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Extracorporeal Photopheresis in Lung Transplantation

David Bennett, Antonella Fossi, Samuele Ferrari, Nicola Lanzarone, Elena Bargagli, Luca Luzzi, Piero Paladini, Paola Rottoli, Piersante Sestini

Respiratory Diseases and Lung Transplantation Unit, Thoracic Surgery Unit - Department of Medical and Surgical Sciences & Neurosciences.
University of Siena, Italy

BACKGROUND

Lung transplantation (LTX) is a justified treatment option for selected patients with endstage pulmonary diseases. Chronic lung allograft dysfunction (CLAD) remains the first cause of mortality in such patients. Different therapeutic approaches have been proposed for CLAD, however an effective treatment is still lacking. Extracorporeal photopheresis (ECP) has been proposed for the treatment of chronic lung rejection, however no clinical randomized trials are yet available.

AIM OF THE STUDY

The aim of the study was to evaluate lung function before and after introduction of ECP in a cohort of CLAD patients at our centre and to identify factors associated with positive response to ECP treatment.

METHODS

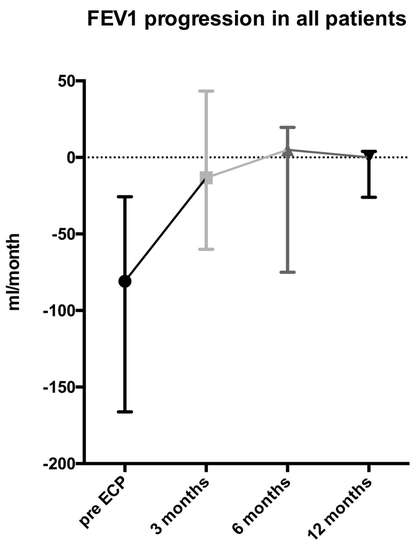
The study population consisted of 25 lung transplant patients diagnosed with CLAD and treated with ECP at our Centre.

Each ECP cycle consisted of two consecutive days of ECP every two weeks for the first three months and subsequently one monthly cycle. The ECP system was an UVAR XTS (Therakos, Exton, PA).

Pulmonary function tests (PFTs) were collected at time of CLAD diagnosis and thereafter at every visit and, since ECP start, 3, 6 and 12 months after.

Patients with a <10% decrease in FEV1 after 6 months of ECP were considered responders. These patients were further divided into stable and improving, the latter group was composed of patients with a FEV1 increase >5%.

RESULTS



Lung function tests before and after the introduction of ECP therapy showed a statistically significant improvement in rates of decline of FEV1 (p=0.0047), FVC (p=0.0089) and FEV1/VC (p=0.0497).

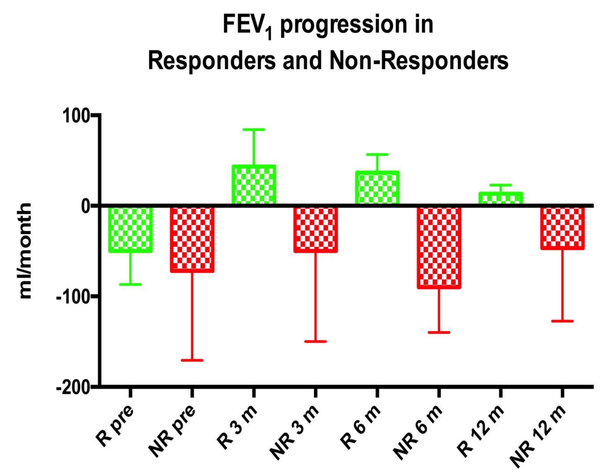
After 6 months of ECP, 11 (44%) patients were classified as responders and 14 (56%) patients as non-responders.

No statistical differences in the pre-operative characteristics of responders and non-responders.
Patients with recurrent respiratory infections and ALAD episodes were more frequent in the non-responders group (18.2% vs. 35.7%; not significant).
The stage of CLAD at the start of ECP was correlated with response to treatment; more non-responders than responders were in stage 3 or 4 (42.9% vs. 18.2%), although the difference was not statistically significant.
All patients with BOS/RAS phenotype (n=4) were non-responders (28.6% vs 0%, not significant); a single case with RAS phenotype was present in the responders and the non-responders groups.

CLAD decline patterns before ECP therapy (fast vs. slow decliners, >100 ml/month) did not show significant difference between responders and non-responders.

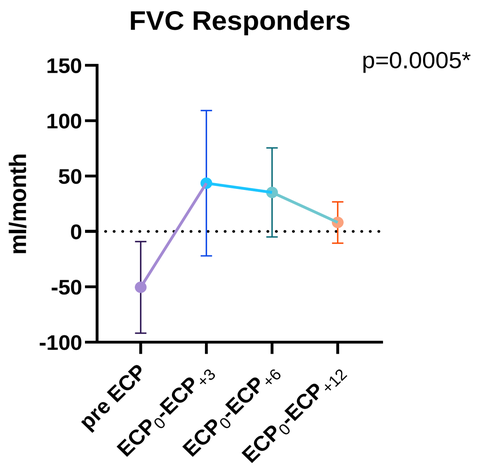
ECP demonstrated to be a safe procedure for CLAD patients. We only observed a case of non-severe blood stream infection by Stenotrophomonas maltophilia correlated to the presence of an indwelling catheter in a colonized cystic fibrosis patient.

Responders patients demonstrated a significantly slower decline in FEV_1, FVC and FEV_1/VC after starting ECP. An increase of FEV_1 and FVC values was reported in 7/10 pts at 3 months, 9/11 at 6 months and n=5/9 at 12 months.



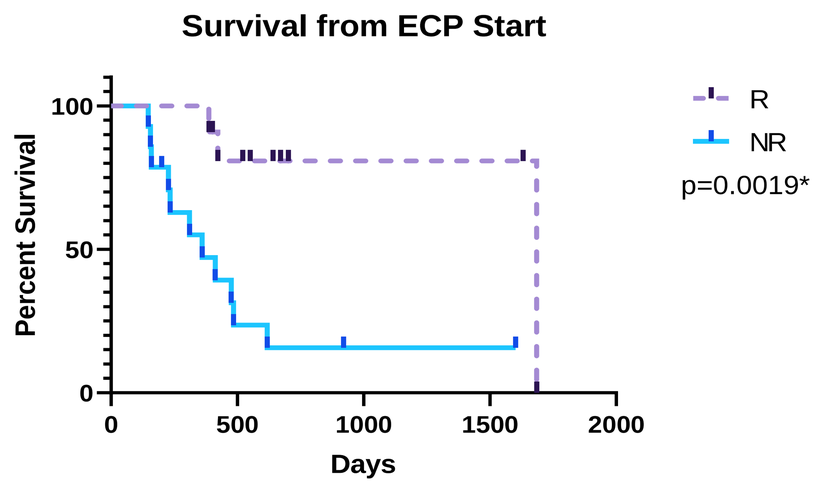
Responders

FEV1
Pre-ECP:
-53.0 ml/month
6 months after ECP:
+12.0 ml/month
12 months after ECP:
+1.0 ml/month



FVC
Pre-ECP:
-50.0 ml/month
ECP+6:
+37.0 ml/month
ECP+12:
+13.0 ml/month

Responders patients had a median survival of 1685 days after starting ECP and this was significantly greater than non-responders (316 days).



CONCLUSION

Our study confirms that in CLAD patients ECP effectively reduces the decline in respiratory function and improves survival, showing a response rate of about 50%. Although no clear clinical profile of responders has yet been defined, BOS phenotype and absence of recurrent respiratory infections before diagnosis of CLAD seem to be associated with a positive response to ECP therapy.