Lung (2019) 197:393–394
https://doi.org/10.1007/s00408-019-00220-9

LETTER TO THE EDITOR

Reply To: A Comment on *Helicobacter pylori* and Lung Transplant Outcome: Is Serology the Ideal Diagnostic Approach?

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Published online: 21 March 2019

Dear Editor,

Recently, we published in this journal the results of a study entitled "*Helicobacter pylori* Infection Does Not Impact on Lung Transplant Outcome" [1].

In our study, we analysed the seroprevalence of *Helicobacter pylori* (HP) infection in a lung transplant cohort and observed a rate of infection that was similar to the one detected in the general population taken as a control (49.25% vs. 51.4%). On the contrary, the prevalence of seropositivity for CagA in infected patients was far lower than that in controls (9% vs. 50.2%, $p < 0.0001$). No correlation was found between HP infection in lung transplant patients and graft outcome: no differences in primary graft dysfunction, acute rejection or bronchiolitis obliterans syndrome-free survival were found. However, HP-positive patients more likely required three or more post-transplant re-hospitalizations. We concluded that the prevalence of HP infection in lung transplant patients was comparable to that of the general population and to that reported in heart and kidney transplant recipients showing no impact on lung allograft outcome [1].

In their correspondence, Patrucco et al. expressed some reservations on our methodology. They commented that serology represents a marker of exposure and not necessarily of active infection and this could have altered our results [2].

Many factors should be considered when choosing a diagnostic test; based on our purposes, when we drawn our study design, serology appeared immediately the most appropriated test considering the following issues.

(A) HP infection very rarely heals spontaneously. Spontaneous healing usually occurs at the first contact, which occurs in almost all cases in childhood; and our cases are all of adults [3]; (B) the infection can heal following an antibiotic treatment aimed at other infections; anyway even in this case, the healings are exceptional [3]. In fact, to eradicate the germ we must associate three antibiotics and similar associations are very rarely used in the treatment of other infections [4]; (C) in case HP infections heal after treatments not aimed at eradicating this microorganism, the serum antibodies disappear within 1–2 years [5, 6] and this greatly reduces the chances that some of the patients and subjects we examined were seropositive in the absence of an ongoing infection; (D) even if we assume that in some cases we were in the presence of past infections, instead of ongoing infections, this does not displace the fact that these patients and controls were enlisted. In fact, the aim was to assess the prevalence of infection in patients and controls and if, instead of individuals with current infection, we had enrolled some people with past infections, this would not have made much difference for comparison purposes; (E) finally, the serological method is the only one that is not affected by the assumption, by patients and controls, of proton pump inhibitors (PPI), drugs that need to be discontinued at least 2–4 weeks before any other diagnostic test of HP infection [7]. In our study, blood samples were taken from all patients on the day of transplant and almost all patients were actively on therapy with PPI so we were bound to use serology to diagnose HP infection. Moreover, it should be considered that it is not ethical to perform gastroscopy to diagnose an HP infection if the patient has no dyspeptic symptoms.

Furthermore, we must note that none of the methods actually used to evaluate the infectious and the CagA status is 100% sensitive and specific [7]. The serological kits used by us had high sensitivity and specificity and the same methods were used for patients and controls. This contributed

This reply refers to the comment available online at https://doi.org/10.1007/s00408-019-00199-3.

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to reducing the possible defects of the serological methods that could have altered the diagnostic reliability parameters. In our study [1], serum IgG antibodies against HP were analysed in patients and controls by ELISA having a sensitivity and specificity of 96% (Diesse Diagnostica Senese, Monteriggioni, Italy), while serum anti-CagA IgG were determined by ELISA with a sensitivity of 95% and a specificity of 90% (CagA–IgG; Genesis Diagnostics Ltd., Cambridgeshire, UK).

The HP IgG antibodies kit has been produced with a glycine extract of two strains isolated in our geographic area: the G21 and G39 strains. G21 is CagA negative and has been chosen out of 20 strains examined for its strong urease activity (this increases the possibility to identify patients with low antibody titres—NF personal observation) [8]. The G39 strain is CagA positive and it was chosen because potentially the most immunogenic due to the high molecular weight of CagA (about 140 kDa). CagA of G39, in fact, contains four EPIYA repeats in the amino-terminal variable region of the protein. This gives CagA of G39 an increased antigenicity [8]. The fact of having used circulating strains in the geographic area populated by the individuals being studied increases the reliability parameters of the serological methods [7, 9].

In conclusion, in our study "*Helicobacter pylori* Infection Does Not Impact on Lung Transplant Outcome" HP infection was diagnosed by serology with high sensibility and specificity. In consideration of the aim of the study and the specificities of the population, this methodology should be considered appropriated and results clearly reliable: HP infection did not prove to be clinically relevant in lung transplant patients.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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