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THE LONG FONTAN CRUSADE

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THE LONG FONTAN CRUSADE
A LONGA CRUZADA DE FONTAN

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In this issue of *The Portuguese Journal of Cardiology,* Chen et al. [1] presented the outcomes for a large cohort of children (n=400) who underwent a Fontan procedure over a period of 20 years at a single institution in China. The aim of their study was to assess early and long-term outcomes and the risk factors for adverse results. Mean age at surgery in the cohort was 5.8 years and the primary diagnosis for two thirds of the patients was univentricular typology and bi-ventricular for the other third. Altogether, left ventricle dominance was present in 36% of patients and two functional ventricles were present in the remaining 29%. Of relevance is the fact that 14% of patients had a heterotaxy arrangement. Most patients (80%) underwent a two-stage procedure, with a bidirectional Glenn for palliation, and fewer had initially either a systemic to pulmonary shunt (5%) or banding (10%). Most of the patients underwent an "extracardiac" type of Fontan and 41% received a fenestration. With a mean follow-up of 8.4 years (range: 3.8-12.3), early mortality at Fontan was 5.5% and late mortality was 4.8%. Survival rates at five, 10, 15 years post-procedure were, respectively, 97.5%, 92.6% and 90%. Freedom from Fontan failure was, respectively, 95.5%, 88.1% and 84.1% at the same intervals. Unexplainably, the rate of transplantation was low for the whole cohort (0.5%). The authors identified heterotaxy with asplenia as a high predictor for early mortality, but also "single stage Fontan" and long bypass times. Regarding late Fontan failure, both heterotaxy and elevated pulmonary pressures were identified as strong predictors.

The Fontan procedure was introduced over fifty years ago as a definitive palliation for patients with only one functional ventricle (initially tricuspid atresia)[2]. Its use has been extended over time also to patients with other univentricular typologies and to patients with two ventricles and challenging bi-ventricular corrections.

Fontan physiology thrives on the delicate hydraulic balances that rely on straight energy-sparing conduits, competent ventricular functions, low resistance and no bottlenecks through the pulmonary circuit. This is the reason why, since first pre-operative Fontan commandments, ventricular function (systolic & diastolic) and pulmonary arterial pressure have remained as the most impactful outcome determinants [3].

Aiming to optimize Fontan circuit design many technical modifications were made to the original operation by Francis Fontan over the years, the most impactful was the Lateral Tunnel modification by my former mentor Marc deLeval [4] and

subsequent evolutions for “Extracardiac Fontan Connections” mainly by Marcelletti[5]. The addition of fenestrations, enabling right side venous decompression into the systemic circuit, have been used and allowed to ease out the post-operative period, reducing the duration of effusion complications; the same for the use of ingenious thoracic duct decompression strategies that we have pioneered in our group[6]. Over the years, early unloading interventions aimed at protecting pulmonary circulation and main pumping ventricle have proven beneficial, which has been the case for bidirectional Glenn shunts in line with two-stage Fontan completions.

Today, it is well known that factors mostly affecting long-term prognosis in Fontan include **the nature of the original cardiac lesion** (poorer for heterotaxy/asplenia and right ventricle typologies), **the early timing of corrections** (namely unloading procedures) and the use of **recent procedures,** namely the ones excluding the atria from excessive venous pressures – the extracardiac conduits. However, despite “perfect” Fontan procedures: those performed in “ideal candidates” - before the age of four, using a two-stage approach and trying to protect pulmonary and ventricular functions early on, the Fontan circulation is invariably prone to late failures, mainly due to the results of chronic systemic venous hypertension, the lack of lung flow pulsation and pumping ventricle failure. All these will lead to liver fibrosis, arteriovenous lung fistulae, atrial distension and arrythmias and, ultimately, cardiac dysfunction, heart failure and death. Failure will typically occur later in life, normally beyond the forties, imposing extracardiac conversions, arrythmia treatment and heart or heart and liver transplants.

Since the late eighties, it has been known that Fontan is a long-standing palliation, not a cure, due to the so-called Fontan attrition effect. After all, nature was right as two ventricles seem to be needed for normal circulation, survival and quality of life, outdating the old concept of a *“*dispensable sub-pulmonary ventricle*”*.

Back to the paper, the authors present their extensive single-center series evidencing results that are not significantly different from those already published. Their early mortality figure is different and clearly higher than the 2% generally published; this is probably due to a high incidence of heterotaxy patients in their cohort (14%). Cumulatively, they have identified heterotaxy/asplenia as the attrition factor for both early and late poor outcomes, a finding in line with a recent paper from the Mayo Clinic [7].

Long-term outcomes in the paper, namely mortality and “freedom from complication” rates up to 15 years, are in line with other published series. However, they do not match the excellent data from the Australian-New Zealand registry, which now has collected close to two thousand Fontan patients, with survival rates at 15 years of, respectively, 80% for atrio-pulmonary connections and well over 90% for the *lateral tunnels* and *extracardiac conduits*.

The authors limited their follow-up analysis to 15 years, a period that is too short to elucidate the “real world” of Fontan outcomes. We now have enough data that extends analysis into the fourth decade and beyond, this being important because we know that survival remains stable till the second-third decade, dropping steadily thereafter. In a classical paper, also from the Mayo Clinic [8], reporting a thousand Fontan cases that were followed for 40 years, survival at 30 years had dropped to 43%... Naturally, this series included earlier patients and classical operations. Predicably new era management will bring us a better scenario. “Lateral tunnels” and “extracardiac” Fontan procedures were introduced just at the turning of the century and their beneficial effects start appearing now, suggesting more promising and uncomplicated long follow-up outcomes. For instance, the Australian and New Zealand Fontan Registry shows survivals in the range of 90% at 20 years, 83 % at 25 years, depicting freedom from Fontan failure, conversion or transplantation of, respectively, 70% and 56% for the same intervals [9]. More importantly, quality of life studies are now showing that adults with Fontan physiology have lower overall health-related QOL compared to normal physiology, a topic that needs to be more addressed extensively[10].

New strategies are now generating reproducible results and more stable outcomes during the first two decades after the procedure, therefore it is critical to refocus on most critical prognostic factors, as the authors underlined, such as the original clinical entity, namely heterotaxy and right ventricle typology. In line with this, I must say that I do not agree with one of the author’s conclusions, stating that two-stage corrections enabled a reduction in early mortality, but do not confer any additional long-term benefits. On the contrary, the Glenn shunt performed as a first stage unloads the ventricle and reduces pulmonary pressures, implicitly improving, not only early outcomes, but particularly overall future outcomes.

Finally, our efforts must now focus on closely following the large number of actual Fontan survivors to timely detect any early heart failure manifestations, arrythmias and liver deterioration, as these are always predictors of a dismal evolution. Particularly important is offering those patients, starting the sliding down ladder, individualized treatment strategies before irreversible organ damage, particularly liver and heart failure, occur. Transplantation is always an option but should be performed earlier rather than later and certainly not when irreversible organ damage is already present.

The paper by Chen et al.[1] presents a rather extensive and well-managed cohort of Fontan patients; I compliment the authors for the quality of their outcomes, but I wish to remind them that the major challenges will start just when their follow-up closes, that being beyond the second decade after the Fontan procedure, if we want to ensure that they remain alive and enjoy good quality of life for the rest of their lives.

I give credit to the authors for the quality of their work in China, and I am sure, Professor Fontan, who passed died in 2018, would be happy to know that “his” surgery, launched in France would enable so many young survivors born with only one ventricle to lead near-normal lives… globally.

It is now our mission to carry the torch and continue looking after these patients into their adult lives, as “the operation” that was never meant to be a cure, is in fact the first hard step to climb in the crusade for long and enjoyable Fontan survival.

References

1. Tianyu Chen, Linjiang Han, Hailong Qiu, Zewen Chen, Jianzheng Cen, Shusheng Wen, Jimei Chen, Xiaobing Liu, Jian Zhuang – 20 years of experience with the Fontan procedure: risk factors for adverse outcomes, Revista Portuguesa de Cardiologia 2025.....
2. 2. Fontan F, Baudet E. Surgical repair of tricuspid atresia. Thorax 1971;26: 240-248.
3. Marc Gewilling Stephen C. Brown, Alexander van de Bruaene, Jack Rychik Providing a framework of principles for conceptualising the Fontan Circulation Acta Paediatrica. 2020;109:651–658.
4. de Leval MR†, Kilner P, Gewillig M, Bull C. Total cavopulmonary connection: a logical alternative to atriopulmonary connection for complex Fontan operations—experimental studies and early clinical experience. J Thorac Cardiovasc Surg.1988;96:682-95.
5. Marcelletti C, Corno A, Giannico S, Marino B. Inferior vena cava-pulmonary artery extracardiac conduit. A new form of right heart bypass. J Thorac Cardiovasc Surg. 1990 Aug;100(2):228–3
6. Marta Antonio, Andreia Gordo, Conceicão Pereira, Fatima Pinto†, Isabel Fragata, and Jose Fragata. - Thoracic Duct Decompression for Protein-Losing Enteropathy in Failing Fontan Circulation - Ann Thorac Surg 2016;101:2370–3
7. Gabriel Graham, Joseph A. Dearani, Talha Niaz, Sheri Crow, Frank Cetta, and Elizabeth H. Stephens Outcomes of Biventricular and Single Ventricle Heterotaxy Patients: A Single Center Five-Decade Experience - Ann Thorac. Surg. 2023;115:1206-12
8. Kavitha N. Pundi, Jonathan N. Johnson, Joseph A. Dearani, Krishna N. Pundi, Zhuo Li. Cynthia A. Hinck, Sonja H. Dahl, Bryan C. Cannon, Patrick W. O’Leary. David J. Driscoll and Frank Cetta - 40-Year Follow-Up After the Fontan Operation Long-Term Outcomes of 1,052 Patients - J Am Coll Cardiol 2015;66:1700–10
9. Mark Dennis,, Diana Zannino, Karin du Plessis, Andrew Bullock, MBBS, Patrick J.S. Disney, Dorothy J. Radford, Tim Hornung, Leeanne Grigg, Rachael Cordina, Yves d’Udekem and David S. Celermajer - Clinical Outcomes in Adolescents and Adults After the Fontan Procedure: JACC Volume 71, Number 9
10. Kate H. Marshall, Yves d'Udekem, David S. Winlaw, Diana Zannino, David S. Celermajer, Robert Justo, Ajay Iyengar, Rachael Cordina, Gary F. Sholler, Susan R. Woolfenden, and Nadine A. Kasparian. Quality of Life and Well-Being in Adults With Fontan Physiology: Findings from the Australian and New Zealand Fontan Registry Quality of Life Study - Journal of the American Heart Association, 2024; Volume 13, Number 15