ESC European Heart Journal - Imaging Methods and Practice (2026) **3**, qyag033
https://doi.org/10.1093/ehjimp/qyag033

SHORT REPORT

# $^{15}$O-water PET perfusion in complex congenital heart disease

**Sanna Kettunen [1,*], Riitta Paakkanen[1], Tiina Ojala [1], Teemu Maaniitty[2,3], and Valtteri Uusitalo[4]**

[1]New Children's Hospital Pediatric Research Center, Helsinki University Hospital and University of Helsinki, PL 347, 00029 HUS, Helsinki, Finland
[2]Turku PET Centre, Turku University Hospital and University of Turku, Turku, Finland
[3]Department of Clinical Physiology, Nuclear Medicine, and PET, Turku University Hospital, Turku, Finland
[4]Clinical Physiology and Nuclear Medicine, Helsinki University Hospital and University of Helsinki, Helsinki, Finland

*Received 30 December 2025; accepted after revision 19 February 2026; online publish-ahead-of-print 27 February 2026*

## Abstract

**Aims** Positron emission tomography (PET) perfusion with $^{15}$O-water is the reference standard for myocardial blood flow (MBF) quantification. Its strengths are low radiation dose, optimal tracer kinetics, and a short imaging protocol. However, the use of $^{15}$O-water or PET perfusion in patients with various complex congenital heart diseases has been rarely studied. We report the initial experiences of $^{15}$O-water PET perfusion in these patients.

**Methods and results** All $^{15}$O-water scans from patients with complex congenital heart disease at Helsinki University Hospital were retrospectively assessed (11/2021–11/2025). Thirteen congenital heart disease patients who underwent adenosine-stress $^{15}$O-water PET were identified. Most common diagnoses were transposition of the great arteries (5/13, 38%), Tetralogy of Fallot (3/13, 23%), and univentricular heart (3/13, 23%). PET perfusion was diagnostic in all cases with no adverse effects reported. The radiation dose for stress protocol was 0.3 mSv for paediatric and 0.6 mSv for adult patients, and double when rest perfusion was also obtained to calculate myocardial flow reserve. The global stress MBF was normal (>2.3 mL/g/min) in 12/13 patients. Eleven patients (85%) had anatomical coronary imaging available, all without significant stenoses. One patient had an apical transmural scar on cardiac magnetic resonance imaging, and both stress and rest $^{15}$O-water PET perfusion was decreased.

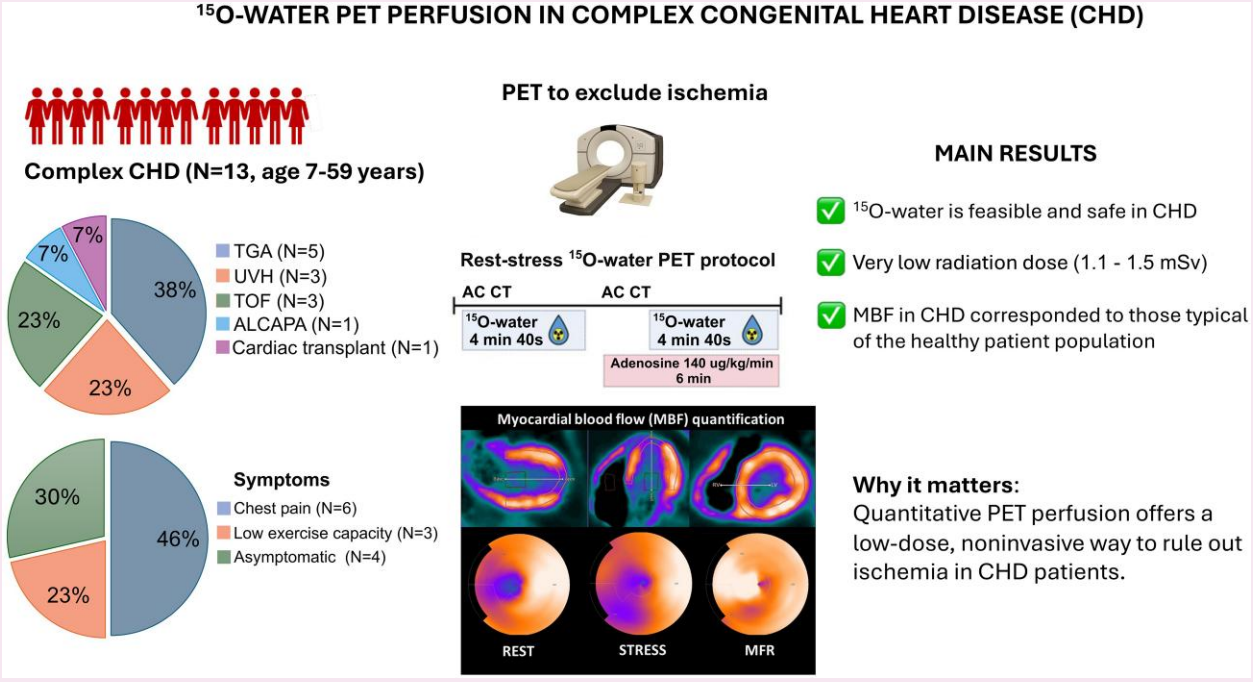
**Conclusion** $^{15}$O-water PET offers a feasible and safe ultra-low-dose approach to quantify myocardial perfusion in complex congenital heart disease and may help identify flow-limiting disease when CT anatomy alone is inconclusive.

**Lay summary** In complex congenital heart disease, myocardial ischaemia can be difficult to confirm. Flow limitation may reflect abnormal coronary anatomy, post-surgical coronary narrowing, or myocardial injury/scar after the surgery, with later atherosclerosis adding a 'double-hit'. Coronary computed tomography (CT) delineates anatomy but does not reliably indicate reduced heart blood flow. In 13 patients, adenosine-stress $^{15}$O-water positron emission tomography (PET) was feasible and safe, enabling measurement of myocardial blood flow with very low radiation dose. Stress myocardial blood flow (MBF) was normal in 12/13 patients; one patient with a scar on cardiac magnetic resonance (CMR) had low rest and stress cardiac blood flow, supporting the use of $^{15}$O-water PET to measure ischaemia when coronary artery anatomy is inconclusive.

* Corresponding author. E-mail: sanna.kettunen@hus.fi
© The Author(s) 2026. Published by Oxford University Press on behalf of the European Society of Cardiology.
This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (https://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

Downloaded from https://academic.oup.com/ehjimp/article/3/3/qyag033/8501041 by Library of Medical Faculty user on 07 April 2026

## Graphical Abstract




The clinical feasibility of 15O-water positron emission tomography (PET) perfusion in complex congenital heart disease (CHD). AC CT, attenuation correction computed tomography; ALCAPA, Anomalous Left Coronary Artery from the Pulmonary Artery; MBF, myocardial blood flow; TGA, transposition of the great arteries; TOF, tetralogy of Fallot; UVH, univentricular heart.

**Keywords** $^{15}$O-water • PET perfusion • congenital heart disease • myocardial perfusion imaging • coronary flow reserve

# Introduction

Myocardial perfusion imaging is clinically performed using SPECT, PET, or stress perfusion CMR. Quantitative PET enables absolute assessment of myocardial blood flow (MBF, mL/g/min) and myocardial flow reserve (MFR), facilitating detection of flow-limiting stenoses and microvascular dysfunction.[1] Patients with congenital heart disease (CHD) are at risk of myocardial ischaemia from CHD-specific mechanisms—abnormal coronary anatomy, post-surgical coronary ostial stenosis, and perioperative myocardial injury—with later-life atherosclerosis adding a 'double-hit susceptibility'.[2] Coronary CT is typically performed first to define anatomy, yet anatomical severity does not reliably indicate haemodynamic significance. Stress perfusion CMR is an important radiation-free alternative, but in complex CHD, interpretability may be limited by postoperative anatomy, susceptibility artefacts, and arrhythmia, and robust absolute flow quantification is not always feasible. $^{15}$O-water PET is a well-validated reference method for MBF quantification with straightforward tracer kinetics and an ultra-low radiation burden due to its 2-min half-life (0.3–0.6 mSv per dose at our centre). We therefore used quantitative $^{15}$O-water PET as a physiological adjunct when CT was considered uncertain and report our initial experience in complex CHD.

# Methods

We retrospectively reviewed the $^{15}$O-water imaging registry for all complex CHD patients in Helsinki University Hospital (November 2021—November 2025). Thirteen patients referred to PET imaging by a cardiologist were identified. Clinical characteristics were gathered from electronic health records. The study was accepted by the local Ethics committee and the institutional research board (HUS/283/2025), and the need for informed written consent was waived due to the retrospective setting. The study was conducted in accordance with the Declaration of Helsinki.

## PET perfusion protocol

All patients were imaged using a standard clinical $^{15}$O-water PET perfusion protocol previously reported in detail.[3] The target radiotracer dose was 300 MBq (0.3 mSv) for paediatric patients and 600 MBq (0.6 mSv) for adults (double for rest-stress protocol). Imaging was done using a digital PET/CT system (Discovery MI PET/CT, GE Healthcare, Waukesha, WI, USA). One patient underwent a stress-only protocol. A standard 6 min adenosine-stress (140 µg/kg/min) was used. Previously validated cut-off values for stress MBF (2.3 mL/min/g) and MFR (2.5) were used.[1]

Downloaded from https://academic.oup.com/ehjimp/article/3/3/qyag033/8501041 by Library of Medical Faculty user on 07 April 2026

**Table 1 Patient characteristics**

| | |
|---|---|
| Demographics | *n* = 13 |
| Age (years) | 27 ± 16 |
| Female | 7 (54) |
| Systemic ventricle ejection fraction (%) | 55 ± 10 |
| **Congenital defects** | |
| TGA | 5 (38) |
| TOF | 3 (23) |
| UVH | 3 (23) |
| ALCAPA | 1 (7) |
| Heart transplant due to CCTGA | 1 (7) |
| **Symptoms** | |
| Chest pain[a] | 6 (46) |
| Decreased exercise tolerance[b] | 3 (23) |
| Asymptomatic, ST-depression in an exercise test[c] | 2 (15) |
| Asymptomatic[d] | 2 (15) |
| **PET results** | |
| Normal global stress MBF (>2.3 mL/g/min) | 12 (92) |
| Normal global MFR | 12 (100) |
| Global rest MBF (mL/g/min) | 1.1 ± 0.3 |
| Global stress MBF (mL/g/min) | 3.5 ± 0.8 |
| MFR (normal >2.5) | 3.3 ± 0.7 |

Data are presented as mean ± standard deviation or number (%). ALCAPA, anomalous left coronary artery from the pulmonary artery; CCTGA, congenitally corrected transposition of the great arteries; MBF, myocardial blood flow; PET, positron emission tomography; TGA, transposition of the great arteries; TOF, Tetralogy of Fallot; UVH, Univentricular heart.
[a]TGA *n* = 1, UVH *n* = 3, TOF *n* = 1, heart transplant *n* = 1.
[b]TGA, TOF, ALCAPA, all *n* = 1.
[c]TGA with previous LAD coronary bypass *n* = 1, TOF *n* = 1.
[d]TGA *n* = 2; one patient with suspected interarterial LAD and one patient with LV dilatation and LV systolic function decrease at 45%.

# Results

## Patient characteristics

The baseline characteristics of 13 patients are depicted in *Table 1*. Six patients were paediatric (≤18 years). The most common diagnoses were transposition of the great arteries (TGA) post arterial switch operation (5/13, 38%), Tetralogy of Fallot (TOF, 3/13, 23%), and univentricular heart (UVH) with Fontan circulation due to hypoplastic left ventricle (3/13, 23%). In addition, one patient had an anomalous left coronary artery from the pulmonary artery (ALPACA), and one patient had undergone heart-lung transplantation (Eisenmenger syndrome, congenitally corrected TGA and ventricular septal defect). The clinical indication for a PET scan in all patients was to exclude myocardial ischaemia (*Table 1*). Three patients (23%) had an ejection fraction of 40–50%, whereas the rest had >50%.

## Feasibility of $^{15}$O-water PET and the imaging results

The PET perfusion study was diagnostic in all cases with no adverse effects reported. None of the patients required sedation. Total radiation dose, including attenuation correction CT, was 1.5 mSv for the adult protocol and 1.1 mSv for the paediatric protocol.

The global stress MBF was normal (>2.3 mL/g/min) in 12/13 patients (92%) (*Table 1*). In one patient who had an apical transmural scar on cardiac magnetic resonance imaging, both stress and rest perfusion were decreased (1.5 and 0.5 mL/g/min, respectively) in the absence of obstructive coronary artery disease (*Figure 1*). Global MFR was normal (≥2.5) in all 12 patients who underwent rest perfusion imaging. The patient with ALCAPA had slightly reduced regional septal perfusion (2.1 mL/g/min, MFR 2.4), attributed to abnormal vascular structures in the corresponding myocardial region. No differences in MBF were detected in different CHD subtypes or in different presentations (*Figure 2*).

# Discussion

To our knowledge, this is the first study to report the feasibility of $^{15}$O-water PET and the absolute quantitative perfusion values for a series of various complex CHD patients. $^{15}$O-water PET was feasible in a wide range of CHD diagnoses, and the absolute global myocardial perfusion values were comparable to the previously reported reference values.[1] Data on typical MBF values in CHD are limited. A similar result to ours for absolute stress MBF was observed in the $^{13}$N-ammonia PET study, but the elevated rest flow was common and attributed to chronic hypoxaemia.[4]

## Complex CHD patients and stress PET perfusion

In patients with CHD, MBF may be impaired through multiple mechanisms, including anomalous coronary artery anatomy, sequelae of surgical interventions—such as perioperative myocardial injury or post-operative complications like stenosis of reimplanted coronary ostia—and the presence of atherosclerotic disease, often described as a 'double-hit' phenomenon.[2] As the number of adult patients with CHD increases, so does the incidence of atherosclerosis in this patient group.

The obstruction of the implanted coronary ostia is a possible complication after the arterial switch in TGA patients, the largest patient group in our study. Although abnormal endothelial function after arterial switch operation has been demonstrated,[5,6] we had normal MBF in all patients.

TOF and UVH were the second most common patient groups. Coronary artery complications are not the most common clinical problem in these patients late after surgery. In our cohort, patients with TOF had symptoms or abnormalities during exercise stress testing that led to perfusion imaging. PET perfusion was performed to rule out ischaemia. In patients with UVH, the indication was to exclude microvascular disease. MBF values in these patients were within the normal range.

## Future prospects of PET perfusion imaging in CHD

The availability of $^{15}$O-water is limited by the need for an on-site cyclotron. The new Fluorine-labeled $^{18}$F-Flurpiridaz perfusion tracer is available as a unit-dose and, due to its 2-h half-life,

Downloaded from https://academic.oup.com/ehjimp/article/3/3/qyag033/8501041 by Library of Medical Faculty user on 07 April 2026

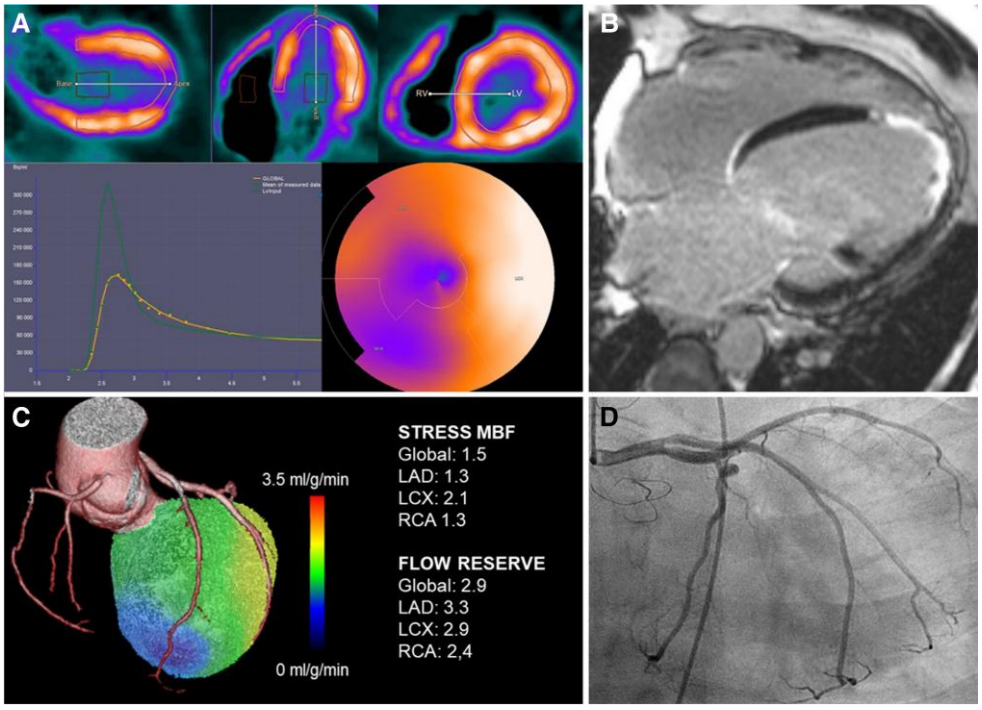



**Figure 1** An example of $^{15}$O-water PET perfusion in a patient with TOF. PET images were segmented, and dynamic flow curves were used to calculate quantitative MBF and perfusion reserve (*A*). There is a post-operative transmural apical scar on CMR imaging (*B*) that can be seen on a PET polar map (*A*) and on a hybrid PET/CTA image and MBF values (*C*). Invasive coronary angiography without coronary stenoses was performed on follow-up, which was concordant with normal perfusion reserve on PET Imaging (*D*).

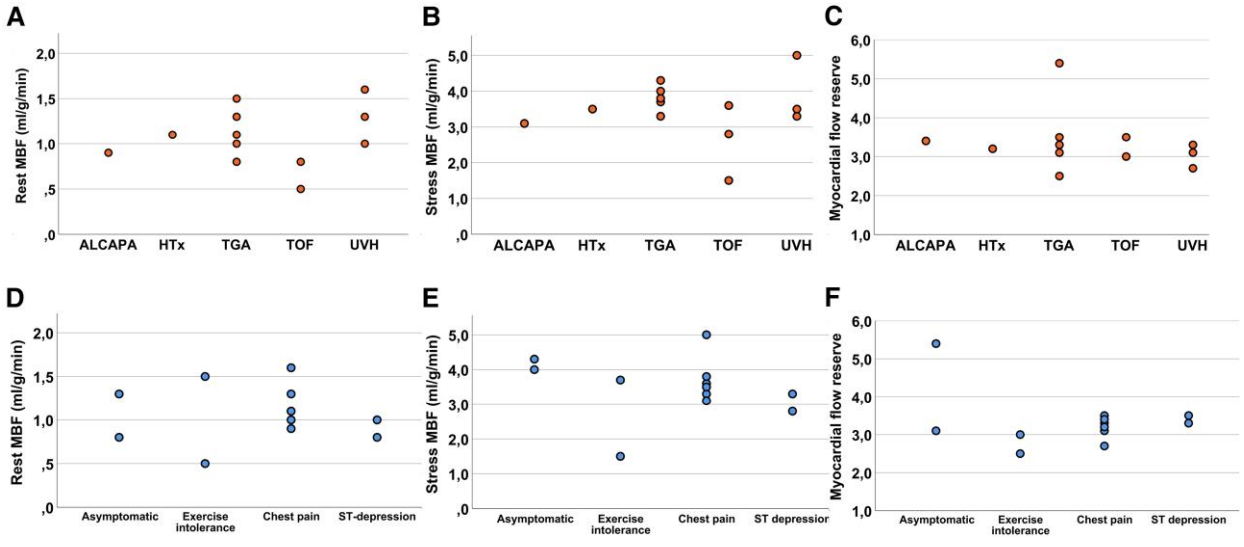



**Figure 2** MBF and MFR in different CHD conditions (*A*–*C*). In the lower panel, MBF and MFR are stratified by presenting symptom (*D*–*F*). There was no statistically significant difference between patients with different heart defects (*A*–*C*) or between different presenting symptoms (*D*–*F*) on the Kruskal-Wallis test. ALCAPA, Anomalous Left Coronary Artery from the Pulmonary Artery; HTx, Heart transplantation; TGA, transposition of the great arteries; TOF, tetralogy of Fallot; UVH, univentricular heart.

Downloaded from https://academic.oup.com/ehjimp/article/3/3/qyag033/8501041 by Library of Medical Faculty user on 07 April 2026

can be delivered outside the cyclotron facility. However, $^{18}$F-Flurpiridaz has a higher radiation dose than $^{15}$O-water but would allow exercise stress (6 mSv vs. 1.5 mSv in adults in our study).[7] Even further reductions in $^{15}$O-water radiation dose could be achieved by reducing the radiotracer dose, favouring stress-only protocols, and adopting PET/MR to eliminate the need for attenuation correction CT.

## Limitations

Our study is limited by the small patient cohort and retrospective study setting. The patient population was heterogeneous. The cut-off values of $^{15}$O-water PET were determined using the adult population.[1] Nevertheless, we believe they reasonably well reflect the threshold of myocardial ischaemia in the younger population. However, we cannot compare the degree of MBF with that of the healthy control population. Our study did not include any patients with ischaemia secondary to a coronary obstruction; the main indication was to exclude myocardial ischaemia.

## Conclusions

$^{15}$O-water PET perfusion is a feasible method for non-invasive assessment of myocardial perfusion in complex congenital heart diseases. In these conditions, perfusion values typically correspond to the previously reported normal MBF values.


## Funding

This work was financially supported by the Finnish Ministry of Social Affairs and Health, The Foundation for Pediatric Research, and The Finnish Foundation for Cardiovascular Research.

**Conflict of interest:** Bayer, steering committee member (T.O.). Bristol-Myers Squibb, Novartis and Astra-Zeneca, lecture fee (R.P.). Pfizer, lecture fee (V.U. and R.P.). No disclosures (S.K. and T.M.).


## Data availability

The data is not publicly available due to limitations imposed by the research permit to protect the privacy of study participants.

## Lead author biography

Sanna Kettunen, MD, is a paediatric cardiologist at Kuopio University Hospital, Finland. She completed her subspecialty training in paediatric cardiology at the University of Helsinki in 2025. In addition to her clinical duties, she is engaged in research at the University of Helsinki and the New Children's Hospital in Helsinki, with a particular focus on cardiovascular imaging and congenital heart diseases.

## References


1. Danad I, Uusitalo V, Kero T, Saraste A, Raijmakers PG, Lammertsma AA *et al.* Quantitative assessment of myocardial perfusion in the detection of significant coronary artery disease: cutoff values and diagnostic accuracy of quantitative [(15)O]H2O PET imaging. *J Am Coll Cardiol* 2014;**64**:1464–75.
2. Jokinen E. Coronary artery disease in patients with congenital heart defects. *J Intern Med* 2020;**288**:383–9.
3. Inkinen SI, Hippeläinen E, Uusitalo V. Adenosine-induced splenic switch-off on [$^{15}$O]$H_2O$ PET perfusion for the assessment of vascular vasodilatation. *EJNMMI Res* 2023;**13**:96.
4. Brunken RC, Perloff JK, Czernin J, Campisi R, Purcell S, Miner PD *et al.* Myocardial perfusion reserve in adults with cyanotic congenital heart disease. *Am J Physiol Heart Circ Physiol* 2005;**289**:H1798–806.
5. Ossner M, Buechel RR, Vontobel J, Mikulicic F, Gräni C, Benz DC *et al.* Myocardial blood flow and cardiac sympathetic innervation in young adults late after arterial switch operation for transposition of the great arteries. *Int J Cardiol* 2020;**299**:110–5.
6. Bengel FM, Hauser M, Duvernoy CS, Kuehn A, Ziegler SI, Stollfuss JC *et al.* Myocardial blood flow and coronary flow reserve late after anatomical correction of transposition of the great arteries. *J Am Coll Cardiol* 1998;**32**:1955–61.
7. Maddahi J. 18F flurpiridaz PET MPI: imaging characteristics and clinical trials. *J Nucl Cardiol* 2025;**45S**:102175.


Downloaded from https://academic.oup.com/ehjimp/article/3/3/qyag033/8501041 by Library of Medical Faculty user on 07 April 2026