure were retrospectively enrolled in the study. Cardiopulmonary exercise testing was performed on Treadmill Ergometer ZAN Ergo 600s (Delmar Reynolds, Irvine, California, United States). Maximal oxygen uptake (VO_2 max) was measured by a modified Bruce protocol. Biochemical data were obtained using standard assay techniques. Collected parameters included serum concentrations of total protein, aspartate and alanine transaminases, total bilirubin, iron, creatinine, thyroid-stimulating hormone, and C-reactive protein. Blood cell tests provided data on hemoglobin levels, platelet and leukocyte counts, and mean corpuscular volume. Additionally, a glomerular filtration rate was estimated. Cardiac magnetic resonance imaging was performed using a 1.5 Tesla scanner (Avanto and Avantofit, Siemens Healthineers, Erlangen, Germany) to evaluate the CO. The CO was calculated according to the following formula: CI = CO / body surface area. Adverse events were identified and followed up for a mean of 4 years. Those events included arrhythmia, nonelective hospitalization, death, heart transplant, lower New York Heart Association (NYHA) functional class, and decreased VO_2 max.

The study protocol was approved by an ethics committee. Patient consent was not required owing to the retrospective design of the study.

Correspondence to:
Małgorzata Kowalczyk, MD, Department of Congenital Heart Diseases, Institute of Cardiology, ul. Alpejska 42, 04-628 Warszawa, Poland, phone: +48 22 34 344 00, email: mkowalczyk1@ikard.pl
Received: August 29, 2020.
Revision accepted: February 5, 2021.
Published online: February 22, 2021.
Kardiol Pol. 2021; 79 (3): 336-338
doi:10.33963/KP.15822

TABLE 1 Clinical and demographic characteristics of the study patients

Characteristics		Patients (n = 34)
Male sex		15 (44)
Single ventricle type	Left	25 (73)
	Right	6 (18)
	Undifferentiated	3 (9)
Age at cardiac MRI, y		25.5 (21.25–30.75)
Time from the Fontan procedure, y		17 (15.25–21)

Data are presented as number (percentage) of patients or median (interquartile range).

Abbreviations: MRI, magnetic resonance imaging

Statistical analysis Study results were analyzed using the Statistica software, version 13.3 (StatSoft, Kraków, Poland). Quantitative variables were expressed as median and interquartile range (IQR). Qualitative variables were presented as numbers and percentages. The Shapiro–Wilk test was used to assess normality. The correlation among biochemical parameters, time from surgery, and CI was assessed using the Spearman rank correlation coefficient. The Mann–Whitney test was used to identify differences in CI between the study groups (Supplementary material, *Table S2*). A *P* value less than 0.05 was considered significant.

Results and discussion Patients' clinical and demographic characteristics are shown in TABLE 1. The median (IQR) CMR-derived CI was 3.37 (2.99–3.87) l/min/m^2 (minimum, 2.1 l/min/m^2; maximum, 6.1 l/min/m^2). Maximal oxygen uptake ranged from 13.16 ml/min/kg to 28.37 ml/min/kg, with a median (IQR) of 19.46 (15.48–21.48) ml/min/kg. During a median (IQR) follow-up of 6 years and 7 months (range, 5 years and 9 months to 7 years and 1 month), 16 events occurred including 9 arrhythmias, 5 nonelective hospitalizations, and a single death. Only supraventricular tachycardia episodes were observed in 4 patients with atrial fibrillation and 2 with atrial flutter. Indications for nonelective hospitalization included arrhythmia episodes, Fontan circulation failure, and diagnostic workup of chest pain. A single patient died 8 days after Fontan conversion to the TCPC procedure. There was no significant relationship between CI and parameters of organ dysfunction (serum creatinine level, glomerular filtration rate, total serum protein level, bilirubin and aminotransferase levels, serum iron level, and blood count) (Supplementary material, *Table S1*). There was also no correlation among age, worsening of the NYHA functional class, and VO_2 max reduction with CI (Supplementary material, *Table S2*). The cardiac index was significantly higher in patients who were not hospitalized compared with those who required nonelective hospitalization (Supplementary material, *Table S2*). A negative correlation between the time from surgery and CI was found.

The SV preload after Fontan palliation depends mainly on pulmonary flow.[7] Lack of a subpulmonary pump to generate the pressure gradient and inward flow to pulmonary arteries causes chronic preload decrease. Filling-volume deprivation leads to concentric hypertrophy, diastolic dysfunction, and, as a consequence, to decreased stroke volume. Patients after TCPC also have a limited heart rate reserve, which is probably an adjustment to abnormal cardiac filling rather than sinus node dysfunction.[6] A reduction of both stroke volume and heart rate leads to decreased CO and CI. Cardiac output and CI are hemodynamic parameters obtained by invasive methods. Hundley et al[8] demonstrated a correlation of CMR-derived CO and standard invasive measurements. There is some evidence on the usefulness of CMR-derived CI in healthy adults and patients with congestive heart failure,[9] as well as in those after the Fontan procedure.[10]

Cardiac output in patients with SV is decreased by 50% to 80% of the normal value for body surface area.[11] Chronically low CO and CI in the case of normal heart anatomy may lead to low arterial and perfusion pressure. We hypothesized that a decreased CI can influence organ function in patients after the Fontan procedure, as organ function deteriorates in patients with congestive heart failure.[12] Mori et al[13] investigated an association between invasively measured hemodynamic parameters (CI and signs of liver and renal dysfunction in patients after the Fontan procedure). Their findings revealed no significant association between the hemodynamic measurements and end-organ dysfunction parameters, which coincides with our findings.

Cardiac output in patients after the Fontan procedure is approximately half of that of healthy controls during exercise.[14] However, we did not find a link between CI and VO_2 max during cardiopulmonary exercise testing. There was also no correlation with the NYHA functional class. This finding may suggest that patients after the Fontan procedure can develop an adaptation to chronic CI decrease.

The CMR-derived CI was found to be a predictor of nonelective hospitalizations. A study of the pediatric population in the Mayo Clinic, Rochester, Minnesota, United States, showed that a low CI and elevated pulmonary vascular resistance obtained during cardiac catheterization can identify patients at high risk of Fontan circulation failure.[15] Our study confirmed that the CMR-derived CI can identify patients at increased risk of Fontan circulation failure.

This study was limited by the small number of patients enrolled. However, SV is a rare disease and the results of this study represent

the experience of only a single medical center. The second limitation of the study was the lack of the parallel invasive measurement of CI. Despite these limitations, the study demonstrated the prognostic value of a noninvasive parameter that can be obtained by routine diagnostic procedures. Our study also provided an insight into the pathophysiology of Fontan circulation deterioration, since CI depends on the time from TCPC palliation.

The CMR-derived CI is not correlated with organ dysfunction parameters. Instead, our evaluation suggested the development of some degree of multiorgan functional tolerance despite chronic organ hypoperfusion. A reduced CMR-derived CI was a predictor of nonelective hospitalizations in the study population.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/kardiologiapolska.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

HOW TO CITE Kowalczyk M, Zieliński P, Marczak M, et al. Cardiac magnetic resonance–derived cardiac index is associated with adverse outcomes in patients with single-ventricle Fontan circulation: a preliminary study. Kardiol Pol. 2021; 79: 336-338. doi:10.33963/KP.15822

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