Pseudomonas aeruginosa eradication after lung transplantation: is it the tip of the iceberg?

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To the Editor:

Chronic lung allograft dysfunction (CLAD) remains the leading cause of death after 1 year post-lung transplantation (LT). As such, every effort to decrease, or to delay, CLAD occurrence must be commended. With this in mind, we read with much interest the study by De Muynck *et al*. [1]. In this retrospective study of 662 LT recipients in the University Hospitals Leuven, the authors show that CLAD-free survival and graft-survival is significantly better in patients in whom *Pseudomonas aeruginosa* was never isolated in the respiratory tract. Moreover, in the 95 patients with at least one episode of *P. aeruginosa* isolation, a significantly better outcome was reported for those whose *P. aeruginosa* was deemed to be "successfully eradicated" and, on the contrary, significantly lower survival, lower CLAD-free survival and graft survival, and a more pronounced decrease in forced expiratory volume in 1 s during the first year was found when *P. aeruginosa* eradication was not achieved. These findings are of utmost interest, and the authors, belonging to a very well-known team, with a long-lasting expertise on LT, should be commended for having conducted this study.

Nevertheless, a few points deserve further insight.

First, information on time from lung transplantation to first episode of *P. aeruginosa* isolation is crucially lacking: *P. aeruginosa* is among the most frequent pathogens isolated in the early post-operative period [2], and the effect of the isolation of *P. aeruginosa* during this period might have been of interest. Clarification of this timing would be of interest, as would time from diagnosis of CLAD to initial isolation. Indeed, the question of *P. aeruginosa* isolation being cause or consequence of CLAD remains: Is *P. aeruginosa* infection or persistence an early marker of an emerging CLAD? Or its by-product?

An indirect sign would be the occurrence of bronchiectasis, and the comparison of computed tomography (CT) findings in both groups. Bronchiectasis has been reported to be one of the CT findings in CLAD, being either obstructive or restrictive [3], and *P. aeruginosa* is one of the most frequently isolated pathogens in the case of bronchiectasis. Furthermore, difficulties in eradicating *P. aeruginosa* are suspected to be different in bronchiectasis patients compared to other kinds of respiratory diseases. We therefore believe that the radiological pattern of CLAD is of utmost importance when discussing the impact of *P. aeruginosa* eradication on the evolution of CLAD, particularly in patients whose CLAD phenotype is expressed with bronchiectasis. Conversely, *P. aeruginosa* eradication might be much easier in patients with undiagnosed, emerging CLAD, a factor which may have led to a bias in the interpretation of the data.

Another concern is about pre-LT colonisation status, which is unfortunately not detailed in this study, and the potential presence of chronic *P. aeruginosa* colonisation of the bronchus and the sinus might have been of interest when discussing successful eradication.

Last but not least, we understand that LT recipients followed up by the Leuven team (and other Belgian teams) cannot benefit from inhaled therapies, such as colistine, to maintain *P. aeruginosa* eradication after a standard antimicrobial course [4], as these therapies are not reimbursed in Belgium after LT. We acknowledge the fact that colistine, as all medications, can carry adverse effects, such as bronchoconstriction, but these effects can be easily prevented by the administration of inhaled β_2-agonists

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Is respiratory *Pseudomonas aeruginosa* infection or persistence in lung transplant recipients an early marker of an emerging chronic lung organ dysfunction? Or its by-product?
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prior to colistine. The exact treatment dose has not been clearly determined [5]. Nevertheless, their efficacy in cystic fibrosis patients is long-established [6]. One might extrapolate this to LT recipients, and offer this treatment after an episode of *P. aeruginosa* isolation.

Taken together, this very interesting paper by the Leuven team calls for complementary data, in order to determine whether a subgroup of LT recipients, with or without ascertained CLAD, could benefit more from *P. aeruginosa* eradication, the objectives being to confirm the findings of this study, and to assess and prove the efficacy of inhaled therapies as means of maintaining eradication.

P. aeruginosa still has to worry about his fine living…

Jonathan Messika[1,2,3], Vincent Bunel[1,2], Gaelle Weisenburger[1,2], Cendrine Godet[1,2] and Hervé Mal[1,2]

[1]APHP.Nord-Université de Paris, Hôpital Bichat-Claude Bernard, Service de Pneumologie B et Transplantation Pulmonaire, Paris, France. [2]Physiopathology and Epidemiology of Respiratory Diseases, UMR1152 INSERM and Université de Paris, Paris, France. [3]Paris Transplant Group, Paris, France.

Corresponding author: Jonathan Messika (jonathan.messika@aphp.fr)

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