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Editorial

The Japanese cohort of adults with a Fontan circulation points to the action plan necessary to improve survival after Fontan

Yves d'Udekem *, Chin L. Poh

Department of Paediatrics, University of Melbourne, Melbourne, VIC, Australia
Murdoch Childrens Research Institute, Heart Research Group, Melbourne, VIC, Australia
Department of Cardiac Surgery, Royal Children's Hospital, Melbourne, VIC, Australia

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More than 50 years have elapsed since the first Fontan procedure [1]. For most of this history, it was feared that the population undergoing this operation would be subjected to a continuous and rapid attrition in early adulthood [2]. The scarcity of information on the cause and mechanism of death of these patients is therefore surprising. We are now realizing that the survival of these patients is far superior to that initially expected and to further extend their survival, the identification of the causes of their demise is essential. The review of this Japanese multi-institutional data [3] is therefore welcome. They restricted their analysis to deaths occurring only in adults. This selection criterium is the best design to enlighten us on the most pressing and yet unsolved question: the cause of mortality intrinsically related to the existence of a Fontan circulation in adults with single ventricle. The follow-up of 600 adults was collected over a five years period. There are interesting new data emerging from this analysis. The relationship between mortality and use of diuretics has been quoted in heart failure [4], but is new for the Fontan population. It may indicate how poorly we are equipped to deal with right-sided heart failure symptoms in the Fontan circulation. The authors classified those as being related to heart failure, but right sided congestion could happen with preserved ventricular function. The fact that low albumin level was associated with mortality even in the absence of PLE may signal that the load on the lymphatic circulation may be an unsuspected causative factor of mortality.

The main finding of this study is the fact that the mortality of this adult population is by far superior to the mortality of their peers. The authors stipulated that currently in Japan, the existence of the Fontan circulation in adults gives them an increased risk of death similar to having an extra 20 to 40 years of age. They also provided causes of death. One should not be too fixated on the relative proportion of these causes of death, because even though this is a large series, the number of deaths was relatively small. Over a total of 33 deaths were observed, the causes of death were heart failure, arrhythmia/sudden death, cancer, reoperation and thrombo-embolic events in 11, 8, 5, 4 and 4 patients. But this manuscript clearly delineates where we should focus our efforts if we want to improve the survival of these patients.

Heart failure. Many of those with a failing Fontan circulation have symptoms of right sided failure and the mechanism leading to those are poorly understood. The authors have recently highlighted the surprising finding that there is a state of failure of the Fontan circulation with a high cardiac output and elevated central pressure [5]. The pathophysiology of failure of the Fontan circulation has to be elucidated.

Sudden death/arrhythmia. It has become clear that arrhythmia is a significant contributor to the demise of this population. Atrial isomerism [6] and having pulmonary atresia and intact ventricular septum and RV dependent coronary circulation [7] have been identified as risk factors for arrhythmia, but we are still poor at predicting those who will develop a serious adverse event. Snapshots provided by punctual ECGs and serial Holter do not seem to predict any of the deaths observed. More in-depth electrophysiological studies including very long recordings of heart rhythms are needed to progress our ability to identify those at highest risk.

Cancer. Developing hepatocellular carcinoma is one of our current fears for our patients after a Fontan completion. Only 4 patients in this series died from hepatocellular carcinoma and seemingly the oldest ones of this group. It is likely that this risk may be alleviated by a timely transplantation, but we are not yet able to determine at which stage we have to intervene. The almost universal presence of fibrosis and vascular nodules makes imaging and detection of early lesions very difficult [8]. We have to proceed with more in-depth prospective investigations into the timing and significance of the development of these lesions.

Reoperations in this population undoubtedly carries a high mortality: 4 of the 22 reoperated patients of this series died. Extracting the data of the Australia and New Zealand Fontan registry made us understand to what extent the valves of these single ventricles will continue to fail at an alarming rate in adulthood (*work submitted*). The presence of atrio-ventricular valve regurgitation precipitates Fontan failure but

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* Corresponding author at: Department of Cardiac Surgery, Royal Children's Hospital, Flemington Road, Parkville, Melbourne, Victoria 3052, Australia.
E-mail address: yves.dudekem@rch.org.au (Y. d'Udekem).

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reoperating on them is associated with a high mortality. We suspect that tackling these issues early rather than late is the only solution to improve their survival.

Thrombo-embolic events. In this series of adults with a high proportion of patients with older forms of the Fontan procedure, it is difficult to distinguish whether the main issue leading to death was the ancient design of the Fontan or anti-thrombotic therapy itself.

Today the Fontan population has been growing at an unexpected pace. We owe this population our complete commitment to improve their survival. Dynamic, in-depth prospective analysis of their end-organ function, their arrhythmic load and the mechanism of their circulatory failure should be intensified if we want to prevent their demise. This Japanese initiative of prospective study of the adult population of patients with a Fontan circulation is welcome and should be extended.

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