

Anatomo-functional Alterations of the Respiratory System in the Surgical Approach to Advanced Pneumopathies

PROGRAM

OBJECTIVES:

To discuss the developments in the dealing with patients with terminal pneumopathies, their therapeutic options, including the pros and cons of each one of them. 2. To foster the research and the development of new experimental models that can be used in the investigation and improvement of the surgical treatment of advanced pneumopathies.

BACKGROUND:

Some lung diseases that evolve with significant functional loss, often irrecoverable, such as severe lung emphysema, advanced pulmonary fibrosis and cystic fibrosis are grouped and named under the label of terminal pneumopathies. The terminal pneumopathies are a major cause of death in the world. Besides the high mortality rate, the life quality of the sick people when submitted to clinical treatment is not satisfactory. Therapeutic surgery was not an option for this group of patients until a few years ago in the whole country. Currently, these therapeutic option has shown a significant growth to become a possibility in some city Centers, and its dissemination is of utmost importance. Lung transplant is indicated for patients with pneumopathies in an advanced stage that do not have a satisfactory response to conventional therapeutic clinical treatments. Encouraging progress in this kind of transplant has been experimented though the years, due to developments achieved in the solutions for organ preservation, surgical techniques, intensive postoperative care, control in the treatment of infections and immunosuppressant schemes. However, some factors are still a hindrance to lung transplant success, such as the lack of viable organs, the difficulties in organ preservation, and the development of ischemic injury and reperfusion. Thus, it is important to discuss and analyze the three main factors that can limit the success of this modality of transplant: the care of the donor lung, the care with patients in the waiting list and the care with transplanted patients. Some pulmonary vascular diseases can also develop with progressive functional loss, such as chronic pulmonary thromboembolism, in which situation the pulmonary thromboendarterectomy is the main therapeutic option. Besides, unidirectional

endobronchial valves are among the non-surgical alternatives for the pulmonary volume reduction, with early encouraging results.

CONTENT (SYLLABUS):

Histopathological aspects of advanced pneumopathies 2. Indications for lung transplant 3. Ideal donor versus marginal donor 4. Technical aspects of the types of lung transplant 5. Immunosuppression in lung transplant: what is the way? 6. Infection in lung transplant: how to deal with it? 7. Pulmonary hypertension: particularities of perioperative and postoperative management of lung transplant. 8. Lung lobar transplant: alternative method? 9. Lung preservation methods. 10. Experimental models of lung transplant 11. Pathophysiology of the ischemia/reperfusion lesion 12. Experimental model of lung ischemia in chronic acute stage: analysis of vascular remodeling 13. Surgical aspects in the treatment of chronic lung thromboembolism 14. Predictors of post-thromboendarterectomy mortality 15. Morphological aspects of pulmonary occlusive vascular disease 16. Role of gene expression markers in thromboembolism and new diagnostic methods. 17. Lung volume reduction surgery: is there still indication for it? 18. Bronchoscopy treatment of the advanced lung emphysema with unidirectional endobronchial valves: current stage of research and clinical practice. 19. Cellular therapy what is new in the national and international scenario.

BIBLIOGRAPHY:

1. Abdalla LG, Braga KA, Nepomuceno NA, Fernandes LM, Samano MN, Pêgo-Fernandes PM. Ex vivo lung perfusion in Brazil. J Bras Pneumol., 2016 apr;42(2):95-8.
2. Samano MN, Iuamoto LR, Fonseca HV, Fernandes LM, Abdalla LG, Jatene FB, Pêgo-Fernandes PM. A simple technique can reduce cardiopulmonary bypass use during lung transplantation. Clinics 2016 Apr 71(4):232-234.
3. Samano MN, Pêgo-Fernandes PM,. Building a lung transplant program. Clinics 2015 DEc 70(12):773-774.
4. Samano MN, Pêgo-Fernandes PM, Fonseca Ribeiro AK, Turuça K, Abdalla LG, Fernandes LM, Correia AT, Jatene FB. Lung Transplantation in patients with cystic fibrosis. Transplant Proc. 2013 Apr 45(3): 1137-1141.
5. Medeiros IL, Pêgo-Fernandes PM, Mariani AW, Fernandes FG, do Vale Unterperfinger F, Canzian M, Jatene FB. Histologic and functional evaluation of

lungs reconditioned by ex vivo lung perfusion. *J Heart Lung Transplant*. 2012 Mar;31(3):305-9.

6. Silva VF, Pazetti R, Soto Sde F, Siqueira MM, Correia AT, Jatene FB, Pêgo-Fernandes PM. Effects of mycophenolate sodium on mucociliary clearance using a bronchial section and anastomosis rodent model. *Clinics (Sao Paulo)*. 2011;66(8):1451-6.
7. Simões EA, Pêgo-Fernandes PM, Cardoso PF, Pazetti R, Werebe E, de Oliveira Braga KA, Menezes A, Nepomuceno N, Soares PR, Correia AT, Jatene FB. Comparing the performance of rat lungs preserved for 6 or 12 hours after perfusion with low-potassium dextran or histidine-tryptophan-ketoglutarate. *Transplant Proc*. 2011 Jun;43(5):1520-4.
8. Pêgo-Fernandes PM, Mariani AW, Medeiros IL, Pereira AE, Fernandes FG, Valle Unterpertinger F, Canzian M, Jatene FB. Ex vivo lung evaluation and reconditioning. *Rev Bras Cir Cardiovasc*. 2010 Oct-Dec;25(4):441-6.
9. Pêgo-Fernandes PM, Samano MN, Fiorelli AI, Fernandes LM, Camargo SM, Xavier AM, Sarmento PA, Bernardo WM, de Castro MC, Jatene FB. Recommendations for the use of extended criteria donors in lung transplantation. *Transplant Proc*. 2011 Jan-Feb;43(1):216-9.
10. Pêgo-Fernandes PM, Werebe EC, Cardoso PF, Pazetti R, Oliveira KA, Soares PR, Jatene FB. Experimental model of isolated lung perfusion in rats: technique and application in lung preservation studies. *J Bras Pneumol*. 2010 Jul-Aug;36(4):490-3.
11. Bugano DD, Campos SV, Afonso JE Jr, Caramori ML, Teixeira RH, Carraro RM, Strabelli TM, Machado CM, Samano MN, Pêgo-Fernandes P, Jatene FB. Impact of cytomegalovirus infection in lung transplant patients under universal prophylaxis: single-center experience in Brazil. *Transplant Proc*. 2010 Mar;42(2):525-30.
12. Pêgo-Fernandes PM, Werebe E, Cardoso PF, Pazetti R, de Oliveira KA, Soares PR, Jatene FB. Experimental model of isolated lung perfusion in rats: first Brazilian experience using the IL-2 isolated perfused rat or guinea pig lung system. *Transplant Proc*. 2010 Mar;42(2):444-7.
13. Pêgo-Fernandes PM, de Medeiros IL, Mariani AW, Fernandes FG, Unterpertinger FD, Samano MN, Werebe ED, Canzian M, Jatene FB. Ex vivo lung perfusion: early report of Brazilian experience. *Transplant Proc*. 2010 Mar;42(2):440-3.
14. Samano MN, Minamoto H, Junqueira JJ, Yamaçake KG, Gomes HA, Mariani AW, Pêgo-Fernandes PM, Jatene FB. Bronchial complications following lung transplantation. *Transplant Proc*. 2009 Apr;41(3):921-6.
15. Jatene FB, Pêgo-Fernandes PM. Challenges in lung transplantation. *J Bras Pneumol*. 2008 May;34(5):249-50.

16. Pazetti R, Pêgo-Fernandes PM, Lorenzi-Filho G, Saldiva PH, Moreira LF, Jatene FB. Effects of cyclosporine A and bronchial transection on mucociliary transport in rats. *Ann Thorac Surg*. 2008 Jun;85(6):1925-9;
17. Fernandes PM, Said MM, Pazetti R, Moreira LF, Jatene FB. Effects of azathioprine on mucociliary clearance after bronchial section and anastomosis in a rat experimental model. *J Bras Pneumol*. 2008 May;34(5):273-9
18. Campos S, Caramori M, Teixeira R, Afonso J Jr, Carraro R, Strabelli T, Samano M, Pêgo-Fernandes P, Jatene F. Bacterial and fungal pneumonias after lung transplantation. *Transplant Proc*. 2008 Apr;40(3):822-4.
19. Samano MN, Minamoto H, Oliveira EQ, Caramori ML, Pêgo-Fernandes PM, Jatene FB. Bronchial stenosis treatment after lung transplantation with a self-expandable silicone stent. *Clinics (Sao Paulo)*. 2007 Oct;62(5):643-4.
20. Terra-Filho M, Mello MF, Lapa MS, Teixeira RH, Jatene FB. Clinical and haemodynamic evaluation of chronic thromboembolic pulmonary hypertension patients scheduled for pulmonary thromboendarterectomy: Is schistosomiasis hypertension an important confounding factor? *Clinics (Sao Paulo)*. 2010;65(11):1155-60.
21. Arnoni RT, Jatene FB, Bernardo WM, Aiello VD, Jatene T, Monteiro R, Demarchi LM. Medial hypertrophy in patients with pulmonary embolism: anatomopathological study. *Arq Bras Cardiol*. 2007 Jun;88(6):660-6.
22. Jatene FB, Bernardo WM. Pulmonary embolic ischemia: clinical and experimental aspects. *Rev Assoc Med Bras*. 2003 Jul-Sep;49(3):342-8.
23. Berger RL, Decamp MM, Criner GJ, Celli BR. Lung volume reduction therapies for advanced emphysema: an update. *Chest* 2010;38(2): 407-17.
24. Cooper JD. "All that glitters...": evaluating interventions for emphysema. *Chest*. 2010 Aug;138(2):243-5.
25. Kemp SV, Polkey MI, Shah PL. The epidemiology, etiology, clinical features, and natural history of emphysema. *Thorac Surg Clin*. 2009 May;19(2):149-58.
26. Shah PL, Slebos DJ, Cardoso PF, Cetti E, Voelker K, Levine B, Russell ME, Goldin J, Brown M, Cooper JD, Sybrecht GW; EASE trial study group. Bronchoscopic lung-volume reduction with Exhale airway stents for emphysema (EASE trial): randomised, sham-controlled, multicentre trial. *Lancet*. 2011 Sep 10;378(9795):997-1005.
27. Thistlethwaite PA, Kaneko K, Madani MM, Jamieson SW. Technique and outcomes of pulmonary endarterectomy surgery. *Ann Thorac Cardiovasc Surg*. 2008 Oct;14(5):274-82.
28. Yao W, Firth AL, Sacks RS, Ogawa A, Auger WR, Fedullo PF, Madani MM, Lin GY, Sakakibara N, Thistlethwaite PA, Jamieson SW, Rubin LJ, Yuan JX. Identification

of putative endothelial progenitor cells (CD34+CD133+Flk-1+) in endarterectomized tissue of patients with chronic thromboembolic pulmonary hypertension. *Am J Physiol Lung Cell Mol Physiol*. 2009 Jun;296(6):L870-8.

29. Jenkins D, Mayer E, Screaton N, Madani M. State-of-the-art chronic thromboembolic pulmonary hypertension diagnosis and management. *Eur Respir Rev*. 2012 Mar 1;21(123):32-9.
30. Kuniyama T, Gerds J, Groesdonk H, Sata F, Langer F, Tscholl D, Aicher D, Schäfers HJ. Predictors of postoperative outcome after pulmonary endarterectomy from a 14-year experience with 279 patients. *Eur J Cardiothorac Surg*. 2011 Jul;40(1):154-61.
31. Rahnnavardi M, Yan TD, Cao C, Vallely MP, Bannon PG, Wilson MK. Pulmonary thromboendarterectomy for chronic thromboembolic pulmonary hypertension: a systematic review. *Ann Thorac Cardiovasc Surg*. 2011 Oct 25;17(5):435-45.
32. Zych B, Popov AF, Amrani M, Bahrami T, Redmond KC, Krueger H, Carby M, Simon AR. Lungs from donation after circulatory death donors: an alternative source to brain-dead donors? Midterm results at a single institution. *Eur J Cardiothorac Surg*. 2012.
33. Lehmann S, Barten MJ, Topf C, Garbade J, Dhein S, Mohr FW, Bittner HB. Donor type impact on ischemia-reperfusion injury after lung transplantation. *Ann Thorac Surg*. 2012 Mar;93(3):913-20.
34. Santana-Rodríguez N, García-Herrera R, Clavo B, Llontop P, Ponce-González MA, Villar J, López-García A, Fiuza MD, Rodríguez-Bermejo JC, García-Castellano JM, Machín RP, Ruíz-Caballero JA, Brito Y, Fernández-Pérez L. Searching for novel molecular targets of chronic rejection in an orthotopic experimental lung transplantation model. *J Heart Lung Transplant*. 2012 Feb;31(2):213-21.
35. Nakajima D, Chen F, Yamada T, Sakamoto J, Ohsumi A, Bando T, Date H. Reconditioning of lungs donated after circulatory death with normothermic ex vivo lung perfusion. *J Heart Lung Transplant*. 2012 Feb;31(2):187-93.
36. Kubo H. Tissue engineering for pulmonary diseases - insights from the laboratory. *Respirology*. 2012 Feb 1. doi: 10.1111/j.1440-1843.2012.02145.x.