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Editorial

Persistent Effort to Control Infection after Lung Transplantation in Korea

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▸ See the article "Infections in Lung Transplant Recipients during and after Prophylaxis" in volume 52 on page 600.

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The first attempt to transplant the lungs (heart and both lungs) was reported by Hardy and Webb in 1963 [1], but the first successful lung transplantation (LT) was performed in 1983. According to the reports of the Korean Network for Organ Sharing, as of 2010, 57 lung transplantations have been performed since the first LT in Korea in 1996. It has increased to more than 30 cases per year after 2011, and more than 100 LTs have been performed every year in Korea since 2019 [2].

Improvements in surgical techniques, perioperative management, and immunosuppressive regimens have increased the quality of life and long-term survival. However, infectious complications remain one of the most important causes of unfavorable outcomes in LT. Infections are the second leading cause of death within 30 postoperative days, and they are the leading cause of death 30 days to 1 year after LT [3]. To prevent postoperative infections, antibacterial, antifungal, and antiviral prophylaxes are administered. Moreover, these protocols for preventing infection after LT vary since the type and frequency of infection after LT differ according to the country or center. An epidemiological report on infection by Bae et al. provided valuable data on infection prevention and control after LT in Korea [4].

Among the bacterial pathogens of infection after LT, antimicrobial-resistant species, including methicillin-resistant *Staphylococcus aureus* (MRSA), Gram-negative bacilli such as *Pseudomonas aeruginosa*, and *Clostridioides difficile*, are often involved. In addition, multidrug-resistant (MDR). *Klebsiella pneumoniae* is an emerging pathogen that is difficult to treat. These bacteria develop resistance due to the patients' prior hospitalizations and the donors' stay in intensive care units. Bae et al. reported that 84 among the 127 episodes of post-LT bacterial infections involved MDR bacteria (66.1%) [4]. It is difficult to treat MDR bacterial infections, such as carbapenem-resistant gram-negative bacilli, and they are associated with a poor prognosis.

Pulmonary infections secondary to MDR bacteria after LT may be treated with aminoglycoside and colistin-based therapy [5]. Colistin can be administered intravenously, through nebulization, or both. However, the use of nebulized colistin (or aminoglycoside) has not yet been approved in Korea. The bactericidal effect of colistin is concentration-dependent, and it exhibits a post-antibiotic effect against *P. aeruginosa*, *Acinebacter baumannii*, and *K. pneumoniae* [6]. However, they have cumulative nephrotoxicity, especially with concomitant calcineurin inhibitor use. New agents, such as ceftolozane-tazobactam and ceftazidime-avibactam, are alternatives. Ceftazidime-avibactam, meropenem, and colistin were compared to treat MDR *Enterobacteriaceae* infections and nosocomial pneumonitis,

including ventilator-associated pneumonia. Ceftazidime-avibactam had better outcomes than colistin and was not inferior to meropenem [7, 8]. However, ceftazidime-avibactam is not available in Korea, and the role of new agents in LT recipients is not yet defined.

Cytomegalovirus (CMV) infection and disease commonly occur in LT and play a critical role in the short-term function of the allograft [9]. CMV prophylaxis with valganciclovir or ganciclovir is established during the immediate postoperative period in susceptible patients, depending on the CMV status of the donor and recipient. Many centers employ viral load monitoring after prophylaxis to detect late-onset CMV infection. However, the cost of prophylaxis and monitoring as well as the side effects of antiviral agents may be limiting. Therefore, a means for identifying high-risk patients for CMV infection using CMV-specific immune monitoring allows for more selective and appropriate use of prophylaxis and monitoring [10]. This results in better transplant outcomes and potential savings with respect to costs and toxicities.

A comprehensive approach that includes pre-transplant evaluation, perioperative prophylaxis, long-term antimicrobial prophylaxis according to infection epidemiology in Korea, and monitoring based on the immunologic response, should be employed to minimize the risk of infection after LT.

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