

COVID-19 Management in Children: Approach in Pediatric Cardiology

Çocuklarda COVID-19 Yönetimi: Çocuk Kardiyolojide Yaklaşım

Ibrahim Ilker CETIN^{1,2}, Hazım Alper GURSU^{1,3}, Ibrahim ECE^{1,3}

¹Ankara Bilkent City Hospital / Children's Hospital, Pediatric Cardiology Clinic, Ankara, Turkey

²Yıldırım Beyazıt University, Department of Pediatrics, Pediatric Cardiology Unit, Ankara, Turkey

³University of Health Sciences, Department of Pediatrics, Pediatric Cardiology Unit, İstanbul, Turkey



ABSTRACT

In children, cardiac involvement can be observed during the course of COVID-19, which is mostly mild, and COVID-19 may develop in children who have previously been known to have congenital or acquired heart disease. The subject of this article is how these children should be evaluated cardiologically, and how the follow-up and treatment of children with heart disease will be managed during the pandemic. Considering the articles and guides published in the literature, some determinations were made and the suggestions developed were presented in this article.

Key Words: Approach, Cardiology, Children, COVID-19, Management

ÖZ

Çocuklarda çoğu zaman hafif seyreden COVID-19 seyri sırasında kardiyak tutulum görülebileceği gibi, daha önce doğumsal yada edinsel kalp hastalığı olduğu bilinen çocuklarda da COVID-19 gelişebilir. Bu çocukların kardiyak açıdan nasıl değerlendirilmesi gerektiği, ayrıca kalp hastalığı bulunan çocukların takip ve tedavilerinin pandemi süresince nasıl yönetileceği bu makalenin konusudur. Literatürde yayınlanmış olan makale ve rehberler dikkate alınarak bazı saptamalar yapılmış ve geliştirilen öneriler bu yazıda sunulmuştur.

Anahtar Kelimeler: COVID-19, Çocuklar, Kardiyoloji, Yaklaşım, Yönetim

INTRODUCTION

COVID-19 is mostly mild in children. Even if children are asymptomatic, there is a high level of contamination (1-14). Cardiac involvement during COVID-19 in children is extremely rare and is often accompanied by multiple organ failure. However, the number of infected children is increasing day by day and new data on cardiac involvement are obtained (15-17). The common idea in the guidelines published recently on how

to manage COVID-19 in children is that unusual (out of routine) approaches should be applied during the pandemic (18-30). In this process, how to use hospital resources more effectively, which patient groups will be prioritized, how to perform patient examination, electrocardiography (ECG) and echocardiography (ECHO) evaluation, as well as how to protect patients and health personnel during interventional and surgical procedures are important issues. In this article, data from current literature and suggestions on how the process should be managed in children will be presented.

CETIN II : 0000-0001-9480-8278
GURSU HA : 0000-0002-0707-2678
ECE I : 0000-0002-3657-2209

Conflict of Interest / Çıkar Çatışması: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Contribution of the Authors / Yazın Katkısı: **CETIN II:** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the Conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. **GURSU HA:** Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar. **ECE I:** Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in necessary literature review for the study, Reviewing the article before submission scientifically besides spelling and grammar.

How to cite / Atıf Yazım Şekli : Cetin II, Gürsu HA, Ece I. Covid-19 Management in Children: Approach in Pediatric Cardiology. Turkish J Pediatr Dis 2020; 14(suppl):60-64.

Correspondence Address / Yazışma Adresi:

I. Ilker CETIN
Ankara Bilkent City Hospital / Children's Hospital,
Pediatric Cardiology Clinic, Ankara, Turkey
E-posta: iicetin@hotmail.com

Received / Geliş tarihi : 15.06.2020

Accepted / Kabul tarihi : 20.07.2020

Online published : 27.07.2027

Elektronik yayın tarihi

DOI: 10.12956/tchd.753060

PEDIATRIC CARDIOLOGY SERVICES DURING PANDEMIC

During the pandemic, routine polyclinic controls should be postponed, and it should be ensured that patients apply to the hospital only in emergency situations. Patients who have been diagnosed and started a specific treatment should be followed up remotely, and they should be asked to come to the hospital when necessary. Every patient admitted to the hospital should be considered as suspected COVID-19, social distance should be preserved while taking history, and protective equipment (mask, gloves, overalls, face shield) should be used during physical examination. Meanwhile, patients and their relatives should be provided to wear masks (1,2,18,19).

Routine ECG and ECHO evaluation is not recommended during pandemic. Protective equipment containing high-level masks (such as FFP1/N80, FFP2/N95 or FFP3/N100) should be ensured, especially when performing ECHO, because of long-term close contact with the patient will be necessary, taking into account that children are mostly asymptomatic and that children who are restless and crying will spread a lot of droplets around them. Echocardiography device, probes and examination table should be cleaned with soapy water after each procedure and then disinfected. Also, rooms, devices and probes used for patients diagnosed with COVID-19 should be separated. Since the risk of contamination will be very high during transesophageal echocardiography (TEE), all TEE procedures should be postponed except for emergencies (24).

Cardiac catheterization is not recommended during pandemic except in emergencies. The procedures of patients in the semi-elective diagnostic group can be delayed as much as possible (several months) depending on the patient load. The procedures of patients in the elective diagnostic group should be postponed absolutely. Urgent, semi-elective and elective diagnostic groups are presented in Table I. It is very important for angiography team to enter the procedures with flexible working order in terms of protection from contamination. Patients and their relatives who

are scheduled for cardiac catheterization should be questioned for the symptoms of COVID-19, and patients and relatives with symptoms should be tested. Informed consent should also be obtained from patients' relatives that they have been informed about the pandemic process as well. If the patient's test result is negative, it is recommended that only anesthesia team use protective equipment, if positive, all angio team should use high-level protective equipment, and if possible, the procedure should be performed in a negative pressure room (21,22,25). General anesthesia should be preferred in order to minimize contamination and reduce the patient's cough and secretions as much as possible. It should be kept in mind that resuscitation may be required during cardiac catheterization, so relevant guidance suggestions should be applied in this regard (26-28).

Electrophysiological study, ablation, pacemaker and implantable cardioverter defibrillator (ICD) applications should be planned separately for the relevant diagnostic groups during the pandemic. Urgent, semi-elective and elective diagnostic groups for rhythm studies in children are presented in Table II. It is recommended that patients who have been ablated or who have been implanted with pacemaker or ICD be discharged as soon as possible (within the first 24 hours if possible) (29).

Surgery of children with heart disease, which is accepted as one of the co-morbid conditions in which the course of COVID-19 is expected severe, should be postponed unless it is urgent. The operations of patients in the semi-elective diagnostic group should be planned in a suitable period. Urgent, semi-elective and elective diagnostic groups for cardiac surgeries to be performed in children are presented in Table III. Patients who develop COVID-19 should be told about the morbidity and mortality could be higher than expected during the heart surgery and intensive care follow-up, and there is also possibility of getting the infection in the hospital, and informed consent should be obtained from patients' relatives that they are informed about that issue as well. Virus test should be performed to patient and accompanying person. Practices

Table I: Urgent, semi-elective and elective groups for cardiac catheterisation during pandemics.

URGENT (Immediately or in 1-2 weeks)	SEMI-ELECTIVE (In 1-3 months)	ELECTIVE (More than 3 months)
Pericardiosentesis TGA – Balloon atrial septostomy, HLHS – Atrial septal decompression ECMO – Atrial septal decompression APCA occlusion – Hemoptysis Duktal stent – PDA dependent KHD Balloon or stent to RVOT Critical AS/PS – Balloon valvuloplasty IVS/PA – Valve perforation PDA closure in prematures OHT – Biopsy in acute rejection	Pulmonary vein stenosis – HF or PH Large PDA – HF or PH Large VSD – HF or PH Severe AS Severe PS Severe aortic coarctation Severe conduit stenosis Pre-Glenn	Secundum ASD closure VSD closure PDA closure Moderate AS Moderate PS Postoperative moderate or severe PR Pre-Fontan OHT – Rutine biopsy

APCA: Aorticopulmonary collateral artery, **AS:** Aortic stenosis, **ASD:** Atrial septal defect, **CHD:** Congenital heart disease, **ECMO:** Extracorporeal membrane oxygenation, **HF:** Heart failure, **HLHS:** Hypoplastic left heart syndrome, **IVS/PA:** Pulmonary atresia with intact ventricular septum, **OHT:** Orthotopic heart transplantation, **PDA:** Patent ductus arteriosus, **PH:** Pulmonary hypertension, **PR:** Pulmonary regurgitation, **PS:** Pulmonary stenosis, **RVOT:** Right ventricular outflow tract, **TGA:** Transposition of great arteries, **VSD:** Ventricular septal defect

Table II: Urgent, semi-elective and elective groups for electrophysiologic study during pandemics.

URGENT (Immediately or in 1-2 weeks)	SEMI-ELECTIVE (In 1-3 months)	ELECTIVE (More than 3 months)
Pacemaker implantation ICD implantation Transcatheter ablation – Resistant case Infected pacemaker/lead extraction Cardioversion – Resistant case	Transcatheter ablation – Hemodynamically stabil SVT/VT Pacemaker replacement	Transcatheter ablation – Stabil case Diagnostic EPS

EPS: Electrophysiologic study, **ICD:** Implantable cardioverter defibrillator, **SVT:** Supraventricular tachycardia, **VT:** Ventricular tachycardia

Table III: Urgent, semi-elective and elective groups for cardiac surgery during pandemics.

URGENT (Immediately or in 1-2 weeks)	SEMI-ELECTIVE (In 1-3 months)	ELECTIVE (More than 3 months)
Pericardial tamponade - Drainage Ductus dependent systemic circulation (AI, HLHS, severe AC, critical AS) Ductus dependent pulmonary circulation (PA, critical PS) Simple TGA Obstructive TAPVC Severe cyanotic CHD Severe Shone complex Large PDA in prematures Postoperative revision ECMO/assists device requirement OHT	Non-obstructive TAPVC TGA with large VSD Truncus arteriosus APW Complete AVSD Tetralogy of Fallot with spell Pulmonary banding Large VSD – HF or PH Large PDA – HF or PH Infective endocarditis Cardiac mass LVOT obstruction HLHS stage II	ASD closure Partial AVSD VSD closure PDA closure Tetralogy of Fallot Glenn operation Fontan operation

AC: Aortic coarctation, **AI:** Aortic interruption, **APW:** Aorticopulmonary window, **AS:** Aortic stenosis, **ASD:** Atrial septal defect, **AVSD:** Atrioventricular septal defect, **CHD:** Congenital heart disease, **ECMO:** Extracorporeal membrane oxygenation, **HF:** Heart failure, **HLHS:** Hypoplastic left heart syndrome, **LVOT:** Left ventricular outflow tract, **OHT:** Orthotopic heart transplantation, **PA:** Pulmonary atresia, **PDA:** Patent ductus arteriosus, **PH:** Pulmonary hypertension, **PS:** Pulmonary stenosis, **TAPVC:** Totally abnormal pulmonary venous connection, **TGA:** Transposition of great arteries, **VSD:** Ventricular septal defect

regarding the use of protective equipment during surgery are the same as in cardiac catheterization. The operations should be done in rooms with negative pressure as much as possible. The room should be disinfected with ultraviolet rays after surgery (30). In the course of COVID-19, the relevant guideline recommendations on extracorporeal membrane oxygenation (ECMO) support practices and advanced life support in children should be implemented (27,28).

Although it is predicted that COVID-19 may progress more severely in children with hemodynamically significant congenital or acquired heart disease, no scientific data supporting this idea has been published yet. It is recommended that patients with COVID-19 have a closer follow-up and be hospitalized at an earlier stage (20,21).

The agent of COVID-19, SARS-CoV-2 virus is known to have high penetration into tissues with high angiotensin converting enzyme-2 (ACE2) expression (heart, lung). Although ACE2 expression is predicted to increase in tissues and increase viral damage in this way in patients using ACE inhibitors (ACEI) or angiotensin receptor blockers (ARB), scientific data supporting this view have not been published yet. Therefore, no consensus has been reached on discontinuation of these medications in

patients taking ACEI or ARB (hypertension, heart failure, valve regurgitation) (16, 20,21).

MANAGEMENT OF CHILDREN WITH COVID-19

Cardiovascular system examination is performed with vital signs (body temperature, heart rate, respiratory rate, blood pressure and oxygen saturation). In the presence of findings suggesting cardiac involvement (heart failure, irregular rhythm), ECG and ECHO evaluation are recommended. The corrected QT (QTc) should be calculated since drugs such as hydroxychloroquine and azithromycin, which are frequently used in the treatment of patients, can lead to QT prolongation and arrhythmia. Cardiac troponin level in the presence of findings indicating myocardial damage at ECG, and BNP level in patients with signs of heart failure or myocardial dysfunction at ECHO, should be studied. Routine and unnecessary ECHO evaluation should be avoided to prevent transmission from patient to physician and also to other patients as there will be prolonged close contact while performing ECHO (24).

In children with COVID-19, cardiac involvement may appear as myocardial damage or rhythm disturbance. In patients, hypoxic damage due to severe lung disease, multiple organ failure and shock due to systemic inflammatory response, and

myocardial damage due to acute viral myocarditis can be seen. Acute myocardial damage is often subclinical in children. In case of progressive or severe damage, heart failure or rhythm disturbances may occur. Patients with severe lung disease may develop right heart failure and pulmonary hypertension. Treatment approaches applied in other viral myocarditis are used in treatment. Intravenous immunoglobulin (IVIG) therapy can be beneficial with both antiviral and immunomodulatory effects. Routine troponin measurement is not recommended for patients with COVID-19 unless evidence suggesting myocardial damage develops. Likewise, routine natriuretic peptide measurement is not recommended for patients without heart failure findings. However, serial monitoring of these biomarkers in patients with severe course can provide information regarding prognosis (3,15,17).

In these patients, rhythm disturbances (such as QT prolongation) may be seen during systemic inflammatory process or as a side effect of some drugs (lopinavir/ritonavir, hydroxychloroquine, azithromycin) used in the treatment of COVID-19. Patients with congenital long QT duration, electrolyte imbalance (hypopotasemia, hypomagnesemia), using another QT-prolonging drug, other heart disease (cardiomyopathy, arrhythmia), kidney or liver failure should be regularly followed-up for QT prolongation.

QT measurement should be done 2-3 hours after the drug is administered. If the QTc duration is longer than 500 ms for those with a QRS duration below 120 ms, and longer than 530 ms for those with a QRS duration above 120 ms, or if the QTc duration has prolonged longer than 60 ms, azithromycin treatment should be discontinued and the hydroxychloroquine dose should be reduced. If QTc prolongation continues at this level, hydroxychloroquine treatment should also be terminated. If there is at least one of the above mentioned risk factors, outpatient follow-up is not recommended. If the QTc duration is over 460 ms at ECG, obtained 2-3 hours after the drug is taken on the 3rd day of treatment, in patients who do not have risk factors and are monitored on an outpatient basis, daily QTc measurement is recommended. In the follow-up, drug reduction and treatment termination criteria are applied in the same way (31-33).

It is also known that, when hydroxychloroquine is used for a long time, it may cause myocardial damage. In addition, hydroxychloroquine and some antiviral drugs (ribavirin) can increase the blood levels of some beta-blocker and anticoagulant drugs, respectively (31,33).

REFERENCES

1. Shen KL, Yang YH, Jiang RM, Wang TY, Zhao DC, Jiang Y, et al. Updated diagnosis, treatment and prevention of COVID-19 in children. *World J Pediatr* 2020 Apr;24:1-8. DOI: 10.1007/s12519-020-00362-4.

2. Zimmermann P, Curtis N. Coronavirus Infections in Children Including COVID-19: An Overview of the Epidemiology, Clinical Features, Diagnosis, Treatment and Prevention Options in Children. *Pediatr Infect Dis J* 2020;39: 355-68.
3. Shi Y, Wang X, Liu G, Zhu Q, Wang J, Yu H, et al. A quickly, effectively screening process of novel corona virus disease 2019 (COVID-19) in children in Shanghai, China. *Ann Transl Med* 2020;8:241. DOI: 10.21037/atm.2020.03.22.
4. Chang TH, Wu JL, Chang LY. Clinical characteristics and diagnostic challenges of pediatric COVID-19: A systematic review and meta-analysis. *J Formos Med Assoc* 2020;119:982-9.
5. Tezer H, Bedir Demirdağ T. Novel coronavirus disease (COVID-19) in children. *Turk J Med Sci* 2020;50: 592-603.
6. She J, Liu L, Liu W. COVID-19 epidemic: Disease characteristics in children. *J Med Virol* 2020;92:747-54.
7. Sinha IP, Harwood R, Semple MG, Hawcutt DB, Thursfield R, Narayan O, et al. COVID-19 infection in children. *Lancet Respir Med* 2020;8:446-7.
8. Zheng F, Liao C, Fan QH, Chen HB, Zhao XG, Xie ZG, et al. Clinical Characteristics of Children with COVID-19 in Hubei, China. *Curr Med Sci* 2020;40:275-80.
9. Hong H, Wang Y, Chung HT, Chen CJ. Clinical characteristics of novel COVID-19 in newborns, infants and children. *Pediatr Neonatol* 2020; 61:131-32.
10. Yasri S, Wiwanitkit V. Clinical features in pediatric COVID-19. *Pediatr Pulmonol* 2020;55(5):1097. DOI: 10.1002/ppul.24737 (2020).
11. Li Y, Guo F, Cao Y, Li L, Guo Y. Insight into COVID-19 for pediatricians. *Pediatr Pulmonol* 2020;55: E1-E4.
12. Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, et al. SARS-CoV-2 Infection in Children. *N Engl J Med* 2020; 382:1663-5.
13. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiology of COVID-19 Among Children in China. *Pediatrics* 2020 Jun;145:e20200702. DOI: 10.1542/peds.2020-0702.
14. Cruz AT, Zeichner SL. COVID-19 in Children: Initial Characterization of the Pediatric Disease. *Pediatrics* 2020; 145(6):e20200834. DOI: 10.1542/peds.2020-0834.
15. Sun D, Li H, Lu XX, Xiao H, Ren J, Zhang FR, et al. Clinical features of severe pediatric patients with COVID-19 in Wuhan: a single center's observational study. *World J Pediatr* 2020 Mar;19:1-9. DOI: 10.1007/s12519-020-00354-4.
16. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. *Nat Rev Cardiol* 2020;17: 259-260.
17. Cui Y, Tian M, Huang D, Wang X, Huang Y, Fan L, et al. A 55-Day-Old Female Infant infected with COVID-19: presenting with pneumonia, liver injury, and heart damage. *J Infect Dis* 2020; 221:1775-81.
18. Li W, Zhou Q, Tang Y, Ren L, Yu X, Li Q, et al. Protocol for the development of a rapid advice guideline for prevention, management and care of children with 2019 novel coronavirus infection. *Ann Palliat Med* 2020; 2020 Feb 24;apm.2020.02.33. DOI: 10.21037/apm.2020.02.33.
19. Shen K, Yang Y, Wang T, Zhao D, Jiang Y, Jin R, et al. Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children. *World J Pediatr* 2020 Feb 7;1-9. DOI: 10.1007/s12519-020-00343-7.
20. COVID-19 Guidance for Vulnerable Groups with Congenital Heart Disease. British Congenital Cardiac Association. March 18, 2020.
21. Coronavirus Guidance for Adult & Pediatric Patients with Congenital Heart Disease. University of Michigan. March 27, 2020.

22. COVID-19 (SARS-CoV2 Enfeksiyonu) Rehberi. T.C. Sağlık Bakanlığı Bilim Kurulu. Nisan 2020.
23. COVID-19 Pandemi Sürecinde Çocuk Kalp Sağlığı Hizmetlerinin Yürütülmesi ve İnfecte Çocukların Kardiyak Yönden Değerlendirilmesi Rehberi. Türk Pediatrik Kardiyoloji ve Kalp Cerrahisi Derneği. Nisan 17, 2020.
24. Kirkpatrick JN, Mitchell C, Taub C, Kort S, Hung J, Swaminathan M. ASE Statement on Protection of Patients and Echocardiography Service Providers During the 2019 Novel Coronavirus Outbreak: Endorsed by the American College of Cardiology. *J Am Soc Echocardiogr* 2020;33:648-653
25. Morray BH, Gordon BM, Crystal MA, Goldstein BH, Qureshi A, Torres AJ, et al. Resource Allocation and Decision Making for Pediatric and Congenital Cardiac Catheterization During the Novel Coronavirus SARS-CoV-2 (COVID-19) Pandemic: A U.S. Multi-Institutional Perspective. *J Invasive Cardiol* 2020;32:E103-E109.
26. Lee-Archer P, von Ungern-Sternberg BS. Paediatric Anaesthetic implications of COVID-19: A Review of Current Literature. *Paediatr Anaesth* 2020 Apr 19;10.1111/pan.13889. DOI: 10.1111/pan.13889.
27. Zhao S, Ling K, Yan H, Zhong L, Peng X, Yao S, et al. Anesthetic Management of Patients with COVID-19 Infections during Emergency Procedures. *J Cardiothorac Vasc Anesth* 2020;34:1125-31.
28. Edelson DP, Sasson C, Chan PS, Atkins DL, Aziz K, Becker LB, et al. Interim Guidance for Basic and Advanced Life Support in Adults, Children, and Neonates With Suspected or Confirmed COVID-19: From the Emergency Cardiovascular Care Committee and Get With The Guidelines-Resuscitation Adult and Pediatric Task Forces of the American Heart Association. *Circulation* 2020; 141:e933-e943.
29. Lakkireddy DR, Chung MK, Gopinathannair R, Patton KK, Gluckman TJ, Turagam M, et al. Guidance for Cardiac Electrophysiology During the COVID-19 Pandemic From the Heart Rhythm Society COVID-19 Task Force; Electrophysiology Section of the American College of Cardiology; And the Electrocardiography and Arrhythmias Committee of the Council on Clinical Cardiology, American Heart Association. *Circulation* 2020;141:e823-e831.
30. Stephens EH, Dearani JA, Guleserian KJ, Overman DM, Tweddell JS, Backer CL, et al. COVID-19: Crisis Management in Congenital Heart Surgery. *Ann Thorac Surg.* 2020;S0003-4975(20)30540-3.
31. Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic treatments for coronavirus disease 2019 (COVID-19). *JAMA* 2020Apr13.DOI: 10.1001/jama.2020.6019.
32. Roden DM, Harrington RA, Poppas A, Russo AM. Considerations for Drug Interactions on QTc in Exploratory COVID-19 Treatment. *JACC.* 2020;141:e906-e907.
33. Chiotos K, Hayes M, Kimberlin DW, Jones SB, James SH, Pinninti SG, et al. Multicenter initial guidance on use of antivirals for children with COVID-19/SARS-CoV-2. *J Pediatric Infect Dis Soc.* DOI: 2020 Apr 22;pii:045. doi: 10.1093/jpids/piaa045.