

World Journal of *Cardiology*

World J Cardiol 2024 January 26; 16(1): 1-48



EDITORIAL

- 1 Development of pulmonary hypertension remains a major hurdle to corrective surgery in Down syndrome
Batta A, Hatwal J
- 5 Venous Doppler flow patterns, venous congestion, heart disease and renal dysfunction: A complex liaison
Di Maria A, Siligato R, Bondanelli M, Fabbian F

MINIREVIEWS

- 10 Unveiling the silent link: Normal-tension glaucoma's enigmatic bond with cardiac blood flow
Ramesh PV, Morya AK, Aradhya AK, Pannersevam P, Gopalakrishnan ST, Ramesh SV, Devadas AK, Krishna N

ORIGINAL ARTICLE**Retrospective Study**

- 16 Do changes in intracoronary pressure aid coronary spasm diagnosis using the spasm provocation test?
Teragawa H, Oshita C, Uchimura Y

SYSTEMATIC REVIEWS

- 27 Safety and effectiveness of neuromuscular electrical stimulation in cardiac surgery: A systematic review
Kourek C, Kanellopoulos M, Raidou V, Antonopoulos M, Karatzanos E, Patsaki I, Dimopoulos S

META-ANALYSIS

- 40 Left bundle branch pacing vs biventricular pacing in heart failure patients with left bundle branch block: A systematic review and meta-analysis
Yasmin F, Moeed A, Ochani RK, Raheel H, Awan MAE, Liaquat A, Saleem A, Aamir M, Hawwa N, Surani S

ABOUT COVER

Peer Reviewer of *World Journal of Cardiology*, Atarodsadat Mostafavinia, PhD, Assistant Professor, Department of Anatomical Sciences, Faculty of Medicine, Tehran Medical sciences, Azad University, Tehran, Iran.
a.mostafavinia@gmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Cardiology* (*WJC*, *World J Cardiol*) is to provide scholars and readers from various fields of cardiology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJC mainly publishes articles reporting research results and findings obtained in the field of cardiology and covering a wide range of topics including acute coronary syndromes, aneurysm, angina, arrhythmias, atherosclerosis, atrial fibrillation, cardiomyopathy, congenital heart disease, coronary artery disease, heart failure, hypertension, imaging, infection, myocardial infarction, pathology, peripheral vessels, public health, Raynaud's syndrome, stroke, thrombosis, and valvular disease.

INDEXING/ABSTRACTING

The *WJC* is now abstracted and indexed in Emerging Sources Citation Index (Web of Science), PubMed, PubMed Central, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for *WJC* as 1.9; IF without journal self cites: 1.8; 5-year IF: 2.3; Journal Citation Indicator: 0.33. The *WJC*'s CiteScore for 2022 is 1.9 and Scopus CiteScore rank 2022: Cardiology and cardiovascular medicine is 226/354.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Hua-Ge Yu; Production Department Director: Xiang Li; Editorial Office Director: Yun-Xiao Jiao Wu.

NAME OF JOURNAL

World Journal of Cardiology

ISSN

ISSN 1949-8462 (online)

LAUNCH DATE

December 31, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Ramdas G Pai, Dimitrios Tousoulis, Marco Matteo Ciccone, Pal Pacher

EDITORIAL BOARD MEMBERS

<https://www.wjnet.com/1949-8462/editorialboard.htm>

PUBLICATION DATE

January 26, 2024

COPYRIGHT

© 2024 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Development of pulmonary hypertension remains a major hurdle to corrective surgery in Down syndrome

Akash Batta, Juniali Hatwal

Specialty type: Cardiac and cardiovascular systems

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Gałeczka M, Poland

Received: November 5, 2023

Peer-review started: November 5, 2023

First decision: November 30, 2023

Revised: December 3, 2023

Accepted: December 18, 2023

Article in press: December 18, 2023

Published online: January 26, 2024



Akash Batta, Department of Cardiology, Dayanand Medical College and Hospital, Ludhiana 141001, Punjab, India

Juniali Hatwal, Department of Internal Medicine, Post Graduate Institute of Medical Education & Research, Chandigarh 160012, India

Corresponding author: Akash Batta, Doctor, MD, Assistant Professor, Researcher, Department of Cardiology, Dayanand Medical College and Hospital, Tagore Nagar, Civil Lines, Ludhiana 141001, Punjab, India. akashbatta02@gmail.com

Abstract

Down syndrome is the most common chromosomal abnormality encountered in clinical practice with 50% of them having associated congenital heart disease (CHD). Shunt lesions account for around 75% of all CHDs in Down syndrome. Down syndrome patients, especially with large shunts are particularly predisposed to early development of severe pulmonary hypertension (PH) compared with shunt lesions in general population. This necessitates timely surgical correction which remains the only viable option to prevent long term morbidity and mortality. However, despite clear recommendations, there is wide gap between actual practice and fear of underlying PH which often leads to surgical refusals in Down syndrome even when the shunt is reversible. Another peculiarity is that Down syndrome patients can develop PH even after successful correction of shunt. It is not uncommon to come across Down syndrome patients with uncorrected shunts in adulthood with irreversible PH at which stage intracardiac repair is contraindicated and the only option available is a combined heart-lung transplant. However, despite the guidelines laid by authorities, the rates of cardiac transplant in adult Down syndrome remain dismal largely attributable to the high prevalence of intellectual disability in them. The index case presents a real-world scenario highlighting the impact of severe PH on treatment strategies and discrimination driven by the fear of worse outcomes in these patients.

Key Words: Down syndrome; Congenital heart disease; Pulmonary hypertension; Cardiac transplantation; Pulmonary vascular resistance; Surgical correction

©The Author(s) 2024. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Down syndrome is the most common chromosomal abnormality with roughly half of them having associated congenital heart disease (CHD). People with Down syndrome are especially predisposed to early development of severe pulmonary hypertension (PH) compared with CHDs in general population. It is not uncommon to come across Down syndrome patients with uncorrected shunts in adulthood with irreversible PH at which stage the only option available is a combined heart-lung transplant. However, despite the guidelines laid by authorities, the rates of cardiac transplant in adults with Down syndrome remain dismal largely attributable to the high prevalence of intellectual disability in them.

Citation: Batta A, Hatwal J. Development of pulmonary hypertension remains a major hurdle to corrective surgery in Down syndrome. *World J Cardiol* 2024; 16(1): 1-4

URL: <https://www.wjgnet.com/1949-8462/full/v16/i1/1.htm>

DOI: <https://dx.doi.org/10.4330/wjc.v16.i1.1>

INTRODUCTION

Down syndrome is the most common chromosomal abnormality encountered in clinical practice[1]. Congenital heart disease (CHD) is present in roughly half of all people with Down syndrome and remains the leading cause of mortality in this population[2]. Amongst the wide variety of CHDs seen in Down syndrome, shunt lesions in particular atrio-ventricular septal defects and ventricular septal defects are the most frequent accounting for 3/4th of all CHDs in this population[3]. People with Down syndrome especially with large shunts are particularly predisposed to early development of severe pulmonary hypertension (PH) compared with CHDs in general population (10 times higher risk) [4,5]. In patients with Down syndrome and large post-tricuspid shunts, PH is present in up to 1/3rd of them within the first year itself[6,7]. The reason for earlier development of significant PH is attributable to genetic predisposition and associated comorbidities (most notably lung developmental disorders). Another peculiarity is the development of PH even after timely corrective repair of the shunt lesions in some patients with Down syndrome[6]. Thus, screening for PH is an essential component of life-long care in Down syndrome.

Therefore, in Down syndrome early surgical repair is critical in preventing the development of PH which once established significantly increases the procedural risks and prohibits surgical repair. Development of severe and irreversible PH (Eisenmenger syndrome) due to structural changes and fibroses in pulmonary vasculature is associated with high morbidity and mortality in these patients. Guidelines recommend management of shunt lesions in Down syndrome similar to general population, however, early development of severe PH often leads to reluctance on the part of surgeon to go ahead with corrective repair. The reluctance is largely driven by the fear of adverse hemodynamic consequences of severe PH in these patients. Further, limited representation of Down syndrome patients in trials of PH reducing therapies (endothelin antagonists and prostacyclin analogues) makes choice of optimal medical therapy difficult which further contributes to poorer outcomes[8,9].

SURGICAL INTERVENTION IN DOWN SYNDROME WITH CHD

Despite, the high-risk nature of intracardiac repair in Down syndrome, there has been progress over the last few decades and now intracardiac repair is increasingly being offered to this subset of patients[10]. In general, patients with Down syndrome are much younger and have lower body weight at the time of intracardiac repair compared to general population[11]. Overall, the increased perioperative risk and high prevalence of non-cardiac developmental diseases has resulted in lack of enthusiasm amongst pediatric cardiac surgeons to take these patients up for intracardiac repair despite the evidence supporting comparable outcomes of cardiac surgery in these patients[12]. As such, presentation at a later stage with severe PH and shunt reversal is not uncommon[4,5]. At this stage given the pulmonary vascular resistance and irreversible nature of PH, intracardiac repair is contraindicated and the only option available is a combined heart-lung transplant. However, this is easier said than done with dismal rates of transplant procedures being performed in these patients. Since the first report of heart-lung transplant in Down syndrome in 1996 after a national wide anti-discrimination campaign, only a handful of Down syndrome patients have undergone cardiac transplant rendering the assessment of outcomes difficult[13,14]. A major reason for low rates of cardiac transplant in adult Down syndrome remains the high prevalence of intellectual disability in them[7]. Another major concern remains the predisposition of Down syndrome to develop oncological disorders which is further aggravated because of the immunosuppressive agents post-transplant and Epstein-Barr virus infection[15]. Nonetheless, the international society for heart-lung transplant and the committee on bioethics has made clear stance that patients with Down syndrome should be given equal right to transplant listings and that discrimination on the basis of intellectual disability or syndrome is unjustified[13,16].

The recent paper by Kong *et al*[17], appropriately reflects the current practice in regards to the management of Down syndrome with CHD. In the index paper, a 13-year-old boy having a large atrial septal defect and patent ductus arteriosus (PDA), underwent PDA closure in childhood. Despite, this he developed severe PH many years later. This in fact highlights the genetic predisposition to develop that these patients have which is not the case in shunt lesions with normal chromosomal structure. Given the high pulmonary vascular resistance, the boy was denied definitive a procedure (heart-lung transplant) at multiple hospitals possibly due to the fear of worse outcome. This is a reflection of the wide gap

between recommendations and actual clinical practice. As mentioned earlier the governing authorities should provide Down syndrome patients with equal opportunities for heart transplantation, which is in fact is hardly ever the case in real world setting[13,16,18]. The authors deserve credit for their decision to offer heart-lung transplant to the index child albeit it did not materialize on this occasion.

CONCLUSION

Down syndrome with CHD is particularly predisposed to develop severe PH early in the course. Hence, timely surgical correction is crucial to improve long term outcomes. Another oddity in these patients is the development of PH even after successful closure of the shunt lesions which highlights the predisposition to develop pulmonary remodeling and fibroses de novo. The index case highlights the same and also raises concern for the discrimination faced by this group of individuals and preferential exclusion from advanced intervention in the form of heart-lung transplantation despite the opposition to the same by the governing bodies.

FOOTNOTES

Author contributions: Batta A and Hatwal J contributed equally to this work.

Conflict-of-interest statement: All the authors declare that they have no conflict of interest.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: India

ORCID number: Akash Batta 0000-0002-7606-5826; Juniali Hatwal 0000-0001-5433-0433.

S-Editor: Liu JH

L-Editor: A

P-Editor: Zhao S

REFERENCES

- 1 **Weijerman ME**, van Furth AM, van der Mooren MD, van Weissenbruch MM, Rammeloo L, Broers CJ, Gemke RJ. Prevalence of congenital heart defects and persistent pulmonary hypertension of the neonate with Down syndrome. *Eur J Pediatr* 2010; **169**: 1195-1199 [PMID: 20411274 DOI: 10.1007/s00431-010-1200-0]
- 2 **Irving CA**, Chaudhari MP. Cardiovascular abnormalities in Down's syndrome: spectrum, management and survival over 22 years. *Arch Dis Child* 2012; **97**: 326-330 [PMID: 21835834 DOI: 10.1136/adc.2010.210534]
- 3 **Kidd SA**, Lancaster PA, McCredie RM. The incidence of congenital heart defects in the first year of life. *J Paediatr Child Health* 1993; **29**: 344-349 [PMID: 8240861 DOI: 10.1111/j.1440-1754.1993.tb00531.x]
- 4 **Bush D**, Galambos C, Dunbar Ivy D. Pulmonary hypertension in children with Down syndrome. *Pediatr Pulmonol* 2021; **56**: 621-629 [PMID: 32049444 DOI: 10.1002/ppul.24687]
- 5 **Bush D**, Galambos C, Ivy DD, Abman SH, Wolter-Warmerdam K, Hickey F. Clinical Characteristics and Risk Factors for Developing Pulmonary Hypertension in Children with Down Syndrome. *J Pediatr* 2018; **202**: 212-219.e2 [PMID: 30025669 DOI: 10.1016/j.jpeds.2018.06.031]
- 6 **Dimopoulos K**, Constantine A, Clift P, Condliffe R, Moledina S, Jansen K, Inuzuka R, Veldtman GR, Cua CL, Tay ELW, Opatowsky AR, Giannakoulas G, Alonso-Gonzalez R, Cordina R, Capone G, Namuyonga J, Scott CH, D'Alto M, Gamero FJ, Chicoine B, Gu H, Limsuwan A, Majekodunmi T, Budts W, Coghlan G, Broberg CS; for Down Syndrome International (DSI). Cardiovascular Complications of Down Syndrome: Scoping Review and Expert Consensus. *Circulation* 2023; **147**: 425-441 [PMID: 36716257 DOI: 10.1161/CIRCULATIONAHA.122.059706]
- 7 **Delany DR**, Gaydos SS, Romeo DA, Henderson HT, Fogg KL, McKeta AS, Kavarana MN, Costello JM. Down syndrome and congenital heart disease: perioperative planning and management. *J Congenit Cardiol* 2021; **5**: 1-14 [DOI: 10.1186/s40949-021-00061-3]
- 8 **Beghetti M**, Rudzinski A, Zhang M. Efficacy and safety of oral sildenafil in children with Down syndrome and pulmonary hypertension. *BMC Cardiovasc Disord* 2017; **17**: 177 [PMID: 28676038 DOI: 10.1186/s12872-017-0569-3]
- 9 **Lindberg L**, Olsson AK, Jögi P, Jonmarker C. How common is severe pulmonary hypertension after pediatric cardiac surgery? *J Thorac Cardiovasc Surg* 2002; **123**: 1155-1163 [PMID: 12063463 DOI: 10.1067/mtc.2002.121497]
- 10 **Stoll C**, Dott B, Alembik Y, Roth MP. Associated congenital anomalies among cases with Down syndrome. *Eur J Med Genet* 2015; **58**: 674-680 [PMID: 26578241 DOI: 10.1016/j.ejmg.2015.11.003]
- 11 **Fudge JC Jr**, Li S, Jaggars J, O'Brien SM, Peterson ED, Jacobs JP, Welke KF, Jacobs ML, Li JS, Pasquali SK. Congenital heart surgery outcomes in Down syndrome: analysis of a national clinical database. *Pediatrics* 2010; **126**: 315-322 [PMID: 20624800 DOI: 10.1542/peds.2009-3245]

- 12 **Hoashi T**, Hirahara N, Murakami A, Hirata Y, Ichikawa H, Kobayashi J, Takamoto S. Current Surgical Outcomes of Congenital Heart Surgery for Patients With Down Syndrome in Japan. *Circ J* 2018; **82**: 403-408 [PMID: [28904256](#) DOI: [10.1253/circj.CJ-17-0483](#)]
- 13 **Statter MB**, Noritz G; COMMITTEE ON BIOETHICS, COUNCIL ON CHILDREN WITH DISABILITIES. Children With Intellectual and Developmental Disabilities as Organ Transplantation Recipients. *Pediatrics* 2020; **145** [PMID: [32312907](#) DOI: [10.1542/peds.2020-0625](#)]
- 14 **Broda CR**, Cabrera AG, Rossano JW, Jefferies JL, Towbin JA, Chin C, Shamszad P. Cardiac transplantation in children with Down syndrome, Turner syndrome, and other chromosomal anomalies: A multi-institutional outcomes analysis. *J Heart Lung Transplant* 2018; **37**: 749-754 [PMID: [29449075](#) DOI: [10.1016/j.healun.2018.01.1296](#)]
- 15 **Liu L**, Zhang X, Feng S. Epstein-Barr Virus-Related Post-Transplantation Lymphoproliferative Disorders After Allogeneic Hematopoietic Stem Cell Transplantation. *Biol Blood Marrow Transplant* 2018; **24**: 1341-1349 [PMID: [29530767](#) DOI: [10.1016/j.bbmt.2018.02.026](#)]
- 16 **Mehra MR**, Canter CE, Hannan MM, Semigran MJ, Uber PA, Baran DA, Danziger-Isakov L, Kirklin JK, Kirk R, Kushwaha SS, Lund LH, Potena L, Ross HJ, Taylor DO, Verschuuren EAM, Zuckermann A; International Society for Heart Lung Transplantation (ISHLT) Infectious Diseases, Pediatric and Heart Failure and Transplantation Councils. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10-year update. *J Heart Lung Transplant* 2016; **35**: 1-23 [PMID: [26776864](#) DOI: [10.1016/j.healun.2015.10.023](#)]
- 17 **Kong MW**, Li YJ, Li J, Pei ZY, Xie YY, He GX. Down syndrome child with multiple heart diseases: A case report. *World J Cardiol* 2023; **15**: 615-622 [DOI: [10.4330/wjc.v15.i11.615](#)]
- 18 **Tong A**, Jan S, Wong G, Craig JC, Irving M, Chadban S, Cass A, Howard K. Rationing scarce organs for transplantation: healthcare provider perspectives on wait-listing and organ allocation. *Clin Transplant* 2013; **27**: 60-71 [PMID: [22994888](#) DOI: [10.1111/ctr.12004](#)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA

Telephone: +1-925-3991568

E-mail: office@baishideng.com

Help Desk: <https://www.f6publishing.com/helpdesk>

<https://www.wjgnet.com>

