Thus, the goal of the study is not the comparison with other therapeutic strategies, such as coronary surgery or conservative therapy.

The study assessed the prognostic impact not only of successful percutaneous coronary intervention (PCI) for a chronic total occlusion (CTO), but also more widely a strategy of complete revascularization in patients with single or multivessel disease and with at least one CTO. Most of these patients had a multivessel coronary disease and multivessel intervention. The imbalance in the two groups according to CTO—PCI success or failure exists, and we cannot also exclude a difference in other variables not collected, or not known, but this is implicit in the nature of the study. However, all clinical, angiographic, procedural, and outcome variables assessed in the study are recognized to have a strong prognostic impact in patients with coronary disease.

The overall population of the registry is a very high risk cohort, not only the CTO—PCI failure group. Thus, the risk for cardiac surgery was very high for the whole cohort of patients, and much more than the attended life-expectancy. Nevertheless, the rate of coronary surgery was more than 9% in the CTO—PCI failure group, and these patients were included in the group of complete coronary revascularization for survival analysis. Thus, it seems reasonable to exclude a supposed ‘clinical judgement’ bias. Furthermore, the multivariable Cox analysis excludes the possibility that the benefit of a complete coronary revascularization is related to a low risk of the patients rather than to the success of the revascularization. All the important variables were tested in a rigorous way, and in the final model, together with age and left ventricular ejection fraction, the completeness of coronary revascularization emerges as an independent prognostic factor, confirming the results of large surgical and PCI retrospective registries in patients with multivessel disease in the current era, while no randomized trial has yet addressed this issue. In the meantime, our study suggests that in the setting of patients with multivessel disease and CTO, the therapeutic target should always be a complete revascularization.

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Effect of sildenafil on haemodynamic response to exercise and exercise capacity in Fontan patients

Giardini et al.1 reported on the increase of peak oxygen uptake at a cardiopulmonary exercise test in Fontan patients after a single dose of sildenafil. This is an excellent study to outline that there are pulmonary vascular changes in these patients. These small but important changes cause an impaired inflow pattern of the single ventricle and curtail the whole cardiovascular performance.

However, there is a misprint in the formula for cardiac output (CO). This formula corrects the pulmonary blood flow (PBF) for probable right-to-left shunting during exercise. It should read

\[
CO = \frac{1}{\left[\text{arterial } O_2 \text{ content} - \text{venous } O_2 \text{ content}\right] / V_O_2 + 1 / PBF}
\]

We assume that the authors used the built-in function of the Innocor™ system that uses the correct formula. Therefore, the results should be correct concerning this issue.

Secondly, concerning the same formula, the values of pulmonary vein saturations obtained in room air during the most recent cardiac catheterization were used in the analysis. We are not sure that pulmonary vein saturation can really substitute pulmonary-endcapillary saturation in Fontan patients. This assumes that there were no intrapulmonary or veno-venous shunts at the catheter assessment. However, veno-venous collateral connections are a common problem in Fontan patients.2

Furthermore, we all assume and the study even showed that there is a pulmonary vascular dysfunction in Fontan patients. However, this might cause a V/Q mismatch with functional shunting of desoxyHb in the lungs at exercise. It is hard to predict whether and how PBF measurement with nitrous oxide dilution is affected by this V/Q mismatch. Therefore, it is questionable whether this functional right-to-left shunt of desoxyHb caused by the V/Q mismatch during exercise should provoke a correction for cardiac output like the authors did.

In summary, there are some doubts on the validity of the cardiac output calculation in that study. Nevertheless, this does not curtail the primary study conclusion that a single dose of sildenafil improves exercise capacity in Fontan patients.

References


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Effect of sildenafil on haemodynamic response to exercise and exercise capacity in Fontan patients: reply

Hager et al. have to be thanked for pointing out that there is a misprint in the formula for the calculation of cardiac output. Indeed, the formula should read: cardiac output = 1/(arterial O2 content – pulmonary end-capillary O2 content/oxygen uptake + 1/pulmonary blood flow).2

The use of pulmonary end-capillary O2 content indeed allows the InnocorTM system to calculate the amount of right-to-left shunt, assuming end-capillary O2 saturation to be equal to 98%. In Fontan patients, the presence of arterial desaturation is usually consequent to the right-to-left shunt because of either a fenestration between the Fontan circuit and the systemic atrium or pulmonary arterio-venous fistulas (anatomical or functional related to ventilation/perfusion mismatch). However, the InnocorTM system is unable to distinguish at which level the right-to-left shunt occurs. In this setting, the knowledge of pulmonary venous saturation allows us to estimate the site and relative contribution of intrapulmonary or intra-cardiac shunting to arterial desaturation (at pulmonary veins level versus at systemic atrial level). This is particularly important as pulmonary vasodilators can theoretically increase the flow in lung areas with reduced ventilation, potentially worsening arterial saturation.

In the referred study,1 an increase in arterial O2 saturation in the first hour after sildenafil administration was observed. Since the effect of sildenafil on intra-cardiac right-to-left shunt is likely to be marginal because of the restrictive nature of the fenestration (4 mm in diameter), and since pulmonary blood flow and cardiac output are known, it is possible to estimate the amount of intrapulmonary shunt after sildenafil administration, and to assess its change from baseline. Of course, this calculation does not pretend to be an accurate measurement, but rather a general guide into the potential effects of sildenafil in this population.

Furthermore, as Hager et al. have pointed out, Fontan patients have a ventilation/perfusion mismatch, which could be anatomical (pulmonary arterio-venous fistulas) or functional. However, contrary to what they suggest, predicting whether and how pulmonary blood flow measurement is affected by the ventilation/perfusion mismatch when using nitrous oxide dilution technique should not be difficult. Indeed, the InnocorTM system, using re-breathing technique, measures only pulmonary blood flow that is directed to ventilated alveoli. Lung areas with abnormally low ventilation and preserved perfusion will produce shunting of deoxygenated blood into the systemic circulation. On the other hand, lung areas with preserved ventilation and reduced perfusion will contribute to nitrous oxide washout only to an extent proportional to the amount of regional pulmonary blood flow.

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