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Title:

Epidemic *Pseudomonas aeruginosa* Infection in Patients with Cystic Fibrosis is Not a Risk Factor for Poor Clinical Outcomes Following Lung Transplantation

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What was your research question?

We set out to determine what percentage of individuals undergoing lung transplantation for end-stage CF-lung disease from our center were infected with an epidemic strain of *Pseudomonas* bacteria termed 'Prairie Epidemic Strain' (PES). By comparing post-transplantation outcomes of those individual with PES to those infected with non-epidemic (uniquely acquired, unrelated strains), we aimed to determine if epidemic *Pseudomonas* infection resulted in poorer outcomes following-transplant.

Why is this important?

Epidemic *Pseudomonas* strains may be transmitted from one CF individual to another. PES is one such strain, and is wide spread in Western Canada. Like other strains of epidemic *Pseudomonas*, individuals with PES infection experience worse clinical outcomes (including more rapid lung function loss, exacerbation frequency and progression to end-stage lung disease) compared to those individuals infected with unique strains of *Pseudomonas*. For those individuals with end-stage lung disease, lung transplantation is a potentially life-saving procedure. However, following transplant, outcomes are variable and are influenced by

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prior infections including Cepacia or other antibiotic resistant bacteria. Whether epidemic Pseudomonas similarly impact lung transplant outcomes is unknown.

What did you do?

Our group collects every bacteria ever isolated from CF sputum from each and every clinical encounter of every single patient attending our clinic (1978-present). This collection – termed a “biobank” - contains almost 40,000 isolates. For those patients who underwent lung transplantation we searched through the biobank to identify their sputum isolates immediately prior to transplantation. We then performed analysis on each bacterial strain to determine the “DNA fingerprint” of each strain and establish if these isolates were related to PES. We classified patients as being infected with epidemic Pseudomonas (PES) or unique (unrelated isolates) bacterial strains and reviewed their post-transplant health outcomes.

What did you find?

Over the course of 22 years, 53 patients from our center underwent lung transplantation. Sixty percent of these patients were infected with PES, and the remainder with unique, unrelated strains of Pseudomonas. Patients with PES were more likely to be transplanted at a younger age. However, following transplant those individuals infected with PES were no longer disadvantaged compared to those with unique strains. Specifically, survival rates at 2, 5 and 10 years were no different. Furthermore, episodes of lung infections, chronic rejection, or progressive kidney disease did not differ amongst those infected with PES relative to those with unique strains.

What does this mean and reasons for caution?

Identifying risk factors for unfavorable outcomes following lung transplantation is important in order to optimize the success of this potentially life-saving procedure. We determined that where patients with epidemic Pseudomonas (and PES in particular) experience worse clinical outcomes relative to those with unique (unrelated) strains before a lung transplant, following lung-transplantation no such disadvantage exists. Patients with epidemic Pseudomonas should therefore be given full consideration for lung transplantation.

What's next?

Identifying epidemic Pseudomonas in individuals with CF remains important for determining those at increased risk of pre-transplant complications and for infection control

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considerations. Confirming that these findings extend to other strains of epidemic Pseudomonas found in other parts of the world is key to ensure their generalizability.

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