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MAJOR ARTICLE

Adenovirus Infections and Disease in Solid Organ Transplant Recipients: Incidence and Outcomes

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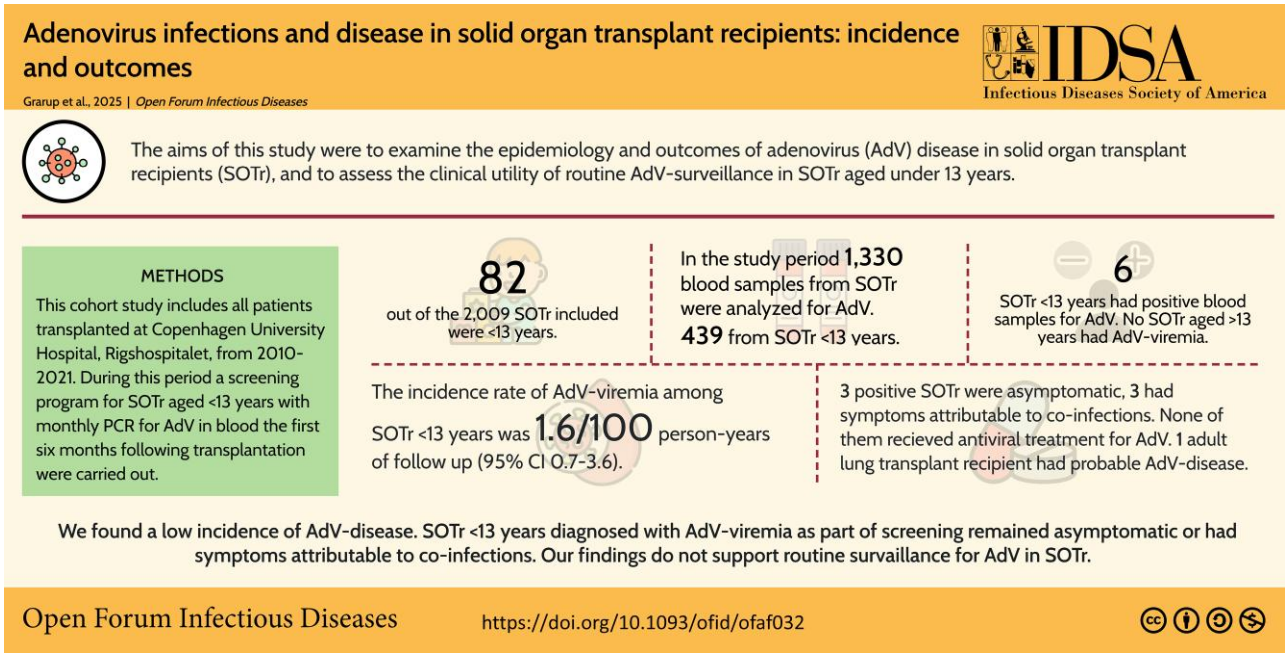
Background. We aimed to examine the epidemiology and outcomes of AdV disease in SOTr and assess the utility of AdV surveillance in SOTr <13 years.

Methods. SOTr transplanted at Rigshospitalet, 2010–2021, were included. The center had a screening program for SOTr <13 years with monthly plasma AdV tests the first 6 months following transplantation.

Results. We included 2009 SOTr (of whom 82 were aged <13 years), and 1330 blood samples from 382 SOTr were analyzed for AdV, of which 10 (0.8%) from 6 SOTr <13 years tested positive. Five out of six were tested as part of the screening program. Three remained asymptomatic, while three had symptoms attributable to co-infections. One adult lung transplant recipient with AdV in BAL had acute exacerbation of chronic graft rejection.

Conclusions. We found a low incidence of AdV disease. SOTr diagnosed with AdV viremia as part of screening remained asymptomatic or had symptoms attributable to co-infections. Our findings do not support routine surveillance for AdV in SOTr.

Graphical Abstract



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Keywords. adenovirus; adenovirus disease; solid organ transplantation; screening program; adenovirus viremia.

Adenovirus (AdV) can cause respiratory, gastrointestinal, hepatic, urethral, or conjunctival infections in individuals who are immunocompetent, and it rarely causes severe disease [1]. In solid organ transplant recipients (SOTr), AdV infections can have manifestations ranging from asymptomatic infections to severe disease with pneumonitis, hepatitis, gastroenteritis, or disseminated infection [1–5]. The incidence of AdV infections is higher among pediatric as compared with adult SOTr [1, 5–8]. Most AdV infections are diagnosed within the first few months after the transplantation [2, 6–8].

Clinical symptoms and severity depend on age [1, 6–8], degree of immunosuppression [1, 2], site of infection, and transplant type [5–7]. Children, patients who are more heavily immunosuppressed, and liver and lung transplant recipients are more affected [7, 9, 10].

Previous studies on outcomes of AdV infections among pediatric SOTr have shown mixed results. Some studies have found that AdV is associated with significant morbidity and mortality and that AdV can affect graft survival [2, 7, 8, 11–14]. Other cohort studies reported no mortality [4, 15] and only limited associated morbidity with AdV infections [4, 16]. Data from large cohorts of adult SOTr are scarce [12].

The main treatment of AdV is supportive care and a decrease in immunosuppressive therapy [1, 6, 7, 12, 17]. The antiviral agent cidofovir is used for treatment of organ-invasive or disseminated AdV disease [1, 6, 17, 18]. Cidofovir can cause nephrotoxicity and bone marrow suppression [1, 17], and it is uncertain whether SOTr with AdV disease benefit from antiviral treatment [11, 12]. There are limited data regarding how often a reduction in immunosuppressive treatment is needed in SOTr diagnosed with AdV [6], and it is unclear if screening of asymptomatic SOTr improves outcomes [4]. The American Society of Transplantation Infectious Diseases Community of Practice offers recommendations for the diagnosis and treatment of AdV in SOTr, but most of these are based on a low level of evidence [6] and management differs among transplantation centers.

In the MATCH program (Management of Posttransplant Infections in Collaborating Hospitals) at Copenhagen University Hospital, Rigshospitalet, SOTr <13 years of age are screened monthly the first 6 months after transplantation. We aimed to examine the incidence, severity, and outcomes of the following: (1) AdV infections diagnosed through this systematic screening program to evaluate the strategy of routine surveillance for AdV in SOTr aged <13 years and (2) AdV disease diagnosed through symptom-directed testing among all SOTr followed in the MATCH program.

METHODS

Study Design and Population

We conducted a retrospective cohort study including all patients with a Danish civil registration number who received a solid organ transplant at Copenhagen University Hospital, Rigshospitalet, between 1 January 2010 and 28 February 2021. Two SOTr were excluded because they had a hematopoietic stem cell transplant (HSCT) prior to their solid organ transplant.

Setting

Rigshospitalet is a tertiary referral hospital, the Danish national transplant center for lung and liver transplantations, and a regional transplant center for kidney and heart transplantations.

Since 2011, systematic surveillance for AdV has been carried out at our center. It involves monthly screening with polymerase chain reaction (PCR) for AdV in blood samples of all SOTr <13 years of age the first 6 months following transplantation. Additional symptom-directed testing for AdV among SOTr has been done at the discretion of the clinicians caring for the patients.

Data Sources

Data on demography and date and type of solid organ transplant were retrieved from the PERSIMUNE data warehouse [19]. Data on AdV tests were obtained from the Danish National Microbiology Database. Data on pathologic examinations were obtained from the Danish National Pathology Database, and data on death and emigration were retrieved from the Danish Civil Registration System.

Medical Records and Clinical Information

SOTr with AdV detected in clinical samples were identified by a systematic electronic search of the Danish National Microbiology Database and the Danish National Pathology Database. The medical records for all SOTr with a positive AdV test result from blood, tissue biopsy, or bronchoalveolar lavage (BAL) were systematically reviewed for information on symptoms and outcomes, with final assessment 180 days after the diagnosis of AdV viremia.

Detection of AdV

Quantitative PCR for AdV was performed on samples of plasma and BAL with the Adenovirus R-gene kit from Argene (67-000/69-010B; bioMérieux).

Definitions

AdV infection and disease were defined according to guidelines from the American Society of Transplantation. Asymptomatic AdV infection was defined as detection of AdV by PCR in the absence of signs and symptoms associated with AdV.

AdV disease was defined as the presence of attributable organ signs and symptoms combined with AdV detection in blood, biopsy specimens, BAL, or cerebrospinal fluid, in the absence of another diagnosis [6].

Statistical Analysis

Data were analyzed by descriptive statistics. Adherence with the AdV screening program was evaluated for SOTr aged <13 years who received a solid organ transplant after 1 January 2011 and were under active follow-up. We assessed whether a PCR test for AdV in blood was performed ±14 days of the planned date.

In analyses of incidence of AdV infection, SOTr were followed from the date of transplantation until the first positive AdV test result (blood, BAL, or tissue), a second transplantation, death, emigration, or 28 February 2021. Analyses were stratified by age (<13 or ≥13 years).

Incidence rates were estimated as the number of events per 100 person-years of follow-up via Poisson regression analysis. Stata 18.5 (StataCorp) was used for the statistical analysis.

Ethical Approvals

The study was approved by the Danish Ethical Committee (H-20071557), the Danish National Board of Health (3-3013-1060/1), and the Danish Data Protection Agency (RH-2016-47).

RESULTS

Characteristics of the Study Population

We included 2009 SOTr who were followed for 9194 person-years (median, 4.1 years; IQR, 1.7–7.1). The number of transplantations was evenly distributed over the study period. Characteristics of the study population are summarized in Table 1.

A total of 82 SOTr (4%) were <13 years of age at the date of transplantation. These patients were followed for 369 person-years (median, 3.4 years; IQR, 0.7–7.9). The median age was 6 years (IQR, 3–10); 49% were female and 51% were male. Transplant types included heart (n = 6), liver (n = 51), kidney (n = 22), and liver-kidney (n = 3). Of the 82 patients, 71 were transplanted after initiation of the AdV screening program and were included in analyses of adherence with the program.

Adherence With the AdV Screening Program

Adherence with the planned screening program was modest, with 53% to 65% of the patient group tested per month in months 1 to 6 posttransplant. Individual patients had a median 50% (IQR, 16.7%–100%) of the planned tests performed (Table 2).

AdV Testing

The total number of AdV tests performed during the study period is summarized in Table 3. A total of 1330 blood samples were analyzed for AdV by PCR. SOTr aged <13 years accounted for 33% of the blood samples tested for AdV. For SOTr aged ≥13 and <13 years, 93% to 96% of all blood tests were performed within the first 6 months posttransplant. The proportions of SOTr who had a blood sample tested for AdV were 17% and 71% for those aged ≥13 and <13 years, respectively.

A total of 5309 nonblood samples were analyzed for AdV by PCR. Overall test-positive rates were low but higher in SOTr aged <13 years than in adults (Table 3).

AdV Viremia

A total of 10 of 1330 blood samples (0.8%) from 6 of 2009 SOTr (0.3%) were positive for AdV DNA. All 6 SOTr with AdV viremia were aged <13 years. Thus, 7.3% of all SOTr aged <13 years were diagnosed with AdV viremia. No adult SOTr were diagnosed with AdV viremia. The incidence rate of AdV viremia among SOTr aged <13 years was 1.6 per 100 person-years of follow-up (95% CI, .7–3.6). Five SOTr tested positive within 6 months posttransplant, and 1 tested positive 18 months posttransplant.

Table 1. Characteristics of the Study Population

Patient Characteristic	Total (n = 2009)	Age <13 y (n = 82)	Age ≥13 y (n = 1927)
Age, y, median (IQR)	50 (38–59)	6 (3–10)	51 (40–59)
Gender			
Male	1192 (59.3)	42 (51.2)	1150 (59.7)
Female	817 (40.7)	40 (48.8)	777 (40.3)
Type of solid organ transplant			
Heart	149 (7.4)	6 (7.3)	143 (7.4)
Lung	324 (16.1)	0 (0)	324 (16.8)
Liver	531 (26.4)	51 (62.2)	480 (24.9)
Kidney	956 (47.6)	22 (26.8)	934 (48.5)
Other	49 (2.4)	3 (3.7)	46 (2.4)
Calendar year of the transplant			
2010–2012	527 (26.2)	25 (30.5)	502 (26.1)
2013–2015	527 (26.2)	20 (24.4)	507 (26.3)
2016–2018	527 (26.2)	21 (25.6)	506 (26.3)
2019–2021	428 (21.3)	16 (19.5)	412 (21.4)

Data are presented as No. (%) unless noted otherwise.

AdV viremia was detected in 5 liver and 1 kidney transplant recipients (Table 4). Patients with AdV viremia were aged 2 to 11 years at the time of infection. Five tested positive for AdV as part of the AdV screening program, and 1 patient was diagnosed with AdV viremia through symptom-directed testing. The viral load was a median 500 copies/mL (range, 185–1100). The 5 SOTr diagnosed with AdV viremia through routine surveillance were not examined for AdV in the upper airways. The patient diagnosed through symptom-directed testing also tested positive for AdV in a nasopharyngeal swab the day prior to diagnosis of AdV viremia.

Table 2. Adherence With the Screening Program for AdV Among SOTr Aged <13 Years

Proportion of Planned AdV Tests Performed	No. (%)
100	21 (30)
60–83	14 (19)
17–50	19 (27)
0	17 (24)

The number of planned AdV tests for SOTr was calculated as 1 test per month under active follow-up for the first 6 months after transplantation.

Abbreviations: AdV, adenovirus; SOTr, solid organ transplant recipients.

Outcomes of AdV Viremia

Three of the 5 patients diagnosed through the AdV screening program were asymptomatic. The positive AdV test result did not change clinical management for 2 of the asymptomatic patients, and for the third, the positive test result led to an additional outpatient follow-up visit.

Two patients had symptoms at the time of the positive blood test result for AdV or within 3 days thereafter. One patient had self-limited fever, malaise, and slight diarrhea and was assessed at an outpatient visit. A fecal test was positive for rotavirus. The other patient developed symptoms with fever and fatigue and was hospitalized. A PCR test of blood was positive for cytomegalovirus (CMV). Immunosuppressive treatment was reduced due to the CMV infection.

The patient diagnosed through symptom-directed testing was hospitalized with fever and septicemia at the time of AdV viremia. The symptoms were most likely attributable to concomitant bacterial and *Candida* bloodstream infections.

None of the patients received antiviral treatment for AdV. Neither graft failure nor graft rejection was observed in any of the 6 patients with AdV viremia.

AdV in Cerebrospinal Fluid, Tissue Biopsy, and BAL

No one in the study population had AdV detected in cerebrospinal fluid or tissue biopsies. AdV was detected in a BAL

Table 3. Adenovirus PCR Tests Performed During the Study Period

	Total (n = 2009)	Age <13 y (n = 82)	Age ≥13 y (n = 1927)
AdV PCR tests: blood	1330 (100)	439/1330 (33.0)	891/1330 (67.0)
SOT recipients with blood AdV PCR tests performed	382/2009 (19.0)	58/82 (70.7)	324/1927 (16.8)
Timing of blood AdV PCR tests, mo posttransplant			
1–6	1260/1330 (94.7)	406/439 (92.5)	854/891 (95.9)
7–12	16/1330 (1.2)	13/439 (3.0)	3/891 (0.3)
>12	54/1330 (4.1)	20/439 (4.5)	34/891 (3.8)
Timing of first positive blood AdV PCR test result, mo posttransplant			
1–6	5/6 (83.3)	5/6 (83.3)	NA
>6	1/6 (16.7)	1/6 (16.7)	NA
AdV PCR tests performed in nonblood specimens, positive/total			
Airway secretions	15/791 (1.9)	12/128 (9.4)	3/663 (0.5)
Bronchoalveolar lavage	1/580 (0.2)	0/13 (0)	1/567 (0.2)
Stool	22/3581 (0.6)	11/552 (2.0)	11/3029 (0.4)
Swab	2/327 (0.6)	1/57 (1.8)	1/270 (0.4)
Cerebrospinal fluid	0/3 (0)	0/2 (0)	0/1 (0)
Other	1/27 (3.7)	1/8 (12.5)	0/19 (0)
Incidence rate per 100 PY of AdV viremia (95% CI)			
Overall	NA	1.6 (0.7–3.6)	0 (—)
Type of SOT			
Heart		0 (—)	
Lung		0 (—)	
Liver		2.4 (1.0–5.7)	
Kidney		0.8 (.1–5.7)	
Other		0 (—)	

Data are presented as No. (%) unless noted otherwise.

Abbreviations: AdV, adenovirus; NA, not applicable; PCR, polymerase chain reaction; PY, person-years of follow-up; SOT, solid organ transplant.

Table 4. Characteristics of Solid Organ Transplant Recipients With AdV Detected in Plasma or BAL

Patient	Age, y	Transplantation		Reason for Testing	Specimen	Peak Viral Load, Copies/mL	Symptoms	Coinfections	Reduction of Immunosuppression	Antiviral Therapy for AdV
		Type	Days From							
1	4	Kidney	121	Screening	Plasma	1100	Fever, malaise, diarrhea[a]	EBV, CMV, rotavirus	No	No
2	3	Liver	118	Screening	Plasma	500	Fever, fatigue[a]	CMV	Yes	No
3	6	Liver	175	Screening	Plasma	500	No	None	No	No
4	9	Liver	92	Screening	Plasma	500	No	None	No	No
5	11	Liver	174	Screening	Plasma	700	No	None	No	No
6	2	Liver	540	Symptoms	Plasma	500	Sepsis[a]	Bacteremia and candidemia, EBV	Yes	No
7	48	Lung	438	Symptoms	BAL	ND	Fever, malaise, dyspnea, cough	CMV, rhinovirus	No	No

Abbreviations: AdV, adenovirus; BAL, bronchoalveolar lavage; CMV, cytomegalovirus; EBV, Epstein-Barr virus; ND, not determined.

[a]Symptoms were most likely attributable to coinfections.

sample from a lung transplant recipient aged 48 years. CMV and rhinovirus were also detected by PCR in the same sample. The BAL was performed as part of a diagnostic workup for pneumonitis and acute exacerbation of chronic graft rejection.

DISCUSSION

In this large cohort study, we examined the incidence and outcomes of AdV disease in SOTr over an 11-year period and evaluated the clinical utility of a systematic AdV surveillance program for SOTr aged <13 years. A large number of PCR tests for AdV were performed during the study period; however, only a few episodes of AdV viremia were diagnosed, and just 1 symptomatic adult lung transplant recipient had AdV detected in BAL. SOTr aged <13 years who tested positive for AdV viremia as part of the routine surveillance program remained asymptomatic or had symptoms that were likely caused by coinfections. None of the patients received antiviral therapy for AdV, and detection of AdV viremia did not change the clinical management.

There are few previous studies of routine surveillance for AdV in SOTr. In a study by Kourí et al, 34 children were monitored systematically for AdV viremia for 34 weeks following a liver or kidney transplantation. AdV viremia was diagnosed in 1 asymptomatic patient [20]. In another study, 75 pediatric SOTr were routinely monitored for AdV viremia for 2 years following transplantation. AdV viremia was detected in 11 SOTr (15%), of whom 5 were symptomatic and 1 was treated with cidofovir. None of the 11 patients developed reduced graft function or graft rejection in relation to the infection [16]. Humar et al prospectively monitored 263 adult SOTr for AdV viremia the first year following transplantation, and 7% tested positive, of whom 58% were asymptomatic and 42% had mild symptoms. All patients recovered spontaneously [9].

Rates of AdV viremia in pediatric patients with HSCT who are routinely monitored for AdV in blood seem to be similar to those observed in SOTr, but the AdV-associated mortality is markedly higher [21]. However, it is not clear that routine surveillance for AdV infection improves outcomes. In a cohort study of pediatric HSCT recipients, 175 were tested for AdV in blood only if clinically suspected, whereas 181 underwent routine surveillance for AdV viremia with weekly testing until day +100 posttransplant. Rates of diagnosis of AdV viremia were significantly higher among those who were routinely screened; yet, those who developed symptoms of the infection already had them at the time of testing or within 5 days, and the AdV-associated mortality was similar between the groups [21]. In another study of pediatric HSCT recipients who underwent routine surveillance for AdV, the detection of AdV viremia preceded development of clinical symptoms by a median >3 weeks, but 82% of patients with AdV viremia died despite early diagnosis [22].

The proportion of SOTr with asymptomatic AdV viremia who will progress to severe disease without reduction of immunosuppression or antiviral therapy has not been quantified but does not seem very high based on the available data [6, 9, 16]. Furthermore, the time from onset of viremia to development of organ-invasive disease is unknown. Reduction in immunosuppression carries a risk of development of graft rejection, and cidofovir, the only marketed antiviral drug that is used for treatment of AdV infections, often causes nephrotoxicity [23, 24]. Thus, these interventions may not be beneficial upon detection of AdV viremia in asymptomatic SOTr. Accordingly, the guidelines from the American Society of

Transplantation does not recommend AdV surveillance in asymptomatic SOTr [6].

We found only modest adherence to the routine AdV surveillance program for SOTr aged <13 years, which likely affects the number of asymptomatic episodes of AdV viremia that were detected. Suboptimal adherence may in part be explained by the challenges in obtaining blood samples in young children. The MATCH program, implemented at Rigshospitalet in 2011 to improve management of viral infections in transplant recipients, also includes systematic surveillance for CMV infections the first year posttransplant in adult and pediatric SOTr. The overall adherence to the surveillance program is high, and we have previously demonstrated the success of this program in reducing rates of CMV disease [25].

We did not detect AdV viremia in any of the 324 adult SOTr who were tested through symptom-directed testing, and only 1 of 567 BAL samples from adult SOTr was positive for AdV. These results are in line with previous studies showing that AdV disease is uncommon in adult SOTr [9]. However, when it does occur, outcomes can be dismal, as was the case for the lung transplant recipient with AdV pneumonia in the present study.

This study has some limitations. It was a single-center study, which may limit the generalizability of findings. The number of SOTr aged <13 years who underwent routine surveillance was limited. There were no pediatric lung or small bowel transplant recipients in the cohort, and these groups are at higher risk of AdV disease. Although it is one of the largest cohort studies of AdV infections in SOTr, the number of episodes of AdV disease detected was very low, prohibiting risk factor and subgroup analyses. It was also a retrospective study, but data were collected prospectively in nationwide registries and the MATCH database. AdV testing outside the routine surveillance program was done at the discretion of clinicians caring for the patients; thus, it is possible that not all episodes of AdV disease were diagnosed. However, the study was performed in a high-resource setting with good access to diagnostic testing.

Strengths of the study include the large study population with almost complete follow-up and the Danish civil registration number, which allows for linkage of data between a local database and nationwide registries of microbiological and pathologic tests. This ensured that results of all relevant tests performed in Danish health care facilities could be captured.

CONCLUSION

We found a low incidence of AdV disease in a large cohort of SOTr. SOTr aged <13 years who tested positive during screening remained asymptomatic without interventions for AdV infection or had symptoms attributable to coinfections. Our findings do not support routine surveillance for AdV in SOTr. The AdV screening program has now been discontinued in our center.

Notes

Patient consent statement. Patient informed consent was not needed for this study according to the national and regional legislation (Team for Journaldata [patient record data], Capital Region of Denmark, Journal-nr R-23022823).

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Potential conflicts of interest. All authors: No reported conflicts.

References

1. Sandkovsky U, Vargas L, Florescu DF. Adenovirus: current epidemiology and emerging approaches to prevention and treatment. Curr Infect Dis Rep **2014**; 16:416.
2. Grasa C, Monteagudo-Vilavedra E, Pérez-Arenas E, et al. Adenovirus infection in hematopoietic and solid organ paediatric transplant recipients: treatment, outcomes, and use of cidofovir. Microorganisms **2023**; 11:1750.
3. Sherman AC, Lu X, Schneider E, et al. Human adenovirus 11 in 2 renal transplant recipients: suspected donor-derived infection. Open Forum Infect Dis **2021**; 8: ofab092.
4. Boge CLK, Fisher BT, Petersen H, et al. Outcomes of human adenovirus infection and disease in a retrospective cohort of pediatric solid organ transplant recipients. Pediatr Transplant **2019**; 23:e13510.
5. Abbas A, Zimmer AJ, Florescu D. Viral enteritis in solid-organ transplantation. Viruses **2021**; 13:2019.
6. Florescu DF, Schaenman JM, AST Infectious Diseases Community of Practice. Adenovirus in solid organ transplant recipients: guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant **2019**; 33:e13527.
7. Florescu DF, Stohs EJ. Approach to infection and disease due to adenoviruses in solid organ transplantation. Curr Opin Infect Dis **2019**; 32:300–6.
8. Hoffman JA. Adenovirus infections in solid organ transplant recipients. Curr Opin Organ Transplant **2009**; 14:625–33.
9. Humar A, Kumar D, Mazzulli T, et al. A surveillance study of adenovirus infection in adult solid organ transplant recipients. Am J Transplant **2005**; 5:2555–9.
10. Ganapathi L, Arnold A, Jones S, et al. Use of cidofovir in pediatric patients with adenovirus infection. F1000Res **2016**; 5:758.
11. Dulek DE. Update on epidemiology and outcomes of infection in pediatric organ transplant recipients. Infect Dis Clin North Am **2023**; 37:561–75.
12. Ison MG. Adenovirus infections in transplant recipients. Clin Infect Dis **2006**; 43: 331–9.
13. Shirali GS, Ni J, Chinnock RE, et al. Association of viral genome with graft loss in children after cardiac transplantation. N Engl J Med **2001**; 344:1498–503.
14. Bridges ND, Spray TL, Collins MH, Bowles NE, Towbin JA. Adenovirus infection in the lung results in graft failure after lung transplantation. J Thorac Cardiovasc Surg **1998**; 116:617–23.
15. de Mezerville MH, Tellier R, Richardson S, Hébert D, Doyle J, Allen U. Adenoviral infections in pediatric transplant recipients: a hospital-based study. Pediatr Infect Dis J **2006**; 25:815–8.
16. Engen RM, Huang ML, Park GE, Smith JM, Limaye AP. Prospective assessment of adenovirus infection in pediatric kidney transplant recipients. Transplantation **2018**; 102:1165–71.
17. Guerra Sanchez CH, Lorica CD, Arheart KL, Perez MM, Tekin A, Gonzalez IA. Virologic response with 2 different cidofovir dosing regimens for preemptive treatment of adenovirus DNAemia in pediatric solid organ transplant recipients. Pediatr Transplant **2018**; 22:e13231.
18. Sudhindra P, Knoll B, Nog R, Singh N, Dhand A. Brincidofovir (CMX001) for the treatment of severe adenoviral pneumonia in kidney transplant recipient. Cureus **2019**; 11:e5296.
19. Centre of Excellence for Personalized Medicine of Infectious Complications in Immune Deficiency. About PERSIMUNE. Available at: http://www.persimune.dk/. Accessed 15 April 2024.
20. Kourí V, Correa C, Martínez PA, et al. Prospective, comprehensive, and effective viral monitoring in Cuban children undergoing solid organ transplantation. SpringerPlus **2014**; 3:247.
21. Ali S, Krueger J, Richardson SE, et al. The yield of monitoring adenovirus in pediatric hematopoietic stem cell transplant patients. Pediatr Hematol Oncol **2019**; 36:161–72.

22. Lion T, Baumgartinger R, Watzinger F, et al. Molecular monitoring of adenovirus in peripheral blood after allogeneic bone marrow transplantation permits early diagnosis of disseminated disease. Blood **2003**; 102:1114–20.
23. Stern A, Alonso CD, Garcia-Vidal C, et al. Safety and efficacy of intravenously administered cidofovir in adult haematopoietic cell transplant recipients: a retrospective multicentre cohort study. J Antimicrob Chemother **2021**; 76:3020–8.
24. Riggsbee DL, Alali M, Kussin ML. Cidofovir for viral infections in immunocompromised children: guidance on dosing, safety, efficacy, and a review of the literature. Ann Pharmacother **2024**; 58:286–304.
25. Ekenberg C, da Cunha-Bang C, Lodding IP, et al. Evaluation of an electronic, patient-focused management system aimed at preventing cytomegalovirus disease following solid organ transplantation. Transpl Infect Dis **2020**; 22:e13252.