

# RGO ET TRANSPLANTATION

Du point de vue du pneumologue....

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**CRCM et Groupe de transplantation pulmonaire**  
**Hôpital Foch, Suresnes**



# RGO ET TRANSPLANTATION

## Pourquoi aborder le sujet ?

Improved lung allograft function after fundoplication in patients with gastroesophageal reflux disease undergoing lung transplantation  
 R. Duane Davis, Jr, Christine L. Lau, Steve Eubanks, Robert H. Messier, Denis Hadjiiladis, Mark P. Steele and Scott M. Palmer  
*J Thorac Cardiovasc Surg* 2003;125:533-542

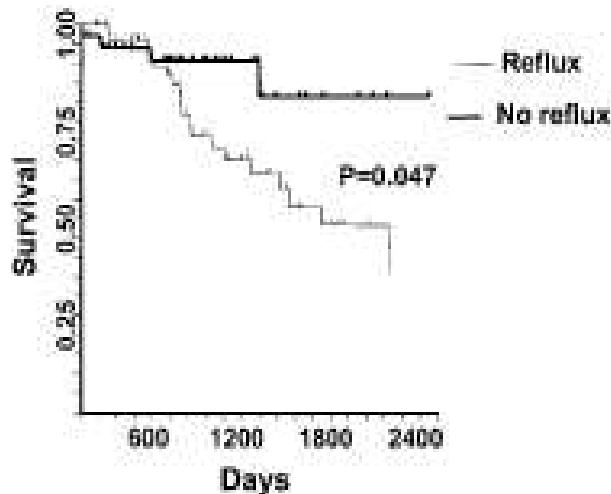


Figure 2. Effect of GERD on survival: Kaplan-Meier actuarial survival curves for overall lung transplant recipients compared with the group of lung transplant recipients who also underwent fundoplication surgery after being evaluated for GERD. The fundoplication group had a significant survival advantage.

Pretransplant gastroesophageal reflux compromises early outcomes after lung transplantation

Stefish C. Murthy, MD, PhD,<sup>a</sup> Edward R. Nowicki, MD, MS,<sup>a</sup> David P. Mason, MD,<sup>a</sup> Marie M. Budev, DO, MPH,<sup>b</sup> Anthony I. Nunez, MD,<sup>a</sup> Lucy Thuita, MS,<sup>c</sup> Jeffrey T. Chapman, MD,<sup>b</sup> Kenneth R. McCurry, MD,<sup>a</sup> Gösta B. Pettersson, MD, PhD,<sup>a</sup> and Eugene H. Blackstone, MD<sup>a,c</sup>

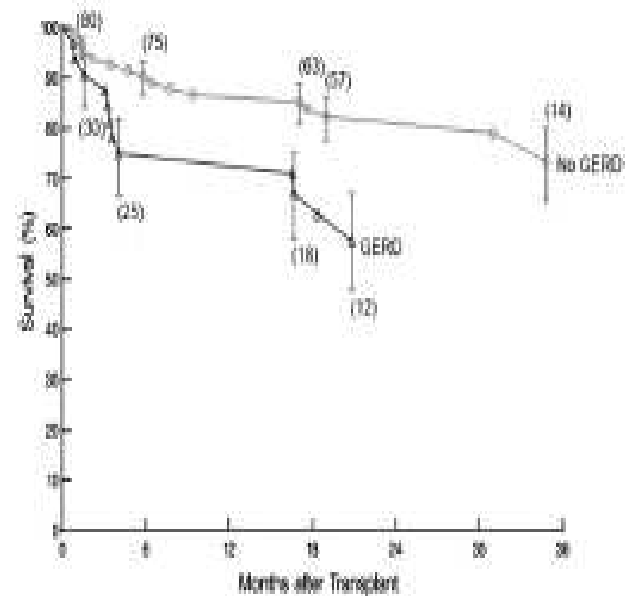


FIGURE 3. Survival after lung transplantation according to presence or absence of gastroesophageal reflux disease (GERD). Each symbol represents a death, vertical bars confidence limits equal to  $\pm 1$  standard error, and numbers in parentheses patients remaining at risk.

# RGO ET TRANSPLANTATION

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**RGO PRE TP:** Prévalence et modalités diagnostiques

**TP:** Rôle aggravant / Gastroparésie

**POST TP :** Conséquences:

- EBO
- RA
- Dysfonction chronique du greffon

**TRAITEMENT**

- Médical
- Chirurgical
- Quand opérer ?

**EXPERIENCE LOCALE**

# RGO AVANT TRANSPLANTATION

- C'est fréquent
- Ça dépend des outils utilisés pour porter le diagnostic
- Ça dépend des pathologies étudiées

**Table 1** Prevalences of abnormal gastro-oesophageal reflux (pH testing) and of delayed gastric emptying (nuclear medicine study)

| Lung disease group           | Study                          | Patient population  | No of patients | Manometry         | Abnormal distal reflux (%)                   | Abnormal proximal reflux (%) | Delayed gastric emptying                              | Comment   |
|------------------------------|--------------------------------|---------------------|----------------|-------------------|--|------------------------------|---|---|
| Usual interstitial pneumonia | Tobin 1998 <sup>15</sup>       | IPF Clinic          | 17             | Selected patients | 88   | 71%                          |   | Manometry not used                                      |
|                              | Raghu 2006 <sup>17</sup>       | IPF Clinic          | 65             | Yes               | 76   | 63                           |   | Some subjects taking PPIs and pH probe placement varied |
|                              | Salvioli 2006 <sup>18</sup>    | IPF Clinic          | 18             | Selected patients | 67   |                              |   | Manometry not used                                      |
|                              | Sweet 2007 <sup>19</sup>       | Pre-transplant      | 30             | Yes               | 67   | 30                           |   |   |
| Cystic fibrosis              | Ledson 1998 <sup>26</sup>      | CF Clinic           | 10             | Yes               | 80   |                              |   | Patients with symptoms selected                         |
|                              | Button 2005 <sup>23</sup>      | Pre-transplant      | 11             | No                | 91   | Undefined                    |   | Some subjects taking PPIs, 1 patient s/p fundoplication |
|                              | Button 2005 <sup>23</sup>      | Post-transplant     | 13             | No                | 85   | Undefined                    |   | Some subjects taking PPIs, 1 patient s/p fundoplication |
|                              | Bodet-Milin 2006 <sup>27</sup> | Pre-transplant      | 30             |                   |  |                              | 67%   |   |
| Connective tissue disease    | Johnson 1989 <sup>10</sup>     | Rheumatology Clinic | 13             | Yes               | 54   | Undefined                    |   |   |
|                              | Bassotti 1997 <sup>28</sup>    | Dermatology Clinic  | 78             | Yes               | 78   |                              |   | Acid suppression not withheld prior to study            |
|                              | Gasper 2007*                   | Transplant Clinic   | 23             | Yes               | 83   | 30                           | 6 of 8 (75%)  |   |
| COPD                         | Andersen 1989 <sup>30</sup>    | COPD Clinic         | 55             | Yes               | 49   |                              |   |   |
|                              | Casanova 2004 <sup>31</sup>    | COPD Clinic         | 42             | Yes               | 62   |                              |   |   |
| Pre-lung transplant          | Cantu 2005 <sup>40</sup>       | Transplant Clinic   | 36             | Yes               | 63   |                              |   | PPI withheld for 5 days                                 |
|                              | D'Ovidio 2005 <sup>24</sup>    | Transplant Clinic   | 78             | Yes               | 32   | 20                           | 13 of 27 (44%)  | PPI withheld for 5 days                                 |
|                              | Sweet 2006 <sup>25</sup>       | Transplant Clinic   | 109            | Yes               | 68   | 37                           |   |   |
| COPD (24) + ILD (47)         | Seccombe, 2013                 | Pre-transplant      | 73             | Yes               | 53% des candidats à la TP (71% OLD, 43% ILD) |                              |   |   |
| COPD(16) +IPF(10)            | Basseri, 2010                  | Pre-transplant      | 30             | Yes               | 36%  | 25%                          | FPI: plus souvent aperistaltisme, reflux acide distal |   |

# LA TRANSPLANTATION AGGRAVE LE RGO

- **Phmetrie:**

35% pré - 65% post (*Young, Chest, 2003*)

32% à M3, 53% à M12 (*D'Ovidio, Am J Transplant, 2006*)

49 % (*Seccombe J, Neurogastroenterol motil, 2013*)

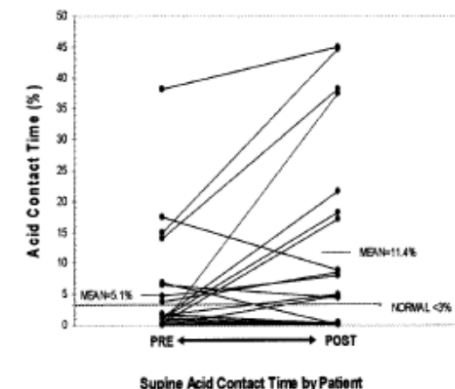
70% (*Hadjiliadis D, Clin Transplant 2003*)

- **Impédancemétrie + pHmétrie**

4/9 patients à 6 mois (*Robertson A, Thorax, 2009*)

49% à M36 (*Blondeau K, Eur Respir J, 2008*), 27% exclusivement non acide

51% (*Davis C, Surgery, 2010*)



## FACTEURS FAVORISANTS

- RGO pré-TP (100%)
- Modification des pressions thoraciques et abdominales
- Traitements et notamment corticoïdes et anticalcineurines
- Gastroparésie
- RE-TP plus que TP (*Davis C, Surgery, 2010*)
- TBP plus que TUP (*Davis C, Surgery, 2010*) ou pas (*Young, Chest, 2003*)

# GASTROPARESIE

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## Incidence variable.....et s'améliore probablement avec le temps

- 36 % TOGD+/-Scan (*Davis C, Surgery, 2010*)
- 77% (*Casper.*)
- 33% si RGO (*Young, Chest, 2003*)
- 93% à 3 mois, 80% à 12 mois (*43 patients- D'Ovidio, Am J Transplant, 2006*)
- 97% MUCOS (*30 patients- Bodet-Millin, JHLT, 2006*)

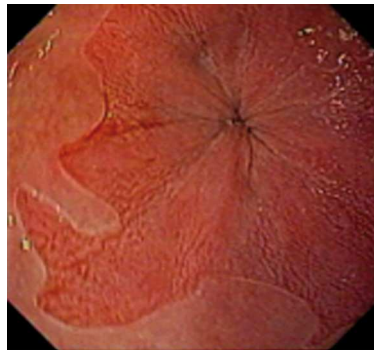
## Mécanismes supposés:

- Lésions nerf vague (mécaniques, ischémiques, complètes ou partielles)
- Traitements et notamment corticoïdes et anticalcineurines

# CONSEQUENCES DU RGO POST TRANSPLANTATION ENDOBRACHYOESOPHAGE

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- 12% (*Davis C, Surgery 2010*)
- 13% (*Bruton PR, Dis. Esophagus 2009*)
- Idem population générale souffrant de RGO (*Winters C, Gastroenterology, 2004*)
- Risque plus élevé de transformation en adénocarcinome (immunosuppression) (*Oka M, Surgery, 1992- Saleh W, J Thorac Cardiovasc Surg 2010*)
- Développement de lésions de métaplasie malgré IPP



# CONSEQUENCES DU RGO POST TRANSPLANTATION

## REJET AIGU: plus fréquent et plus grave

### Gastroesophageal Reflux Disease Is Associated With an Increased Rate of Acute Rejection in Lung Transplant Allografts

N.S. Shah, S.D. Force, P.O. Mitchell, E. Lin, E.C. Lawrence, K. Easley, J. Qian, A. Ramirez, D.C. Neujahr, A. Gal, K. Leeper, and A. Pelaez

Transplantation Proceedings, 42, 2702-2706 (2010)

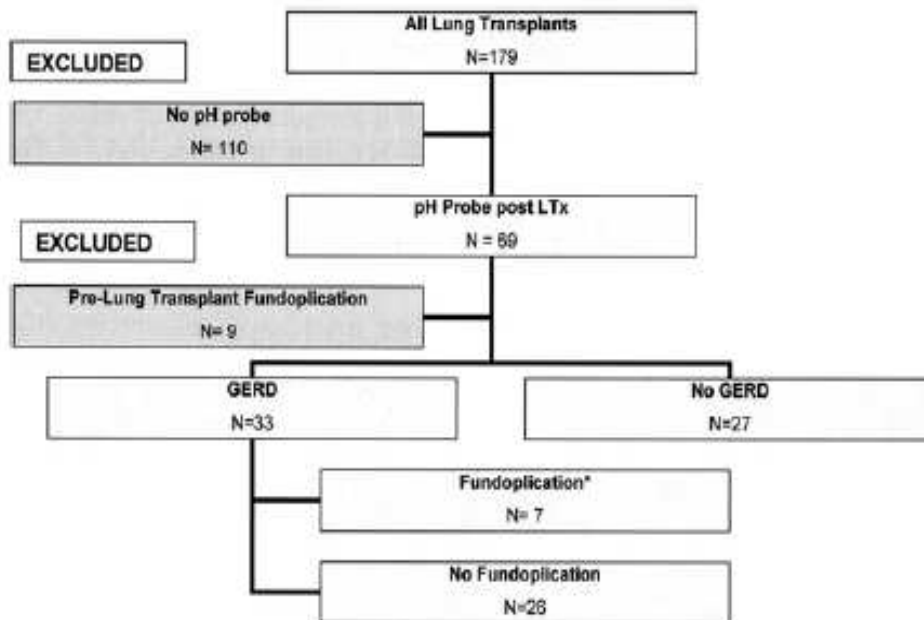
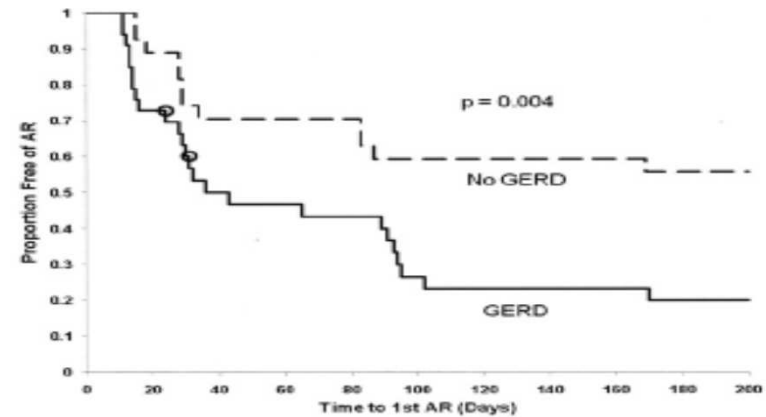


Fig 1. Selection criteria. \*Episodes of AR and patient-days after gastric fundoplication in this group were excluded.



| Number of patients at risk at day | 0  | 10 | 20 | 40 | 80 | 120 | 160 | 200 |
|-----------------------------------|----|----|----|----|----|-----|-----|-----|
| No GERD                           | 27 | 27 | 25 | 20 | 20 | 17  | 17  | 15  |
| GERD                              | 33 | 33 | 24 | 16 | 14 | 8   | 8   | 6   |

Fig 2. Time to first acute rejection episodes (ARE).  $P = .004$  calculated by log-rank test; GERD = gastroesophageal reflux disease; O = censored if fundoplication before to ARE.

Table 3. Secondary Analysis

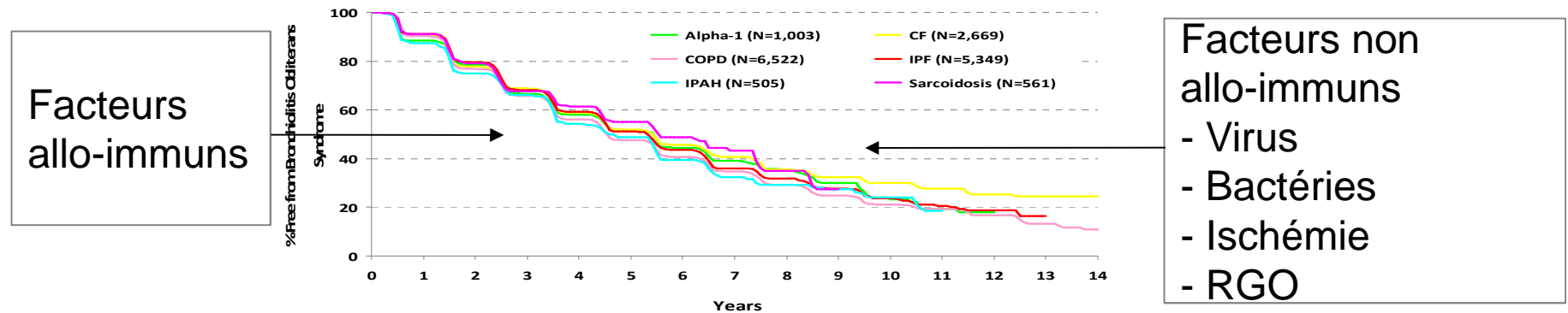
|                                      | GERD (n = 33)<br>(95% CI) | No GERD (n = 27)<br>(95% CI) | P Value |
|--------------------------------------|---------------------------|------------------------------|---------|
| $\geq 2$ ARE                         | 12 (36.4%)                | 0                            | <0.0001 |
| Incidence density by severity of ARE |                           |                              |         |
| A1                                   | 3.48 (1.99-5.66)          | 0.86 (0.23-2.20)             | .011    |
| A2                                   | 4.14 (2.49-6.46)          | 1.29 (0.47-2.80)             | .013    |
| A3                                   | 0.44 (0.05-1.57)          | 0                            | .49     |
| A4                                   | 0                         | 0                            | .35     |
| B1                                   | 1.31 (0.48-2.84)          | 0.86 (0.23-2.20)             | .74     |
| B2                                   | 0.44 (0.05-1.57)          | 0                            | .49     |

Abbreviations as in Tables 1 and 2.



# CONSEQUENCES DU RGO POST TRANSPLANTATION

## DYSFONCTION CHRONIQUE DU GREFFON



### QUEL LIEN ENTRE RGO ET DYSFONCTION CHRONIQUE DU GREFFON ?

- Modèle animal d'inhalation de liquide gastrique (rat tp)
- Cytologie et histologie pulmonaire
- Marqueurs d'inhalation dans le LBA
- Corrélations RGO/Fonction respiratoire
- Effets du traitement du RGO

# CONSEQUENCES DU RGO POST TRANSPLANTATION DYSFONCTION CHRONIQUE DU GREFFON

## Aspect histologique

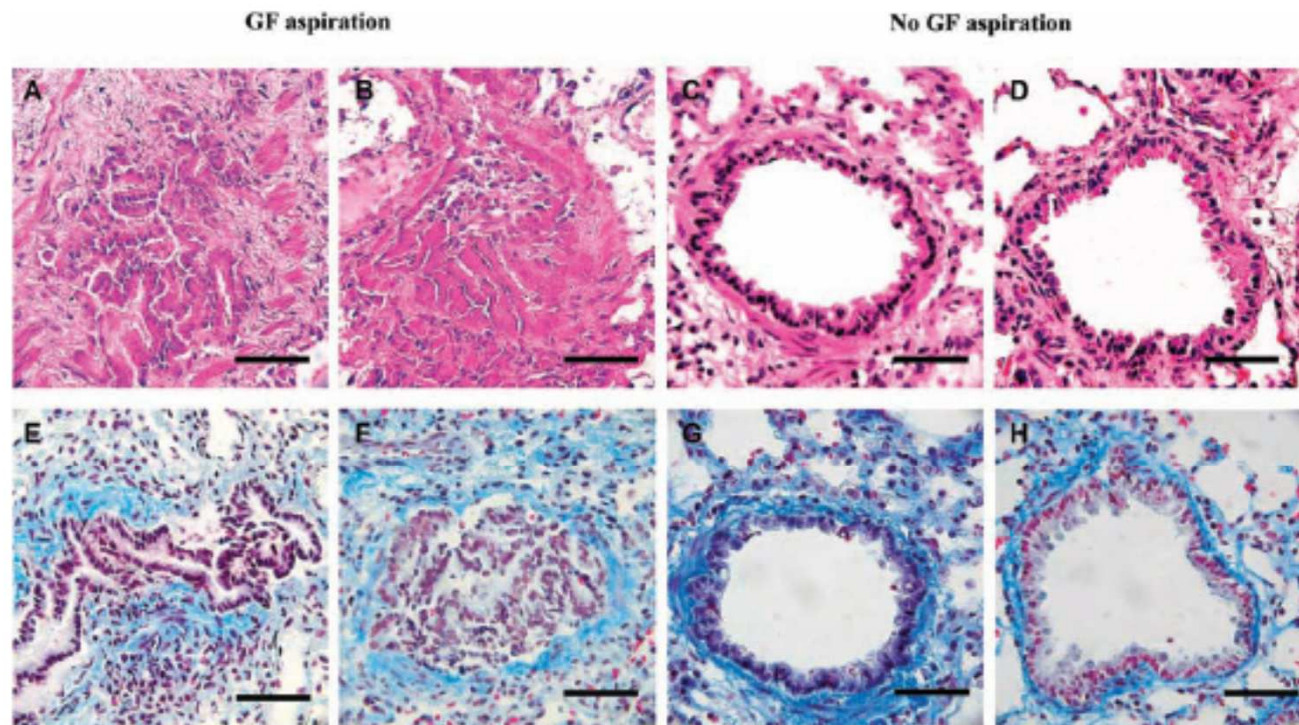
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- Abernathy, Human Pathol 1991
- 11 TCP (autopsies, explant)
- 7 BOS,
- 3 patients greffés depuis >6mois: fibrose concentrique des bronchioles terminales, relativement acellulaire
- 4 patients greffés depuis <6 mois: lésions focales et cellulaires, extension alvéolaire, matériel d'inhalation avec granulomes à corps étranger

# CONSEQUENCES DU RGO POST TRANSPLANTATION DYSFONCTION CHRONIQUE DU GREFFON Modèle animal

## Chronic Aspiration of Gastric Fluid Induces the Development of Obliterative Bronchiolitis in Rat Lung Transplants

*American Journal of Transplantation 2008; 8: 1614-1621*



**Figure 1: Histological evidence consistent with the development of obliterative bronchiolitis associated with gastric fluid (GF) aspiration.** In lung allografts with gastric fluid aspiration (A, B, E, F), fibroproliferative tissue significantly reduced the size of the bronchiolar lumen, whereas the lumen remained normal in allografts (C, G) and isografts (D, H) not receiving aspiration. A mild degree of peribronchiolar cell infiltration was observed in allografts receiving gastric fluid aspiration (A, B, E, F). Trichrome staining (lower panels) demonstrated a substantially greater extent of fibroproliferation surrounding the bronchioles of allotransplants with gastric fluid aspiration (E, F) compared to those observed in allotransplants (G) and in isotransplants (H) without gastric fluid aspiration. (Bar represents 250  $\mu$ m.)

# CONSEQUENCES DU RGO POST TRANSPLANTATION DYSFONCTION CHRONIQUE DU GREFFON Lien entre RGO et Inhalation

## Oil red O stain of alveolar macrophages is an effective screening test for gastroesophageal reflux disease in lung transplant recipients

The Journal of Heart and Lung Transplantation, Vol 29, No 8, August 2010

**METHODS:** Our investigation was a prospective analysis of 34 lung transplant patients who were transplanted between April 1999 and July 2006 at a single institution. All patients with recurrent respiratory infections, recurrent acute rejection, unexplained graft dysfunction or newly diagnosed OB had Oil red O staining of alveolar macrophages on BAL specimens at bronchoscopy and 24-hour esophageal pH monitoring. A quantitative assessment called the lipid index was performed resulting in a score from 0 to 400. Abnormal 24-hour pH studies were defined as acid exposure >3.4% in the distal and/or >1% in the proximal esophageal site.

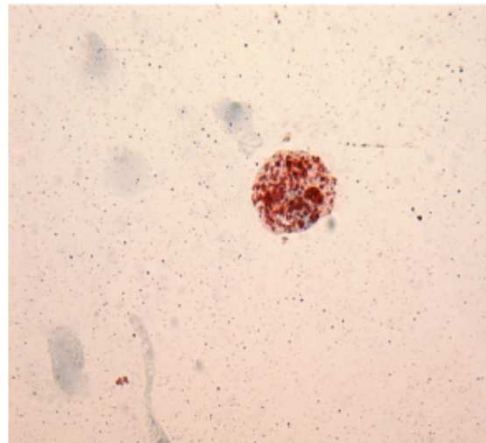


Figure 1 Oil red O staining of alveolar macrophages with varying degrees of intracellular lipid.

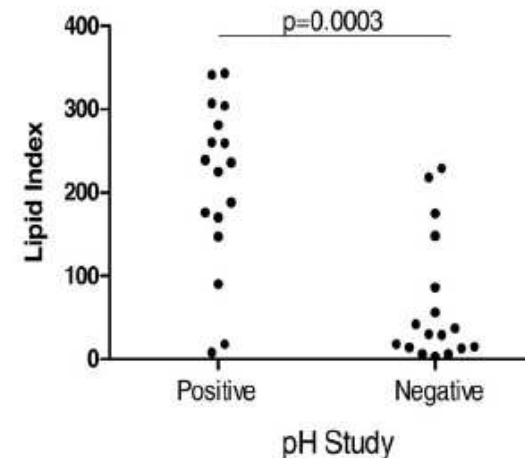


Figure 2 Distribution of lipid index according to pH study data.

# CONSEQUENCES DU RGO POST TRANSPLANTATION DYSFONCTION CHRONIQUE DU GREFFON

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## Marqueurs biologiques: la pepsine

Enzyme protéolytique activée à partir de son zymogène quand  $\text{pH} < 4$

- Élevée dans le LBA des greffés sans rapport avec reflux et BOS (*Ward, Thorax 2005- Stovold, AJRCCM 2007*)
- Présence dans le LBA non influencée par les IPP (*Blondeau, ERJ 2008*)
- Taux non corrélé avec la présence ou la sévérité de la BOS (*Blondeau, ERJ 2008*)
- Taux peut être corrélé à l'existence d'un rejet aigu (*Stovold, AJRCCM 2007*)

→ **Plutôt un marqueur de reflux que le chaînon physiopathologique manquant**

**CONSEQUENCES DU RGO POST TRANSPLANTATION  
DYSFONCTION CHRONIQUE DU GREFFON  
Marqueurs biologiques: les acides biliaires**

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**Marqueurs biologiques: les Acides biliaires**

- Destruction membrane des pneumocytes de type II (*Oleberg, Lung 1990*)
- Lésions des jonctions serrées de la barrière épithéliale (*Chen, Am J Physiol Gastrointest Liver Physiol, 2011*)
- Diminution de l'activité des macrophages alvéolaires (*D'Ovidio, Dis Esphagus, 2006 et Chang Proc Natl Acad Sci USA, 2004*)
- Altération des phospholipides et du surfactant (*D'Ovidio, Dis Esphagus, 2006*)
- Diminution des protéines A et D du surfactant (*D'Ovidio, Am J Transplant 2006*)
  
- Présence dans le LBA corrélée à l'existence d'un RGO documenté et plus souvent élevé si BOS (*Blondeau, JHLT 2009*)
- Augmentation locale des taux d'IL8 et des PNN (LBA) (*D'ovidio, J Thorac Cardiovasc Surg, 2005*)
- Présence dans le LBA associée à la survenue de BOS et à la survie (*D'ovidio, J Thorac Cardiovasc Surg, 2005 - Mertens, AJt 2011*)

# CONSEQUENCES DU RGO POST TRANSPLANTATION DYSFONCTION CHRONIQUE DU GREFFON Marqueurs biologiques: les acides biliaires

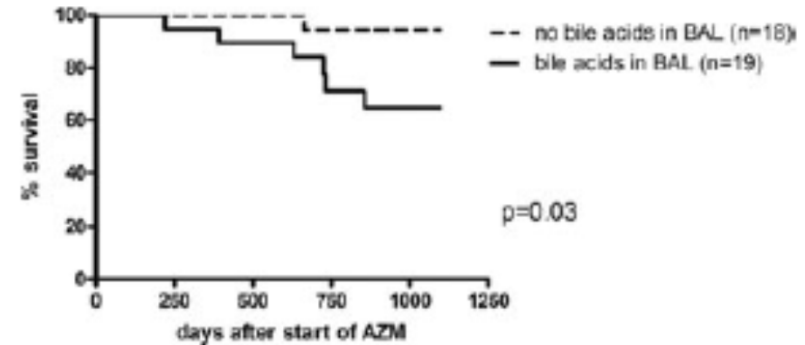
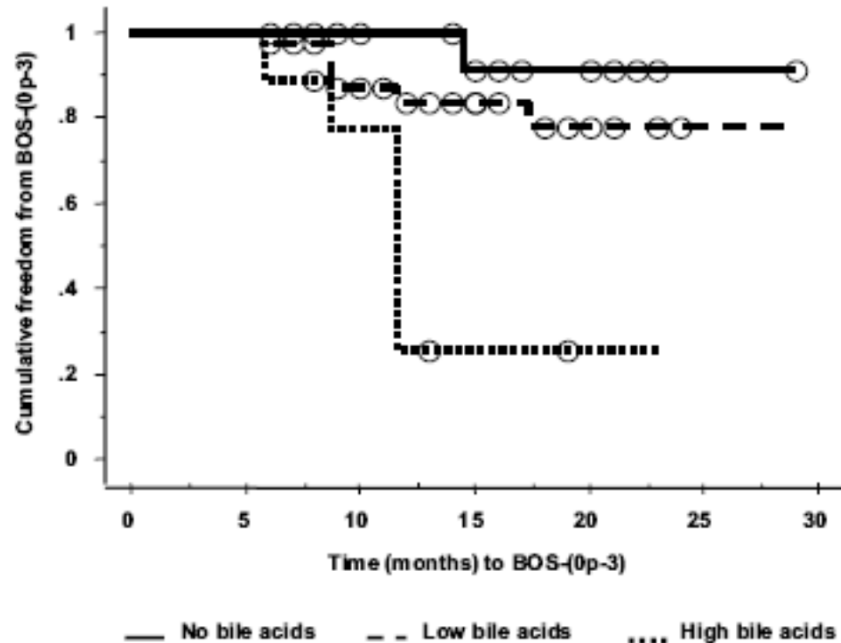


Figure 4: Kaplan-Meier survival curve: effect of bile acids in BAL on survival. The percentage of patients surviving without reLTx, either with (solid line) or without (dashed line) bile acids in BAL ( $p = 0.03$ ).

## Bile acid aspiration and the development of bronchiolitis obliterans after lung transplantation

Frank D'Ovidio, MD, Marco Mura, MD, Melanie Tsang, MSc, Thomas K. Waddell, MD, Michael A. Hutcheon, MD, Lianne G. Singer, MD, Denis Hadjiiladis, MD, Cecilia Chaparro, MD, Carlos Gutierrez, MD, Andrew Pierre, MD, Gail Darling, MD, Mingyao Liu, PhD, and Shaf Keshavjee, MD

The Journal of Thoracic and Cardiovascular Surgery • May 2005

## Bile Acids Aspiration Reduces Survival in Lung Transplant Recipients with BOS Despite Azithromycin

V. Mertens<sup>a</sup>, K. Blondeau<sup>a</sup>, L. Van Oudenhove<sup>a</sup>, B. Vanaudenaerde<sup>b</sup>, R. Vos<sup>b</sup>, R. Farre<sup>a</sup>, A. Pauwels<sup>a</sup>, G. Verleden<sup>b,c</sup>, D. Van Raemdonck<sup>c</sup>, D. Sifrim<sup>a,d</sup> and L. J. Dupont<sup>b,e\*</sup>

American Journal of Transplantation 2011; 11: 329-335

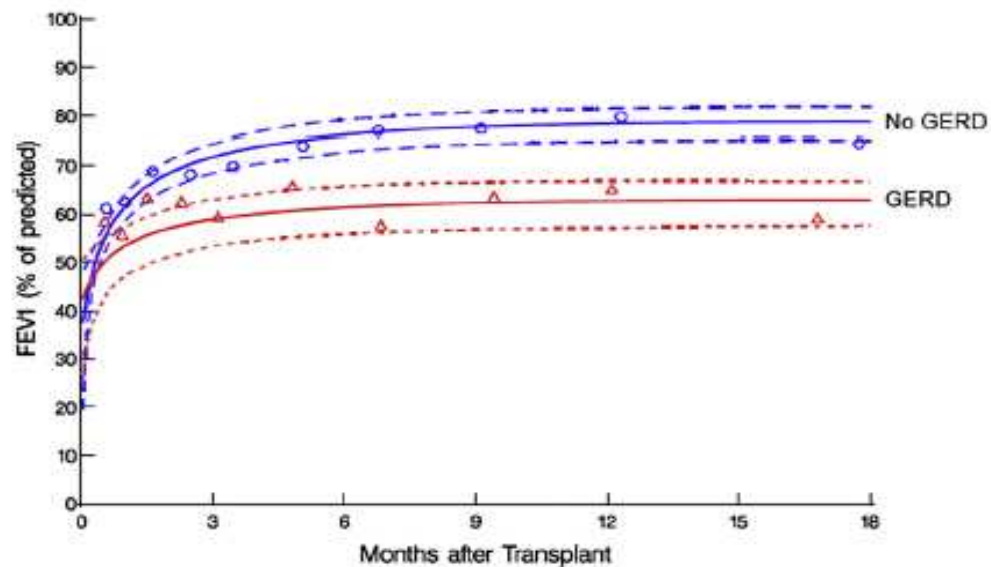
# CONSEQUENCES DU RGO POST TRANSPLANTATION

## DYSFONCTION CHRONIQUE DU GREFFON

### Corrélation avec la fonction respiratoire

#### Pretransplant gastroesophageal reflux compromises early outcomes after lung transplantation

Sudish C. Murthy, MD, PhD,<sup>a</sup> Edward R. Nowicki, MD, MS,<sup>a</sup> David P. Mason, MD,<sup>a</sup> Marie M. Budev, D.O., MPH,<sup>b</sup> Anthony I. Nunez, MD,<sup>a</sup> Lucy Thuita, MS,<sup>c</sup> Jeffrey T. Chapman, MD,<sup>b</sup> Kenneth R. McCurry, MD,<sup>a</sup> Gösta B. Pettersson, MD, PhD,<sup>a</sup> and Eugene H. Blackstone, MD<sup>a,c</sup>





# CONSEQUENCES DU RGO POST TRANSPLANTATION DYSFONCTION CHRONIQUE DU GREFFON Corrélation avec la fonction respiratoire

## Fundoplication After Lung Transplantation Prevents the Allograft Dysfunction Associated With Reflux

Matthew C. Hartwig, MD, Deverick J. Anderson, MD, Mark W. Onaitis, MD, Shekur Reddy, MD, Laurie D. Snyder, MD, Shu S. Lin, MD, PhD, and R. Duane Davis, MD

Division of Thoracic Surgery, Division of Infectious Diseases, and Division of Pulmonary and Critical Care Medicine, Department of Medicine, Duke University Medical Center, Durham, North Carolina

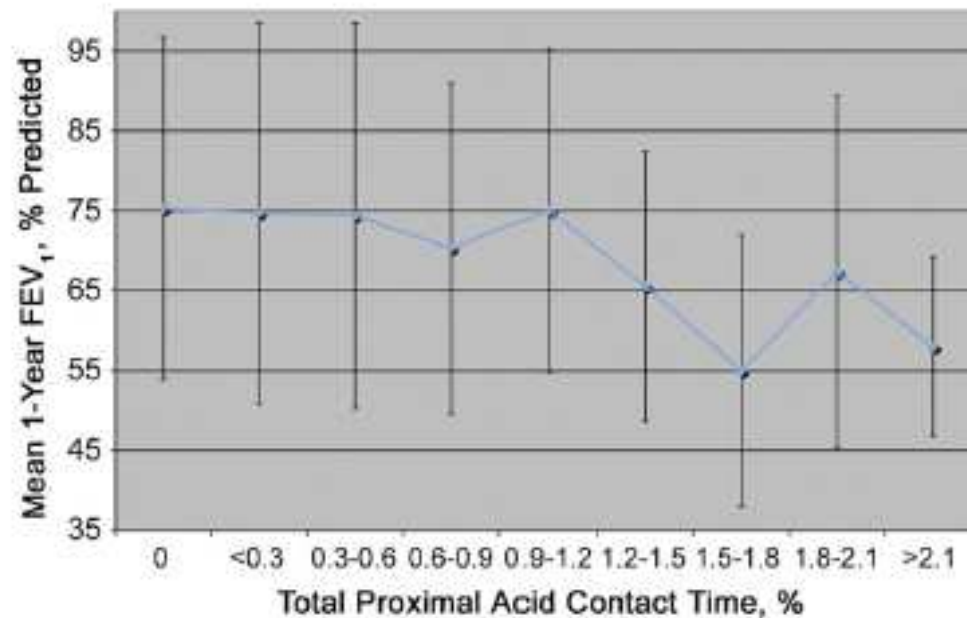


Fig 1. Relationship of total proximal acid contact time to the mean percent predicted 1-year forced expiratory volume in first second of expiration (FEV<sub>1</sub>). Notably, the mean 1-year FEV<sub>1</sub> decreases with total proximal acid contact times greater than 1.2%.

# TRAITEMENT DU RGO

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## TRAITEMENT MEDICAL:

- IPP ....reflux non acides, aucun effet sur marqueurs bio
- AZITHROMYCINE : amélioration de la fonction via le RGO ? *(Murphy, Thoax, 2007)*
- PROKINETIQUES (rôle aggravant de la gastroparésie)
  - Domperidone 12 greffés RGO+Gastroparésie
  - Amélioration des symptômes à 6 mois
  - Amélioration objective de la gastroparésie (6 patients)
  - Pas d'effets secondaires
  - Effets à plus long terme sur dysfonction du greffon ?

Domperidone for delayed gastric emptying  
in lung transplant recipients with and without  
gastroesophageal reflux

Anne O. Lidor, MD, MPH,  
Christopher R. Ensor,  
PharmD, Amy J. Sheer, MPH,  
Jonathan B. Orens, MD,  
John O. Clarke, MD,  
John F. McDyer, MD

Progress in Transplantation, Vol 24, No. 1, March 2014

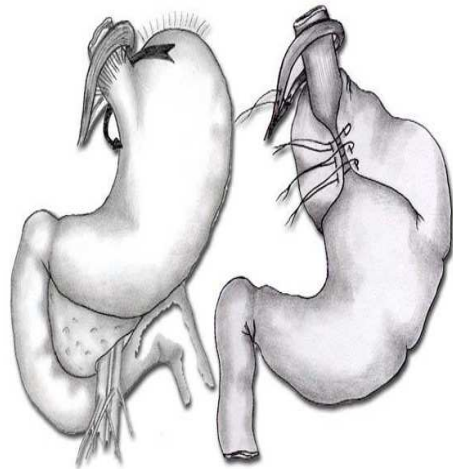


# TRAITEMENT DU RGO

## CHIRURGIE



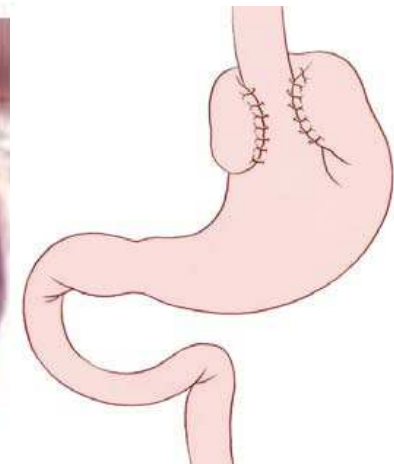
Figure 3. Fundoplicature totale circulaire



NISSEN



Figure 4. Fundoplicature partielle postérieure



TOUPET

# TRAITEMENT CHIRURGICAL DU RGO

## EFFETS SECONDAIRES ET COMPLICATIONS

- similaires autres populations
- cas particulier du BMI
- 1 seule série (28 pts) : durée séjour plus longue et réadmissions <J30 plus fréquentes (Burton, JHLT 2007)

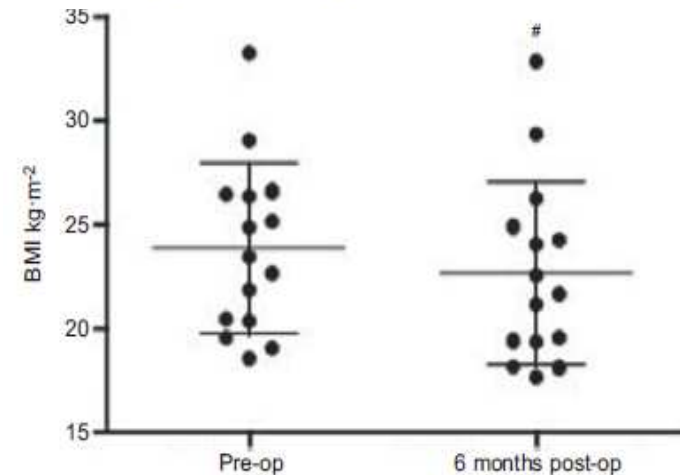
### Gastroesophageal Reflux Disease Treatment: Side Effects and Complications of Fundoplication

**Table 1.** Prevalence of Medical and Surgical Complications of Antireflux Surgery

|   |            |
|---|------------|
| Mortality (<30 days)                                | 1% or less |
| Perioperative and immediate postoperative morbidity | 8%–17%     |
| Open conversion rate                                | 0%–24%     |
| Early postoperative complications                   |            |
| Bowel perforation                                   | 0%–4%      |
| Bleeding and splenic injury                         | <1%        |
| Pneumothorax  | 0%–10%     |
| Severe postoperative nausea and vomiting            | 2%–5%      |
| Late postoperative complications                    |            |
| Gas-bloat syndrome                                  | 1%–85%     |
| Dysphagia   |            |
| Early   | 10%–50%    |
| Late  | 3%–24%     |
| Diarrhea  | 18%–33%    |
| Recurrent heartburn                                 | 10%–62%    |
| Need for revisional surgery                         |            |
| Laparoscopic Nissen fundoplication                  | 0%–15%     |
| Laparoscopic Toupet fundoplication                  | 4%–10%     |

### Anti-reflux surgery in lung transplant recipients: outcomes and effects on quality of life

A.G.N. Robertson\*, A. Krishnan\*, C. Ward<sup>#</sup>, J.P. Pearson<sup>†</sup>, T. Small<sup>#</sup>, P.A. Corris<sup>#</sup>, J.H. Dark<sup>#,†</sup>, D. Karat\*, J. Shenfine\* and S.M. Griffin\*



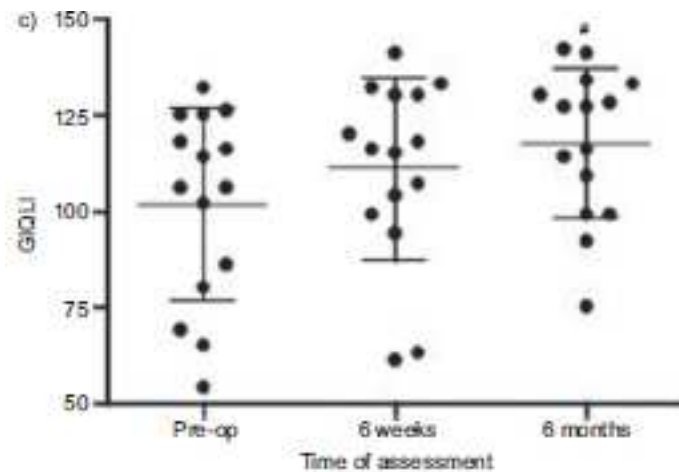
**FIGURE 2.** Body mass index (BMI) score pre-operatively (pre-op) and at 6 months post-fundoplication (post-op). Horizontal lines represent the mean and error bars represent the standard deviation. #: p=0.001 compared with pre-op.

# TRAITEMENT CHIRURGICAL DU RGO

## ■ EFFETS SUR LA QUALITE DE VIE

Anti-reflux surgery in lung transplant recipients: outcomes and effects on quality of life

A.G.N. Robertson<sup>\*</sup>, A. Krishnan<sup>\*</sup>, C. Ward<sup>®</sup>, J.P. Pearson<sup>†</sup>, T. Small<sup>®</sup>, P.A. Corris<sup>®</sup>, J.H. Dark<sup>®\*</sup>, D. Karat<sup>\*</sup>, J. Shenfine<sup>\*</sup> and S.M. Griffin<sup>\*</sup>



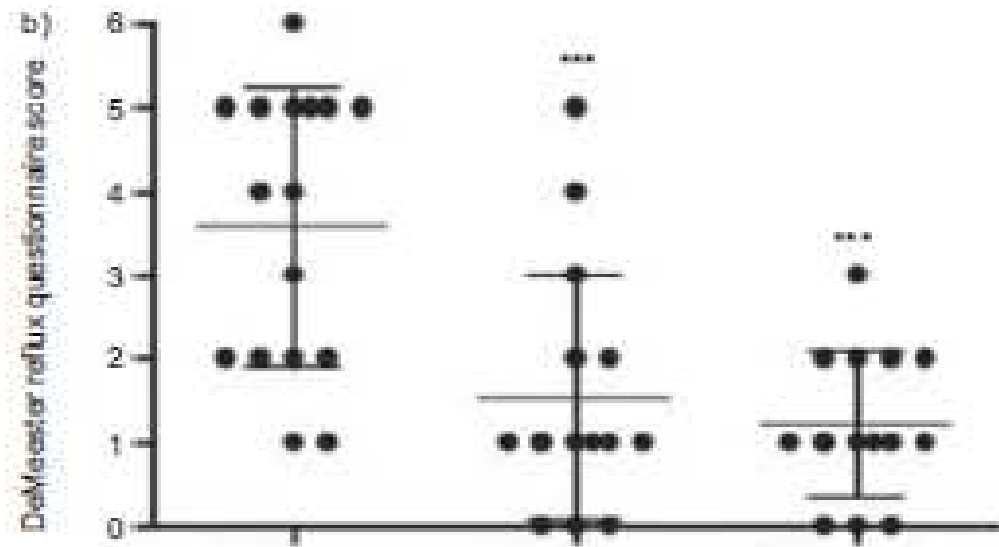
**FIGURE 1.** a) Reflux Symptom Index (RSI) scores, b) DeMeester Reflux Questionnaire Score and c) Gastro-intestinal Quality of Life Index (GIQLI) score over the first 6 months post-transplantation. The dotted line indicates a score of 115, the cut-off for a normal/abnormal score. Horizontal lines represent the mean and error bars represent the standard deviation. Pre-op: pre-operative. \*\*\*:  $p < 0.001$  compared to pre-op; <sup>®</sup>:  $p = 0.006$  compared to pre-op.

# TRAITEMENT CHIRURGICAL DU RGO

EFFET SUR.....LE RGO ?

Anti-reflux surgery in lung transplant recipients: outcomes and effects on quality of life

A.G.N. Robertson<sup>\*</sup>, A. Krishnan<sup>\*</sup>, C. Ward<sup>®</sup>, J.P. Pearson<sup>†</sup>, T. Small<sup>®</sup>, P.A. Corris<sup>®</sup>, J.H. Dark<sup>®\*</sup>, D. Karat<sup>\*</sup>, J. Shenfine<sup>\*</sup> and S.M. Griffin<sup>\*</sup>



# TRAITEMENT CHIRURGICAL DU RGO

## EFFET SUR LES INFECTIONS ET LE REJET AIGU

### Antireflux Surgery Preserves Lung Function in Patients With Gastroesophageal Reflux Disease and End-stage Lung Disease Before and After Lung Transplantation

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**Table 3. Pulmonary Function Test Results Before and After ARS in Patients With ESLD**

| Variable  | Before ARS        | After ARS         | P Value           |
|---|-------------------|-------------------|-------------------|
| <b>Post-LTx patients (n= 22)</b>                |                   |                   |                   |
| FEV <sub>1</sub> , % predicted <sup>a</sup>     | 81.5 (61.3-92.8)  | 92.5 (65.8-102.5) | <.01 <sup>b</sup> |
| FVC, % predicted <sup>a</sup>                   | 77.5 (63.5-87.3)  | 81.5 (70.5-94.5)  | .04 <sup>b</sup>  |
| FEF <sub>25-75</sub> , % predicted <sup>a</sup> | 53.5 (31.3-100.3) | 58 (44.5-118)     | .03 <sup>b</sup>  |
| Pneumonia, No./total No. (%)                    | 7/24 (29)         | 1/24 (4)          | .08 <sup>b</sup>  |
| Rejection, No./total No. (%)                    | 8/24 (33)         | 1/24 (4)          | .08 <sup>b</sup>  |
| <b>Pre-LTx patients (n= 13)</b>                 |                   |                   |                   |
| FEV <sub>1</sub> , % predicted <sup>a</sup>     | 55 (44.3-76.3)    | 68 (49-82)        | .02 <sup>b</sup>  |
| FVC, % predicted <sup>a</sup>                   | 61 (50-71)        | 71 (52-75)        | <.01 <sup>b</sup> |
| FEF <sub>25-75</sub> , % predicted <sup>a</sup> | 49.5 (19.3-78.8)  | 70 (23-81)        | .26               |
| Pneumonia, No./total No. (%)                    | 6/16 (38)         | 3/16 (19)         | .09               |

# TRAITEMENT CHIRURGICAL EFFETS SUR LA FONCTION RESPIRATOIRE

## Gastroesophageal Reflux as a Reversible Cause of Allograft Dysfunction After Lung Transplantation\*

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Victor F. Tapson, MD, FCCP; and  
Robert D. Davis, MD, FCCP

Improved lung allograft function after fundoplication in patients with gastroesophageal reflux disease undergoing lung transplantation  
R. Duane Davis, Jr, Christine L. Lau, Steve Eubanks, Robert H. Messier, Denis Hadjiliadis, Mark P. Steele and Scott M. Palmer  
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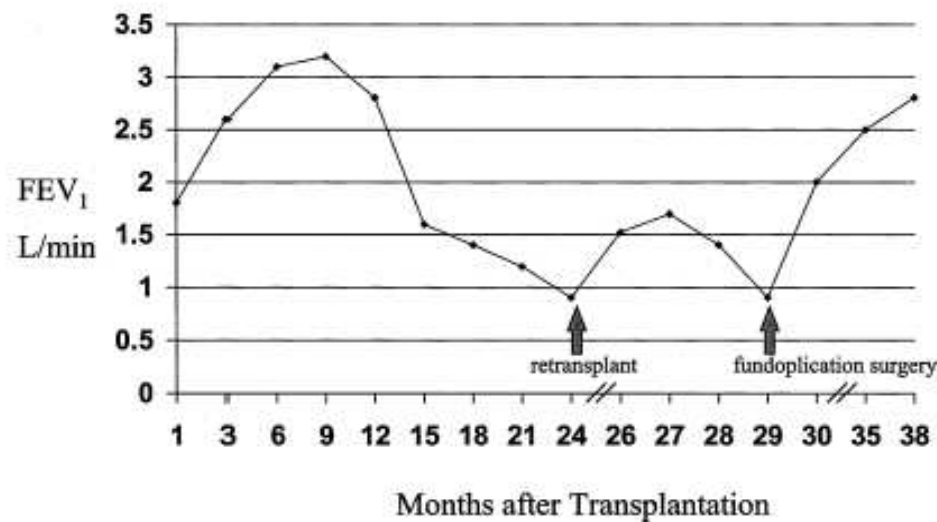
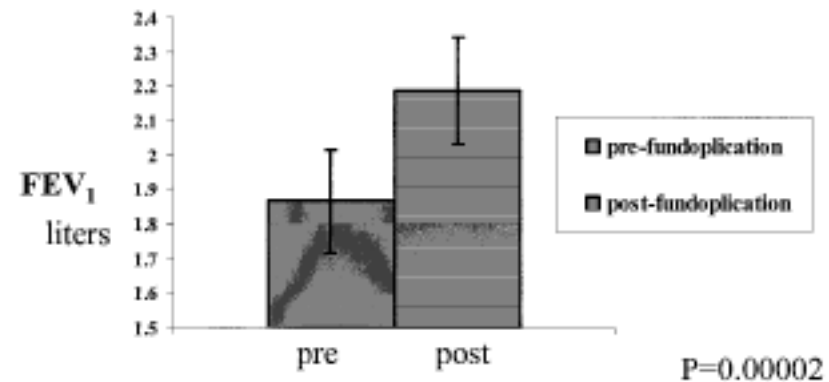


FIGURE 1. Lung function before and after fundoplication.

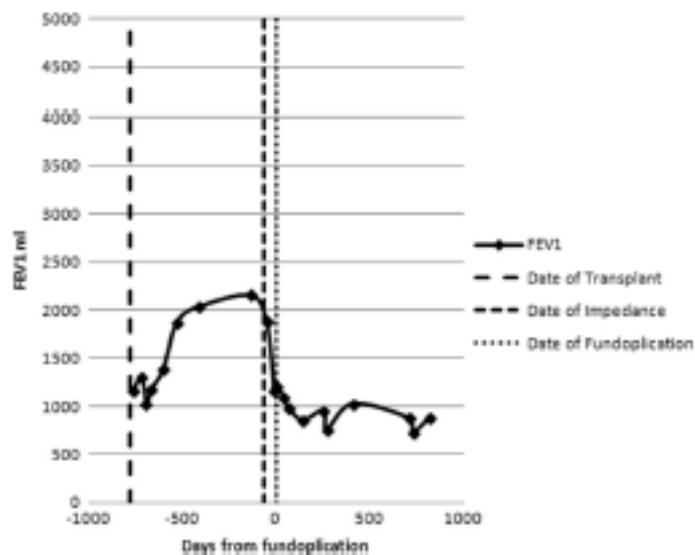




# TRAITEMENT CHIRURGICAL EFFETS SUR LA FONCTION RESPIRATOIRE

Anti-reflux surgery for lung transplant recipients in the presence of impedance-detected duodenogastroesophageal reflux and bronchiolitis obliterans syndrome: A study of efficacy and safety

Nima Abbassi-Ghadi, MRCS,<sup>2</sup> Sacheen Kumar, MRCS,<sup>2</sup> Billy Cheung, MBBS,<sup>2</sup> Anne McDermott, MSc,<sup>2</sup> Alison Knaggs, FRCA,<sup>2</sup> Emmanouil Zacharakis, FRCS,<sup>2</sup> Krishna Moorthy, FRCS,<sup>2</sup> Martin Carby, FRCP,<sup>2</sup> and George B. Hanna, FRCS,<sup>2</sup>



Medium-term outcome of fundoplication after lung transplantation

P. R. Burton,<sup>1</sup> B. Button,<sup>2</sup> W. Brown,<sup>1</sup> M. Lee,<sup>1</sup> S. Roberts,<sup>3</sup> S. Hassen,<sup>1</sup> M. Bailey,<sup>2</sup> A. Smith,<sup>1</sup> G. Snell<sup>2</sup>

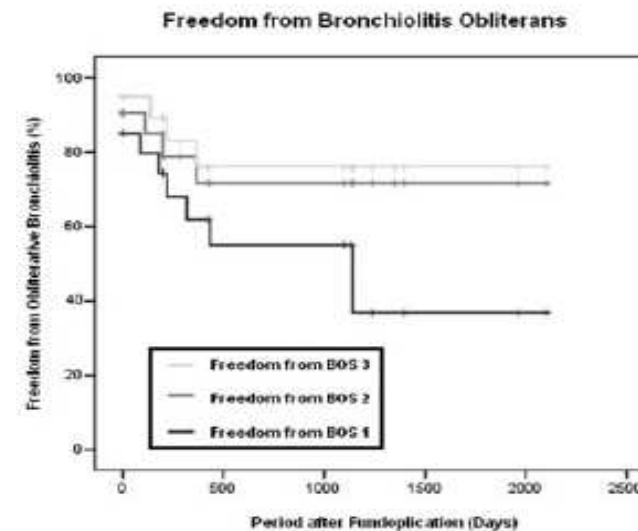


Fig. 1 Kaplan-Meier curve demonstrating freedom from the BOS stages 1, 2, and 3. Notably, there was a relatively rapid progression to BOS 1 following fundoplication. There did, however, appear to be stabilization of lung function, without further progression to BOS stage 2 or 3. BOS, bronchiolitis obliterans syndrome.

# TRAITEMENT CHIRURGICAL EFFETS SUR LA SURVIE

Improved lung allograft function after fundoplication in patients with gastroesophageal reflux disease undergoing lung transplantation  
 R. Duane Davis, Jr, Christine L. Lau, Steve Eubanks, Robert H. Messier, Denis Hadjiliadis, Mark P. Steele and Scott M. Palmer  
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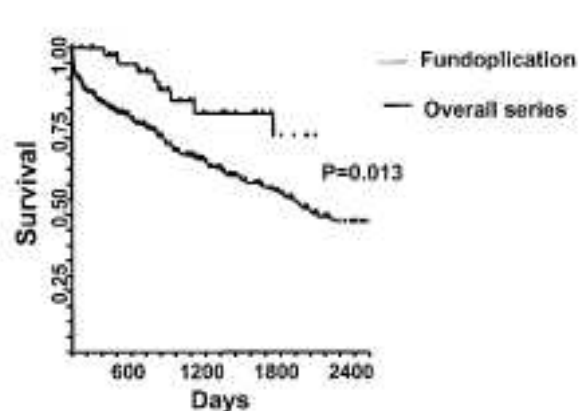


Figure 3. Effect of fundoplication on survival. Kaplan-Meier actuarial survival curves for patients evaluated for reflux by 24-hour pH studies, comparing the group with documented reflux versus the group with no reflux. A significant survival advantage was seen in the patients with normal pH studies.

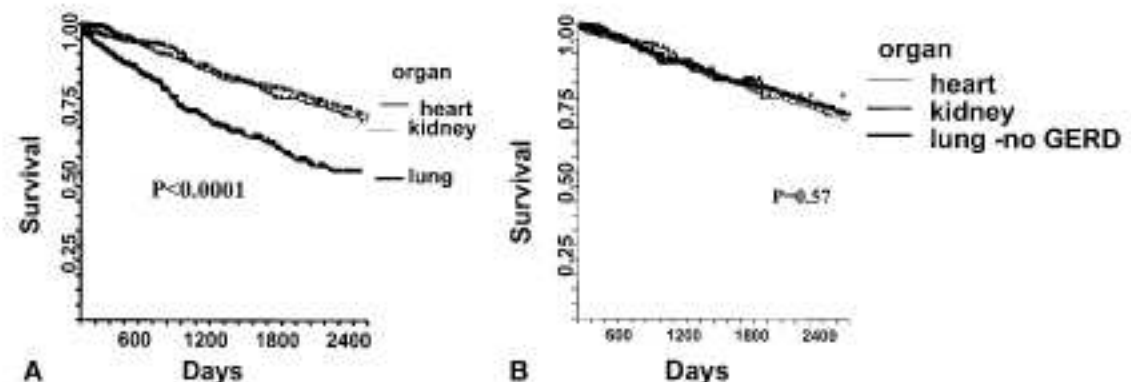


Figure 4. Kaplan-Meier actuarial allograft survival curves: allograft survival of at least 6 months to adjust for differences between organs on the basis of early technical variables. A, Overall allograft survival (6-month survivors) for patients undergoing kidney, heart, and lung transplantation, documenting a worse outcome in lung transplant recipients. B, Overall allograft survival in lung transplant recipients who did not have reflux or whose reflux was corrected by means of fundoplication compared with recipients of kidney or heart transplants. Allograft survival among the 3 groups was almost identical.

# QUAND OPERER ? AVANT OU APRES LA GREFFE ?

## Both Pre-Transplant and Early Post-Transplant Antireflux Surgery Prevent Development of Early Allograft Injury After Lung Transplantation

Wai-Kit Lo<sup>1,2,3</sup> · Hilary J. Goldberg<sup>4,5</sup> · Jon Wee<sup>3,6</sup> · P. Marco Hatzellia<sup>4,6</sup> ·  
Walter W. Chu<sup>1,2</sup>

**Table 3** Kaplan-Meier log-rank *p* values demonstrating significant association of late post-transplant surgical fundoplication and increased early allograft injury compared to early post-transplant and pre-transplant ARS

| Fundoplication timing and early allograft injury | Kaplan-Meier log-rank <i>p</i> value |
|--|--------------------------------------|
| Late post-transplant vs pre-transplant           | 0.007                                |
| Late post-transplant vs early post-transplant    | 0.05                                 |
| Early post-transplant vs pre-transplant          | 0.27                                 |

# QUAND OPERER ? TOT APRES LA GREFFE ?

## Early Fundoplication Prevents Chronic Allograft Dysfunction in Patients With Gastroesophageal Reflux Disease

Edward Cantu III, MD, James Z. Appel III, MD, Matthew G. Hartwig, MD, Hiwot Woreta, BA, Cindy Green, PhD, Robert Messier, MD, PhD, Scott M. Palmer, MD, MPH, and R. Duane Davis, Jr, MD

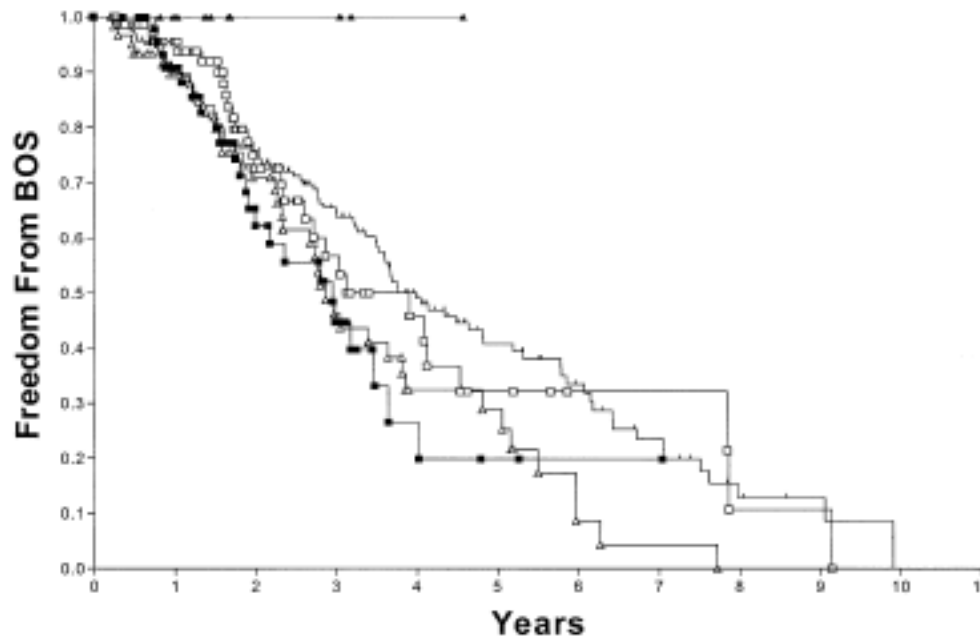


Fig 3. Freedom from BOS in pH confirmed subgroups. ■ - normal pH study; □ - reflux, no surgery; ▲ - reflux, early surgery; △ - reflux, late surgery; ○ - unknown. (BOS - bronchiolitis obliterans syndrome.)

| Patients at risk at year | 0   | 1   | 2   | 3  | 4  | 5  | 6  | 7  | 8  | 9 | 10 |
|--------------------------|-----|-----|-----|----|----|----|----|----|----|---|----|
| Normal pH Study          | 47  | 44  | 33  | 20 | 10 | 4  | 2  | 1  | 1  | 0 | 0  |
| Reflux no Surgery        | 79  | 68  | 48  | 26 | 15 | 10 | 5  | 3  | 3  | 1 | 1  |
| Reflux Early Surgery     | 14  | 12  | 8   | 5  | 3  | 1  | 0  | 0  | 0  | 0 | 0  |
| Reflux Late Surgery      | 62  | 57  | 44  | 30 | 17 | 10 | 8  | 2  | 1  | 0 | 0  |
| Unknown                  | 180 | 158 | 131 | 97 | 72 | 44 | 29 | 20 | 12 | 4 | 3  |

# QUAND OPERER ? INTERET SI BOS INSTALLEE ?

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- 43 procédures chir
- 26 BOS
- 13=50% BOS 1
- 7=27% BOS 2 - 43% amélioration
- 6=23% BOS 3 – 17% amélioration

## ANTI-REFLUX SURGERY FOR GASTROESOPHAGEAL REFLUX DISEASE AFTER LUNG TRANSPLANTATION : BENEFIT FOR LUNG FUNCTION, ACUTE REJECTIONS AND RESPIRATORY INFECTIONS

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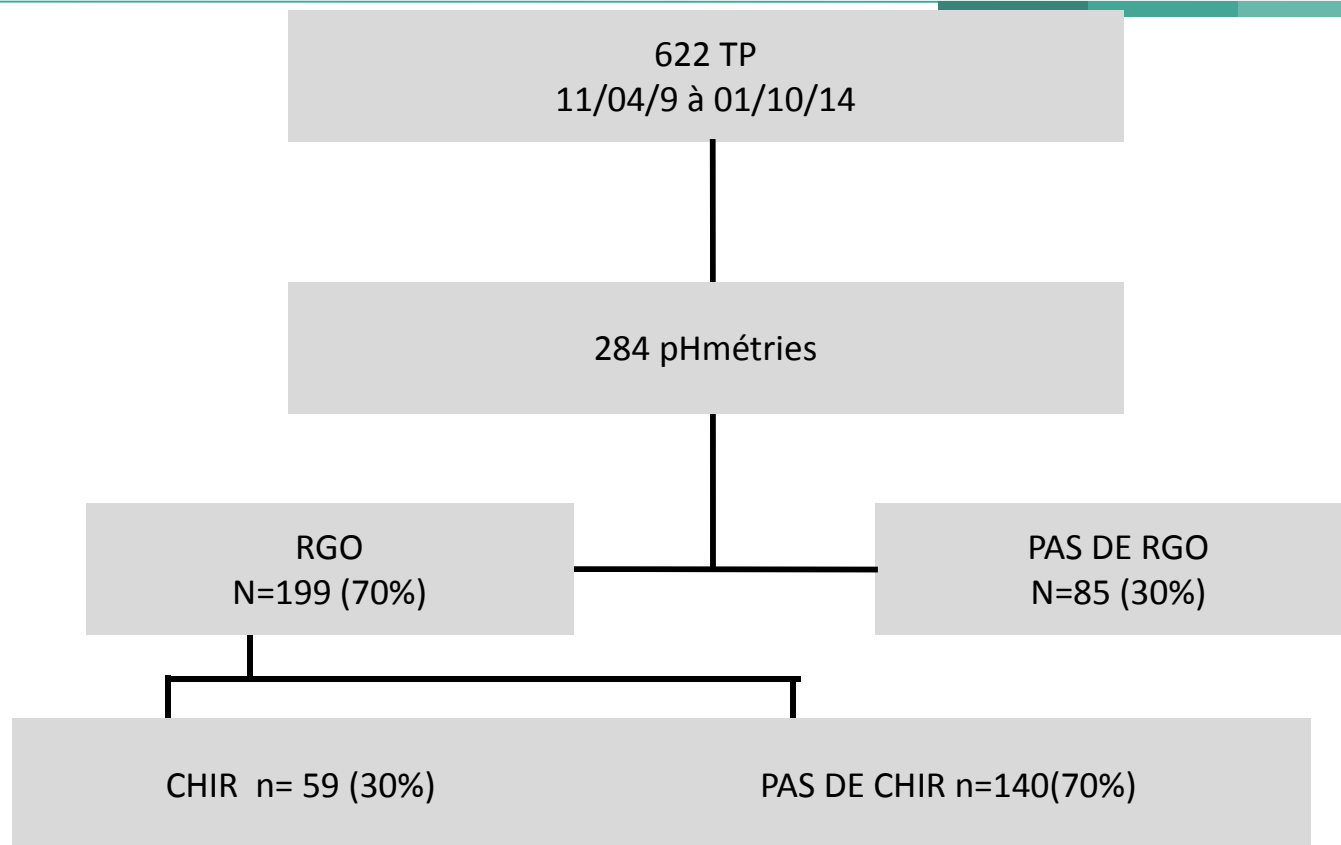
Am Hamid (MD), A Roux (MD PhD), O Boche (MD), J Leport (MD), M Stern (MD), S De Miranda (MD), D Grenet (MD), L Azuar-Beaumont (MD), B Douvry (MD), D Usturoi (MD), E Cuquemelle (MD), E Sage (MD PhD), A Chapelier (MD PhD), C Picard (MD)

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- Etude monocentrique retrospective
- 622 TP entre 1991 et 2014
- 284 pHmétries
- RGO si score de de Meester >14.7.
- **Indication chirurgicale: RGO (symptomatique ou non) et déclin du VEMS eT/ou infections pulmonaires récurrentes**
  
- Evaluation:
  - 1- Evolution de la fonction respiratoire (VEMS et CVF) 6 mois après la chirurgie du reflux :
    - amélioration (>110% fonction pré-op)
    - stabilisation (91-109%)
    - deterioration (<90%).
  - 2- Incidence du rejet aigue (RA) prouvé ou fonctionnel et des infections respiratoires 1 an après chirurgie vs 1an avant.

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- Result are shown as median [IQR25-75] or mean±SD.
  - Data were compared with non parametric testing (Wilcoxon, Man Whitney) and Khi square test when appropriate.





- RGO chez 199/284 patients (70%)
- Phmétrie faite à 4.5 mois [3.1; 9.6] de la greffe
- 59 patients (30%) opérés, 20 [13; 43] mois après la greffe

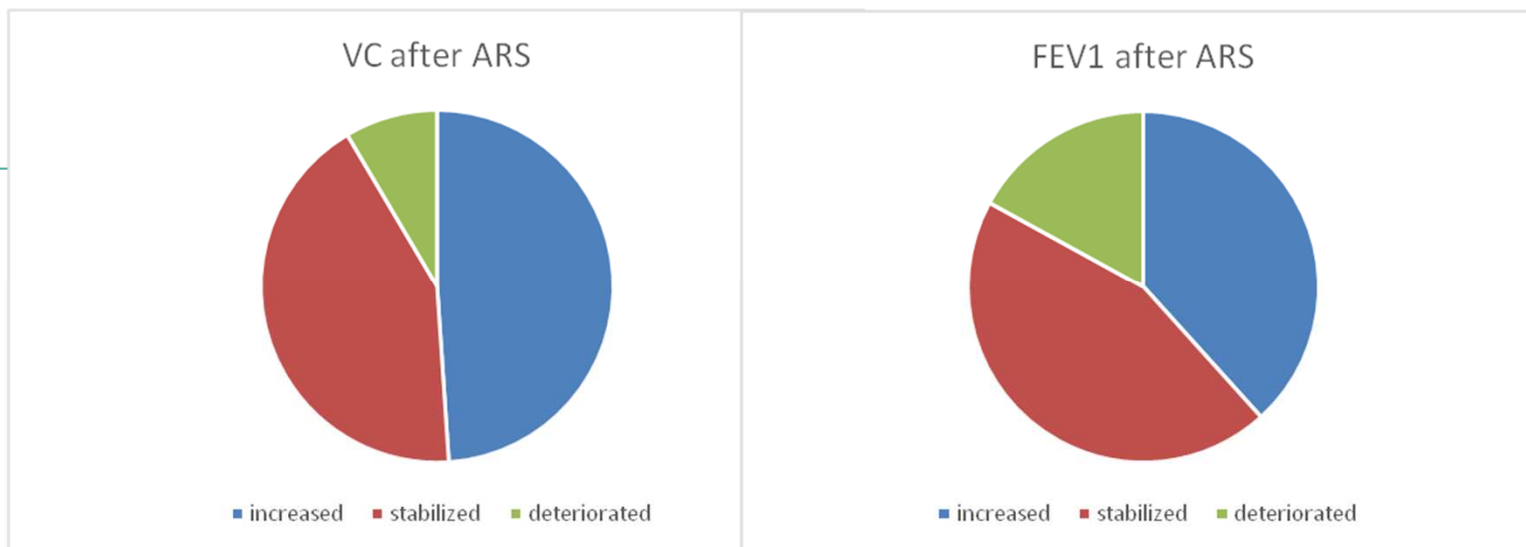
|                      | Total<br>(n=284) | Pas de RGO<br>(n=85) | RGO<br>(n=199) |                  |
|----------------------|------------------|----------------------|----------------|------------------|
| <b>Age (années)</b>  | 35 [26 ; 51]     | 46.6 [34 ; 53]       | 31.6 [25 ; 46] | <b>&lt;0.001</b> |
| <b>Sex ratio H/F</b> | 144/140          | 45/40                | 99/100         | 0.5              |

### Pathologie

|                      |     |    |     |                  |
|----------------------|-----|----|-----|------------------|
| <b>Mucoviscidose</b> | 166 | 32 | 134 |                  |
| <b>PID</b>           | 35  | 15 | 20  |                  |
| <b>BPCO</b>          | 56  | 24 | 32  | <b>&lt;0.001</b> |
| <b>HTAP</b>          | 2   | 1  | 1   |                  |
| <b>Re-TP</b>         | 1   | 0  | 1   |                  |
| <b>Autres</b>        | 24  | 13 | 11  |                  |

|                                   |                  |                 |                 |                  |
|-----------------------------------|------------------|-----------------|-----------------|------------------|
| <b>Transplantation</b>            |                  |                 |                 |                  |
| <b>Bilatérale</b>                 | 262              | 75              | 187             | 0.2              |
| <b>Unilatérale</b>                | 21               | 10              | 11              |                  |
| <b>Cardiopulmonaire</b>           | 1                | 0               | 1               |                  |
| <b>Délai pHmétrie (mois)</b>      | 4.6 [3.1 ; 9.6]  | 4.6 [3.1 ; 9.4] | 4.5 [3.1 ; 9.6] | 0.7              |
| <b>De Meester</b>                 | 21 [10 ; 40]     | 7.4 [4 ; 11]    | 36 [25 ; 56]    | <b>&lt;0.001</b> |
| <b>Nombre de reflux</b>           | 93 [48 ; 153]    | 40 [20 ; 57]    | 131 [85 ; 185]  | <b>&lt;0.001</b> |
| <b>Meilleure CVF (ml)</b>         | 3.3 [2.6 ; 3.9]  | 3.3 [2.6 ; 3.9] | 3.3 [2.6 ; 3.9] | 0.75             |
| <b>Meilleur VEMS (ml)</b>         | 2.65 [2.1 ; 3.2] | 2.7 [2 ; 3.3]   | 2.7 [2.2 ; 3.2] | 0.56             |
| <b>Délai meilleur VEMS (mois)</b> | 27.3 [12 ; 61]   | 23 [9 ; 42]     | 31 [14 ; 67]    | <b>0.03</b>      |





➤ VEMS à 6 mois:

- Amélioration 37%
- Stabilisation 44%
- Détérioration 17%

➤ BOS : diminution de 51 (86.4%) à 28 (47.4%) patients (n=59, p<0,0001).

|                                 | Before ARS   | After ARS    | P            |
|---------------------------------|--------------|--------------|--------------|
| <b>Rejet aigu épisodes/an</b>   | 1.04 +/-0.98 | 0.42 +/-0.99 | <b>0.001</b> |
| <b>Infections episodes/an</b>   | 0.75+/-1.04  | 0.33+/-0.6   | <b>0.007</b> |
| <b>Jours sous antibiotiques</b> | 8.2+/-12.3   | 2.5+/- 6     | <b>0.002</b> |

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## Complications de la chirurgie :

- Mortalité J30= 0
- Baisse significative du BMI:20.65+/-4.2vs 21.58+/-4.3 (p<0.001)

## Conclusion

- Forte incidence de RGO (70%) en particulier chez les patients greffés pour mucoviscidose (81% vs 55% p<0.001).
- Chirurgie associée à:
  - Diminution des rejets aigus et des infections respiratoires
  - Une stabilisation ou amélioration de la fonction respiratoire

# EN CONCLUSION

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- RGO fréquent avant et après TP, aggravé par la gastroparésie.
- Il influence le pronostic via la dysfonction chronique du greffon (mécanisme?).
- Le traitement chirurgical est globalement bien toléré.
- Il est efficace sur les épisodes de rejet aigu et les épisodes infectieux respiratoires (peu rapportés).
- Il est efficace sur la dysfonction chronique du greffon d'autant plus qu'il est réalisé précocement mais peut améliorer certains patients avec BOS évoluée.
- Il n'y a probablement pas d'intérêt à opérer les patients avant la greffe (en tous cas dans pas dans le but d'améliorer le pronostic de celle-ci).

MERCI DE VOTRE ATTENTION

