CHU UCL NAMUR

Quel avenir pour la chirurgie thoracique et de la transplantation pulmonaire

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Service de Chirurgie Cardio-Vasculaire, Thoracique & Transplantation Pulmonaire

« La minimal invasive c'est nouveau et c'est l'avenir de la chirurgie thoracique··· »

VATS: une nouveauté?

Del Med J. 1992 Apr;64(4):267-72.
Video-assisted thoracic surgery: our first 20 cases.
Davies AL, Panasuk DB.

Video-assisted thoracic surgery has been performed in 20 patients at the Medical Center of Delaware. Operations included seven pulmonary wedge resections, one mediastinal procedure, and 12 pleural procedures. In all cases, a definitive diagnosis was made or the lesion was removed. One postoperative atypical pneumonia occurred. One patient whose wedge resection proved to be squamous cell carcinoma on frozen section underwent a formal thoracotomy and lobectomy. Estimated savings in the eight patients who formerly would have undergone a thoracotomy incision is estimated at $30,000 for room cost alone. We foresee a markedly expanded role for this technique in major pulmonary resections, esophageal procedures, and cardiac surgery in the near future

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Il y a...
25 ans !

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Chest Surg Clin N Am. 1994 Feb;4(1):185-94.
Thymoma. The use of minimally invasive resection techniques.
Kaiser LR.

Surgery remains the cornerstone of therapy for thymoma whether the lesion is encapsulated or invasive. Video-assisted thoracic surgical techniques may be applicable in a number of patients with encapsulated thymoma for definitive therapy, especially when combined with a transcervical approach to achieve total thymectomy. Initial experience with a minimally invasive approach for resection of thymomas is described. The development of new instrumentation facilitates the performance of these procedures.

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J Thorac Cardiovasc Surg. 1992 Dec;104(6):1679-85; discussion 1685-7.
Video-assisted thoracic surgical resection of malignant lung tumors.
Lewis RJ, Caccavale RJ, Sisler GE, Mackenzie JW.

Forty patients with malignant pulmonary disease underwent evaluation, staging, and a biopsy or resection by means of video-assisted thoracic surgery. There were 20 men and 20 women whose ages ranged from 27 to 82 years. Eight patients had a wedge resection for metastatic carcinoma, three a lobectomy for primary carcinoma, six exploration of the thorax, five biopsy of the aortopulmonary window, and eighteen a sublobar resection for primary carcinoma of the lung. There was no mortality. Three patients had air leaks that lasted an average of 8 days. Video-assisted thoracic surgery seems to be useful for more precise staging of carcinoma of the lung, and, in some patients, resectional operations can be performed.

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Thorax. 1993 Sep;48(9):921-4.
Thoracoscopy assisted pulmonary lobectomy.
Walker WS[1], Carnochan FM, Tin M.

This report describes a preliminary experience with six patients undergoing video imaged thoracoscopic pulmonary lobectomy.
Three left upper lobectomies, and one each of right upper, right lower and left lower lobectomy were undertaken. The resections were performed as orthodox dissectional lobectomy procedures but were carried out under videothoracoscopic imaging with instruments introduced through two stab incisions. The entire resected lobe was delivered through a 7 cm submammary intercostal incision.
There were no operative deaths or complications attributable to the technique. In three other patients conversion to an open thoracotomy was required because of bleeding (two cases) or obscure anatomy (one case). Post-operative pain in those undergoing thoracoscopic resection was less than that encountered with standard thoracotomy and early clinic review showed the patients to be pain free with excellent shoulder movement.
Major pulmonary resection according to standard cancer practices is feasible with videothoracoscopic techniques. This approach is likely to offer considerable functional benefit to patients. Specimen delivery through the submammary incision imposes a 5 cm primary lesion size limitation. Detailed mediastinal assessment is necessary to exclude N2 status before undertaking thoracoscopic surgery.

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Il y a...
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Robotic lobectomy: une nouveauté?

J Thorac Cardiovasc Surg. 2003 Jul;126(1):292-3.
Robot-assisted lobectomy.
Ashton RC Jr, Connery CP, Swistel DG, DeRose JJ Jr.

Video-assisted thoracoscopic surgery (VATS) for ana- tomic pulmonary resections continues to develop since its application in the early 1990s.1-5 Using the da Vinci Surgical System (Intuitive Surgical, Inc., Mountain View, Calif), we performed an anatomic right lower lobectomy for stage Ia non–small cell lung cancer.

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Il y a...
14 ans !

La minimal invasive n'est pas une démarche nouvelle…

Questions…

- Y-a-t-il un intérêt autre que la performance manuelle à faire de la chirurgie moins invasive?
- Quelles sont les répercussions sur la société?
- Comment la démarche peut elle être efficiente?

Fast-Track Chirurgie

- *Récupération rapide des patients après chirurgie*

  = *Réhabilitation précoce*
  = *Fast-track-surgery*
  = *Enhanced recovery after surgery*

- Vise la reprise d'une autonomie active et complète du patient, le plus rapidement possible après sa chirurgie.
- C'est une médecine fondée sur les faits, validée par des publications scientifiques.

Fast-Track Chirurgie

- Méta-analyse d'essais randomisés contrôlés pour la chirurgie colo-rectale…
  - ↘ 30 % la durée de séjour,
  - ↘ 50 % les complications péri-opératoires.
- Chaque étape, chaque soin y est optimisé et organisé autour de l'opéré.
- Elle a été initialement développée par le Pr H Kehlet au Danemark en 1995 pour la chirurgie colique.
- La récupération rapide après chirurgie se combine idéalement avec les techniques chirurgicales mini-invasives telles que la cœlioscopie.

Ca fait 20 ans qu'on fait ça…

- Kehlet a eu l'intuition que de nombreuses étapes de la prise en charge classique en chirurgie reposaient plus sur le poids des habitudes et sur les traditions que sur une analyse systématique des bénéfices apportés aux patients.
- Il a donc analysé chacune de ces étapes et de rechercher quel était le niveau de preuve scientifiquement publié justifiant la présence ou l'absence d'une étape donnée dans les protocoles utilisés.
- Il a pu prouver que de nombreux actes réalisés étaient non seulement inutiles mais délétères pour la plupart des patients opérés du côlon.

Un patient acteur…

- L'autre pilier de la réflexion de Kehlet est l'association du patient à ses soins.
- Dans le schéma classique, le patient a une posture passive. Les décisions sont prises par les praticiens; le patient est informé.
- Dans la récupération rapide après chirurgie, le patient reçoit une information très approfondie sur les différents temps du traitement. La patient est inscrit dans un partenariat.
- Le patient est donc réellement un moteur de sa propre réhabilitation et peut influencer les décisions en fonction de ses propres sensations et du retour d'information qu'il donne aux professionnels de santé.

Tous pour un malade…
Un malade pour tous!

- Pluridisciplinarité de la prise en charge…
- Au delà du binôme habituel chirurgie-anesthésiste, il associe le personnel infirmier, les kinésithérapeutes, les diététiciens, les assistants sociaux, les coordinateurs de soins, etc…
- Chacun va apporter son expertise de façon coordonnée pour atteindre les objectifs fixés et communiquer pour ajuster la prise en charge si besoin.
- Cette pluridisciplinarité se trouve formalisée sous forme de protocoles/parcourts de soins rigoureux dont l'exécution est régulièrement évaluée.

Des principes…

- Réduire le stress physique et psychique lié à l'intervention.
- Prévenir les dysfonctions organiques secondaires de la chirurgie
  - Nausées,
  - Somnolence,
  - Vomissements,
  - Dyspepsie et iléus paralytique postopératoire,
  - Douleur...

Des principes…

- Combinaison de mesures : jeûne pré-opératoire limité, utilisation de drogue d'anesthésie à courte durée d'action, prévention de l'hypothermie, analgésie multimodale au plus proche de la source, gestion individualisée des apports liquidiens, utilisation limitée de drains, utilisation limité de sondage urinaire, réalimentation précoce, mobilisation rapide…
- C'est l'ensemble de ces mesures et la coordination de l'équipe de prise en charge qui permet au patient de retrouver plus vite son autonomie.

Des principes…

- Le retour à l'autonomie du patient lui permet non seulement de rentrer plus rapidement à la maison, mais aussi de pouvoir mieux gérer ce retour à domicile hors du cocon protecteur de l'hôpital ou de la clinique.
- L'ensemble de l'organisation est formalisé sous forme de procédures et protocoles standardisés. Ils suivent la trajectoire du patient et prennent souvent le nom de itinéraire clinique qui comprend par exemple les documents d'information qui seront remis au patient et les scores qui permettent d'évaluer son état et de décider de sa sortie.

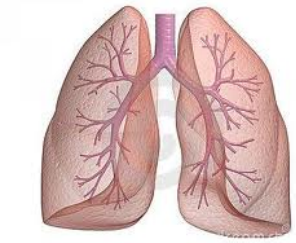
Des retombées importantes…

- Les publications scientifiques montrent que la satisfaction des patients est excellente et que les taux de complications et réadmissions sont identiques (voire meilleurs) qu'avec une prise en charge traditionnelle.
- Le patient retrouve un confort plus rapidement et la durée d'hospitalisation est limitée ainsi les coûts diminuent.
- Dans les pays où elle est largement diffusée, elle réduit le nombre de lits de chirurgie nécessaires pour faire face à la demande de la population du fait de la baisse de la durée moyenne de séjour, sans que les dépenses soient reportées sur la médecine de ville ou les centres de rééducation. Les ressources ainsi libérées peuvent donc être consacrées à d'autres besoins sanitaires.

Des retombées importantes…

- Cette approche est plébiscitée aujourd'hui par le National Health service (NHS) et est devenue la norme en Grande Bretagne.
- Depuis la fin 2011, la récupération rapide après chirurgie pour la prothèse totale de hanche et la prothèse du genou bénéficie ainsi d'une tarification spéciale en Grande Bretagne dans le cadre des "best practice tarifs ».
- Un nombre croissant de centres adopte également la récupération rapide après chirurgie à travers le monde mais elle reste confidentielle en Belgique malgré les preuves de son efficience.

Et la chirurgie thoracique?

Anesthésie & Gestion de la douleur	Diététique	Revalidation
Service social		Soins intensifs
Nursing	Tabacologie	Chirurgie

Démarche(s)…

- Tout doit être systématiquement remis en cause…
- Etablir une liste des étape du processus pour chaque spécialité.
- Pour chaque étape, faire une revue de la littérature exhaustive pour dégager les méthodes qui donnent le moins de dysfonctions organiques secondaires.

  Abandonner les traditions, implémenter des attitudes basées sur l'*evidence based medicine*.
- Etablir des protocoles pour chaque entité impliquée.
- Etablir un parcourt de soins qui articule chaque spécialité avec les autres.
- Etablir un parcourt de « communication » dans l'équipe et avec le patient.

Pour la chirurgie…

La survie est conditionnée par …

- La qualité de la résection : R_0, R_1…
- La qualité du curage ganglionnaire et du staging…

Staging médiastinal pré-op?

EUS/EBUS combinés en première intention

Chest. 2014 Aug;146(2):389-97.
Endosonographic mediastinal lymph node staging of lung cancer.
Liberman M, Sampalis J, Duranceau A, Thiffault V, Hadjeres R, Ferraro P.

It is unclear whether endoscopic mediastinal lymph node (LN) staging techniques are equivalent to surgical mediastinal staging (SMS) techniques in patients with potentially operable non-small cell lung cancer (NSCLC).
A total of 166 patients with confirmed or suspected NSCLC who required SMS based on current guidelines were enrolled in this prospective controlled trial comparing endosonographic mediastinal LN staging with SMS. Each patient served as his or her own control. All patients underwent endobronchial ultrasound (EBUS), endoscopic ultrasound (EUS), and SMS during a single procedure. Results of EBUS, EUS, and combined EBUS/EUS were compared with SMS (gold standard) and in patients with negative LN staging results, with LN sampling at pulmonary resection.

The combined EBUS/EUS procedure can replace surgical mediastinal staging in patients with potentially resectable NSCLC.
Additionally, endosonography leads to improved staging compared with SMS because it allows the biopsy of LNs and metastases unattainable with SMS techniques.

Staging médiastinal pré-op?

Une place pour la médiastinoscopie?

Interact Cardiovasc Thorac Surg. 2013 Nov;17(5):823-8.

Mediastinal staging in daily practice: endosonography, followed by cervical mediastinoscopy. Do we really need both?

Verhagen AF, Schuurbiers OC, Looijen-Salamon MG, van der Heide SM, van Swieten HA, van der Heijden EH.

In patients with lung cancer, endosonography has emerged as a minimally invasive method to obtain cytological proof of mediastinal lymph nodes, suspicious for metastases on imaging. In case of a negative result, it is currently recommended that a cervical mediastinoscopy be performed additionally. However, in daily practice, a second procedure is often regarded superfluous. The goal of our study was to assess the additional value of a cervical mediastinoscopy, after a negative result of endosonography, in routine clinical practice.
In a retrospective cohort study, the records of 147 consecutive patients with an indication for mediastinal lymph node staging and a negative result of endosonography were analysed. As a subsequent procedure, 124 patients underwent a cervical mediastinoscopy and 23 patients were scheduled for an intended curative resection directly. The negative predictive value (NPV) for both diagnostic procedures was determined, as well as the number of patients who needed to undergo a mediastinoscopy to find one false-negative result of endosonography (number needed to treat (NNT)). Clinical data of patients with a false-negative endosonography were analysed.

In patients with a high probability of mediastinal metastases, based on imaging, and negative endosonography, cervical mediastinoscopy should not be omitted, not even when the aspirate seems representative.

Staging médiastinal pré-op?

Quelle technique de médiastinoscopie?

J Thorac Cardiovasc Surg. 2013 Oct;146(4):774-80.
Video-assisted mediastinoscopic lymphadenectomy is associated with better survival than mediastinoscopy in patients with resected non-small cell lung cancer.
Turna A, Demirkaya A, Ozkul S, Oz B, Gurses A, Kaynak K.

We aimed to analyze the accuracy of video-assisted mediastinoscopic lymphadenectomy (VAMLA) as a tool for preoperative staging and the impact of the technique on survival in patients with non-small cell lung cancer (NSCLC) undergoing pulmonary resection.
Between May 2006 and December 2010, 433 patients underwent pulmonary resection for NSCLC, 89 (21%) had VAMLA before resection and 344 (79%) had standard mediastinoscopy. The patients who had negative VAMLA/mediastinoscopy results underwent anatomic pulmonary resection and systematic lymph node dissection.
The median and mean numbers of resected lymph node stations were 5 and 4.9 in the VAMLA group and 4

Video-assisted mediastinoscopic lymphadenectomy was associated with better survival (odds ratio, 1.34; 95% VAMLA was associated with improved survival in NSCLC patients who had resectional surgery.

Staging médiastinal pré-op?

Quelle(s) technique(s)? Quand? Comment?

Eur J Cardiothorac Surg. 2014 May;45(5):787-98. **Revised ESTS guidelines for preoperative mediastinal lymph node staging for non-small-cell lung cancer.**
De Leyn P, Dooms C, Kuzdzal J, Lardinois D, Passlick B, Rami-Porta R, Turna A, Van Schil P, Venuta F, Waller D, Weder W, Zielinski M.

1. In case of computed tomography (CT)-enlarged or positron emission tomography (PET)-positive mediastinal lymph nodes, tissue confirmation is indicated.

    a. Endosonography [endobronchial ultrasonography (EBUS)/esophageal ultrasonography (EUS)] with fine-needle aspiration (FNA) is the first choice (when available), since it is minimally invasive and has a high sensitivity to rule in mediastinal nodal disease.

    b. If negative, surgical staging with nodal dissection or biopsy is indicated. Video-assisted mediastinoscopy is preferred to mediastinoscopy. The combined use of endoscopic staging and surgical staging results in the highest accuracy.

2. When there are no enlarged lymph nodes on CT and when there is no uptake in lymph nodes on PET or PET-CT, direct surgical resection with systematic nodal dissection is indicated for tumours ≤ 3 cm located in the outer third of the lung.

3. In central tumours or N1 nodes, preoperative mediastinal staging is indicated. The choice between endoscopic staging with EBUS/EUS and FNA or video-assisted mediastinoscopy depends on local expertise to adhere to minimal requirements for staging.

4. For tumours >3 cm, preoperative mediastinal staging is advised, mainly in adenocarcinoma with high standardized uptake value.

5. For restaging, invasive techniques providing histological information are advisable. Both endoscopic techniques and surgical procedures are available, but their negative predictive value is lower compared with the results obtained in baseline staging. An integrated strategy using endoscopic staging techniques to prove mediastinal nodal disease and mediastinoscopy to assess nodal response after induction therapy needs further study.

Résection pulmonaire

VATS lobectomy: Technique sûre et efficace?

Zhonghua Yi Xue Za Zhi. 2013 Oct 8;93(37):2972-5.

[A comparative study of complete video-assisted thoracoscopic lobectomy and video-assisted mini-thoracotomy in treatment of lung cancer].

Zhang Y, Li YB, Liu BD, Chen DH, Wang RT, Liu L, Qian K, Zhi XY.

To explore the clinical application value of complete video-assisted thoracoscopic (cVATS) lobectomy in the mini-invasive treatment of lung cancer.
90 patients with non-small cell lung cancer (NSCLC) who had undergone lobectomy were reviewed. According to surgical approach, complete video-assisted thoracoscopic lobectomy group (cVATS, n = 47) and video-assisted mini-thoracotomy group (VAMT, n = 43) were studied. Numbers of dissected lymph nodes, operation duration, volumes of intraoperative bleeding, duration of postoperative catheter drainage, length of postoperative hospital stay, incidence rates of postoperative complications, postoperative pain scores of patients were compared between the two groups retrospectively.

Complete video-assisted thoracoscopic lobectomy is safe and effective surgical strategy for lung cancer patients with advantage of rapid recovery.

Résection pulmonaire

Robotic lobectomy: Technique sûre et efficace?

Ann Surg. 2017 Feb;265(2):431-437.

Long-term Survival Based on the Surgical Approach to Lobectomy For Clinical Stage I Nonsmall Cell Lung Cancer: Comparison of Robotic, Video-assisted Thoracic Surgery, and Thoracotomy Lobectomy.

Yang HX1, Woo KM, Sima CS, Bains MS, Adusumilli PS, Huang J, Finley DJ, Rizk NP, Rusch VW, Jones DR, Park BJ.

To compare the long-term outcomes among robotic, video-assisted thoracic surgery (VATS), and open lobectomy in stage I nonsmall cell lung cancer (NSCLC).

Survival comparisons between robotic, VATS, and open lobectomy in NSCLC have not yet been reported. Some studies have suggested that survival after VATS is superior, for unclear reasons.

Three cohorts (robotic, VATS, and open) of clinical stage I NSCLC patients were matched by propensity score and compared to assess overall survival (OS) and disease-free survival (DFS). Univariate and multivariate analyses were performed to identify factors associated with the outcomes.

Minimally invasive approaches to lobectomy for clinical stage I NSCLC result in similar long-term survival as thoracotomy. Use of VATS and robotics is associated with shorter length of stay, and the robotic approach resulted in greater lymph node assessment.

Résection pulmonaire

VATS, Est-ce efficace d'un point de vue oncologique?

Ann Thorac Surg. 2014 Jul;98(1):197-202.
Thoracoscopic approach to lobectomy for lung cancer does not compromise oncologic efficacy.
Berry MF, D'Amico TA, Onaitis MW, Kelsey CR.

We compared survival between video-assisted thoracoscopic surgery (VATS) and thoracotomy approaches to lobectomy for non-small cell lung cancer.
Overall survival of patients who had lobectomy for any stage non-small cell lung cancer without previous chemotherapy or radiation from 1996 to 2008 was evaluated using the Kaplan-Meier method and multivariate Cox analysis. Propensity scoring was used to assess the impact of selection bias.

The thoracoscopic approach to lobectomy for non-small cell lung cancer does not result in worse long-term survival compared with thoracotomy.

Résection pulmonaire

Y a-t-il une alternative efficace au VATS si conversion?

Eur J Cardiothorac Surg. 2014 Oct;46(4):614-9. doi: 10.1093/ejcts/ezu050. Epub 2014 Feb 26.
The comparison of complication, pain, quality of life and performance after lung resections with thoracoscopy and axillary thoracotomy.
Erus S, Tanju S, Kapdağlı M, Özkan B, Dilege Ş, Toker A.

The aim of this prospective study was to compare the effects of axillary thoracotomy (AT) and video-assisted thoracoscopic surgery (VATS) on acute-phase responses, performance status and quality of life in patients undergoing pulmonary resection.
Fifty-five patients with peripherally located lung lesions were enrolled into this study. Surgery was done by VATS or AT. Forced expiratory volume, smoking habits, complications, Charlson comorbidity index, sex, age, length of incision, length of operation, length of hospital stay, length of drainage, length of air leakage, preoperative and postoperative C-reactive protein (CRP) values, visual analogue scale, quality of life and performance status of the patients were measured and compared.

Axillary thoracotomy is a technique equivalent to VATS in terms of early complications,, performance status and quality of life; VATS provided a shorter postoperative stay.

Résection pulmonaire

VATS vs Mini-thoracotomie d'un point de vue douleur….

Eur J Eur J Cardiothorac Surg. 2014 Nov;46(5):907-12. doi: 10.1093/ejcts/ezu092. Epub 2014 Mar 18.
Postoperative pain control: videothoracoscopic versus conservative mini-thoracotomic approach.
Andreetti C, Menna C, Ibrahim M, Ciccone AM, D'Andrilli A, Venuta F, Rendina EA.

The management of postoperative pain in thoracic surgery is an open issue. The aim of this study was to compare postoperative pain after a videothoracoscopic lobectomy versus a mini-thoracotomy approach. Between April 2011 and January 2013 we enrolled in a prospective, non-randomized study 145 patients undergoing pulmonary lobectomy with lymphadenectomy for Stage I lung cancer. In 75 cases (Group A), surgery was performed through a videothoracoscopic approach. In 70 cases (Group B), surgery was undertaken through a conservative mini-thoracotomy. Pain was assessed by visual analogue scale and lung function by spirometry and six-minute walking test (6MWT) before surgery, at 48 h and 1 month after surgery.

The videothoracoscopic approach in the treatment of Stage I lung cancer reduces postoperative pain, which seems to allow a rapid functional recovery of patients.

Résection pulmonaire

VATS vs thoracotomie: Résultats…

PLoS One. 2013 Dec 31;8(12):e82366.
Thoracoscopic lobectomy versus open lobectomy in stage I non-small cell lung cancer: a meta-analysis.
Cai YX, Fu XN, Xu QZ, Sun W, Zhang N.

The objective of the present meta-analysis was to evaluate the survival, recurrence rate, and complications in patients with stage I non-small cell lung cancer (NSCLC) who received video-assisted thoracoscopic surgery (VATS) or open lobectomy.

Patients with stage I NSCLC undergoing VATS lobectomy had longer survival and fewer complications than those who received open lobectomy.

Résection pulmonaire

VATS vs thoracotomie: Coûts…

Ann Thorac Surg. 2014 Jul;98(1):191-6.
Ninety-day costs of video-assisted thoracic surgery versus open lobectomy for lung cancer.
Farjah F, Backhus LM, Varghese TK, Mulligan MS, Cheng AM, Alfonso-Cristancho R, Flum DR, Wood DE.

Complications after pulmonary resection lead to higher costs of care. Video-assisted thoracoscopic surgery (VATS) for lobectomy is associated with fewer complications, but lower inpatient costs for VATS have not been uniformly demonstrated. Because some complications occur after discharge, we compared 90-day costs of VATS lobectomy versus open lobectomy and explored whether differential health care use after discharge might account for any observed differences in costs.
A cohort study (2007-2011) of patients with lung cancer who had undergone resection was conducted using

VATS lobectomy is associated with lower 90-day costs--a relationship that appears to be mediated by lower rates of PLOS. Although VATS may lead to lower rates of PLOS among patients undergoing lobectomy, observational studies cannot verify this assertion. Strategies that reduce PLOS will likely result in cost-savings that can increase the value of thoracic surgical care.

Résection pulmonaire

VATS/Robotic: L'épargne pulmonaire, ca marche?

J Thorac Oncol. 2017 Jan 20

Comparison of Segmentectomy and Lobectomy in Stage IA Adenocarcinomas.

Zhao ZR1, Situ DR2, Lau RW1, Mok TS3, Chen GG1, Underwood MJ1, Ng CS4

Recent studies have suggested that segmentectomy may be an acceptable alternative treatment to lobectomy for surgical management of smaller lung adenocarcinomas. The objective of this study was to compare survival after lobectomy and segmentectomy among patients with pathological stage IA adenocarcinoma categorized as stage T1b (>0 to ≤20 mm) according to the new eighth edition of the TNM system.

Patients who underwent segmentectomy may have survival outcomes no different than those of some patients who received lobectomy for pathological stage IA adenocarcinomas at least 10 but no larger than 20 mm in size. These results should be further confirmed through prospective randomized trials.

Résection pulmonaire

VATS/Robotic: L'épargne pulmonaire, ca marche?

Eur J Cardiothorac Surg. 2017 Apr 11.

Stage I non-small-cell lung cancer: long-term results of lobectomy versus sublobar resection from the Polish National Lung Cancer Registry†.

Dziedzic R1, Zurek W1, Marjanski T1, Rudzinski P2, Orlowski TM2, Sawicka W3, Marczyk M4, Polanska J4, Rzyman W1.

Anatomical lobar resection and mediastinal lymphadenectomy remain the standard for the treatment of early stage non-small-cell lung cancer (NSCLC) and are preferred over procedures such as segmentectomy or wedge resection. However, there is an ongoing debate concerning the influence of the extent of the resection on overall survival. The aim of this article was to assess the overall survival for different types of resection for Stage I NSCLC.

We performed a retrospective analysis of the results of the surgical treatment of Stage I NSCLC. Between 1 January 2007 and 31 December 2013, the data from 6905 patients who underwent Stage I NSCLC operations were collected in the Polish National Lung Cancer Registry (PNLCR) and overall survival was assessed. A propensity score-matched analysis was used to compare 3 groups of patients, each consisting of 231 patients

Wedge resection was associated with significantly lower 3-year and 5-year survival rates compared to the other methods of resection. There was no significant difference in 3-year or 5-year survival rates between lobectomy and segmentectomy. Segmentectomy, but not wedge resection, could be considered an alternative to lobectomy in the treatment of patients with Stage I NSCLC.

Résection pulmonaire

VATS vs robotic: Coûts… Effet du volume opératoire.

Chest. 2017 Feb;151(2):329-339.

Hospital Volume and Outcomes of Robot-Assisted Lobectomies.

Tchouta LN1, Park HS2, Boffa DJ1, Blasberg JD1, Detterbeck FC1, Kim AW3..

The positive impact of hospital operative volume on outcomes following video-assisted thoracoscopic surgery has been established. The goal of this study was to determine whether or not this volume/outcome relationship translates to robot-assisted thoracoscopic surgery (RobATS) lobectomy.
Patients who underwent RobATS lobectomy were identified between 2008 and 2013 in the Healthcare Cost and Utilization Project National Inpatient Sample database. Hospital volume, as well as demographic, clinical, and health-care system-related factors were selected as potential predictors of outcomes. Outcome variables included length of stay (LOS), inpatient mortality, and complications. Hospitals were designated by quartiles according to annual case volume, with very low-volume defined as the first quartile and high-volume defined as the fourth quartile. Regression analyses were used to identify independent predictors of the outcomes of interest.

Undergoing lobectomy at high-volume RobATS centers confers favorable mortality and LOS outcomes compared with very low-volume centers. However, the beneficial effect of volume on mortality suggests a need for the careful adoption of this promising technology.

Staging per-op

VATS vs thoracotomie: Curage ganglionnaire…

J Thorac Dis. 2014 Jan;6(1):45-51.

Comparative study of systematic thoracoscopic lymphadenectomy and conventional thoracotomy in resectable non-small cell lung cancer.

Wang W, Yin W, Shao W, Jiang G, Wang Q, Liu L, Liu D, Wang Z, Zhu Z, Chen H, He J.

To assess the feasibility and safety of the video-assisted thoracoscopy surgery (VATS) systematic lymph node dissection in resectable non-small cell lung cancer (NSCLC).

The clinical data of patients with NSCLC who underwent VATS or thoracotomy combined with lobectomy and systematic lymphadenectomy from January 2001 to January 2008 were retrospectively analyzed to identify their demographic parameters, number of dissected lymph nodes and postoperative complications.

For patients with resectable NSCLC, VATS systematic lymph node dissection is safe and effective with fewer postoperative complications, and significantly faster postoperative recovery compared with traditional open chest surgery.

Staging per-op

VATS vs thoracotomie vs robotic: Curage ganglionnaire…?

Ann Surg. 2017 Feb;265(2):431-437.

Long-term Survival Based on the Surgical Approach to Lobectomy For Clinical Stage I Nonsmall Cell Lung Cancer: Comparison of Robotic, Video-assisted Thoracic Surgery, and Thoracotomy Lobectomy.

Yang HX1, Woo KM, Sima CS, Bains MS, Adusumilli PS, Huang J, Finley DJ, Rizk NP, Rusch VW, Jones DR, Park BJ.

To compare the long-term outcomes among robotic, video-assisted thoracic surgery (VATS), and open lobectomy in stage I nonsmall cell lung cancer (NSCLC).

Survival comparisons between robotic, VATS, and open lobectomy in NSCLC have not yet been reported. Some studies have suggested that survival after VATS is superior, for unclear reasons.

Three cohorts (robotic, VATS, and open) of clinical stage I NSCLC patients were matched by propensity score and compared to assess overall survival (OS) and disease-free survival (DFS). Univariate and multivariate analyses were performed to identify factors associated with the outcomes.

Minimally invasive approaches to lobectomy for clinical stage I NSCLC result in similar long-term survival as thoracotomy. Use of VATS and robotics is associated with shorter length of stay, and the robotic approach resulted in greater lymph node assessment.

Staging per-op

Peut on encore être moins invasif?

J Thorac Cardiovasc Surg. 2017 Feb 10

A novel technique for tumor localization and targeted lymphatic mapping in early-stage lung cancer.

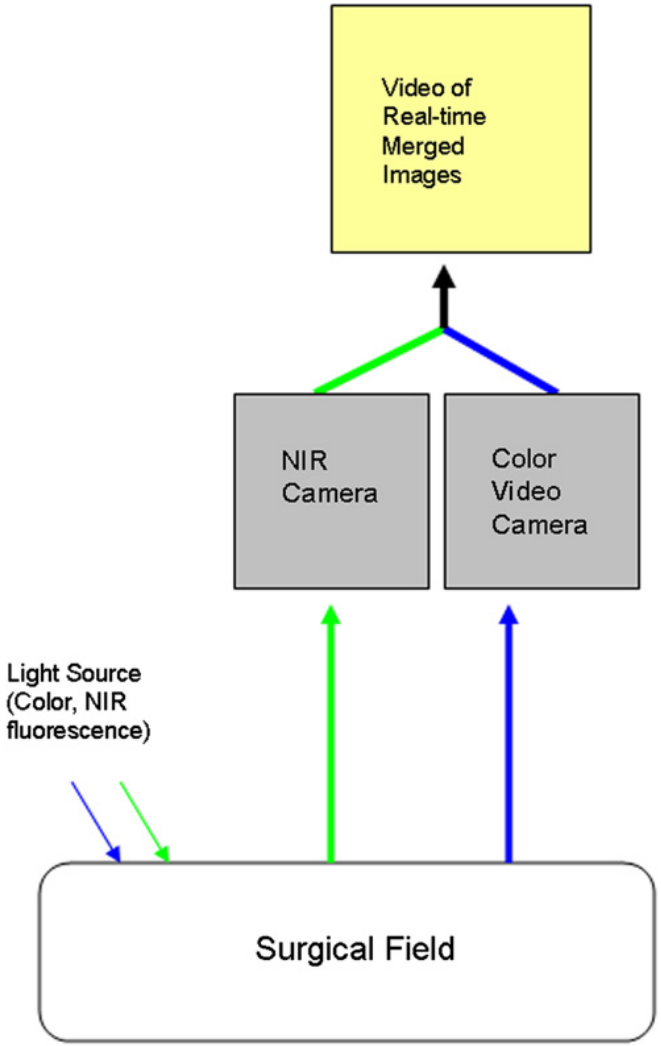
Hachey KJ1, Digesu CS1, Armstrong KW1, Gilmore DM2, Khullar OV3, Whang B1, Tsukada H1, Colson YL4.

To investigate safety and feasibility of navigational bronchoscopy (NB)-guided near-infrared (NIR) localization of small, ill-defined lung lesions and sentinel lymph nodes (SLN) for accurate staging in patients with non-small cell lung cancer (NSCLC).

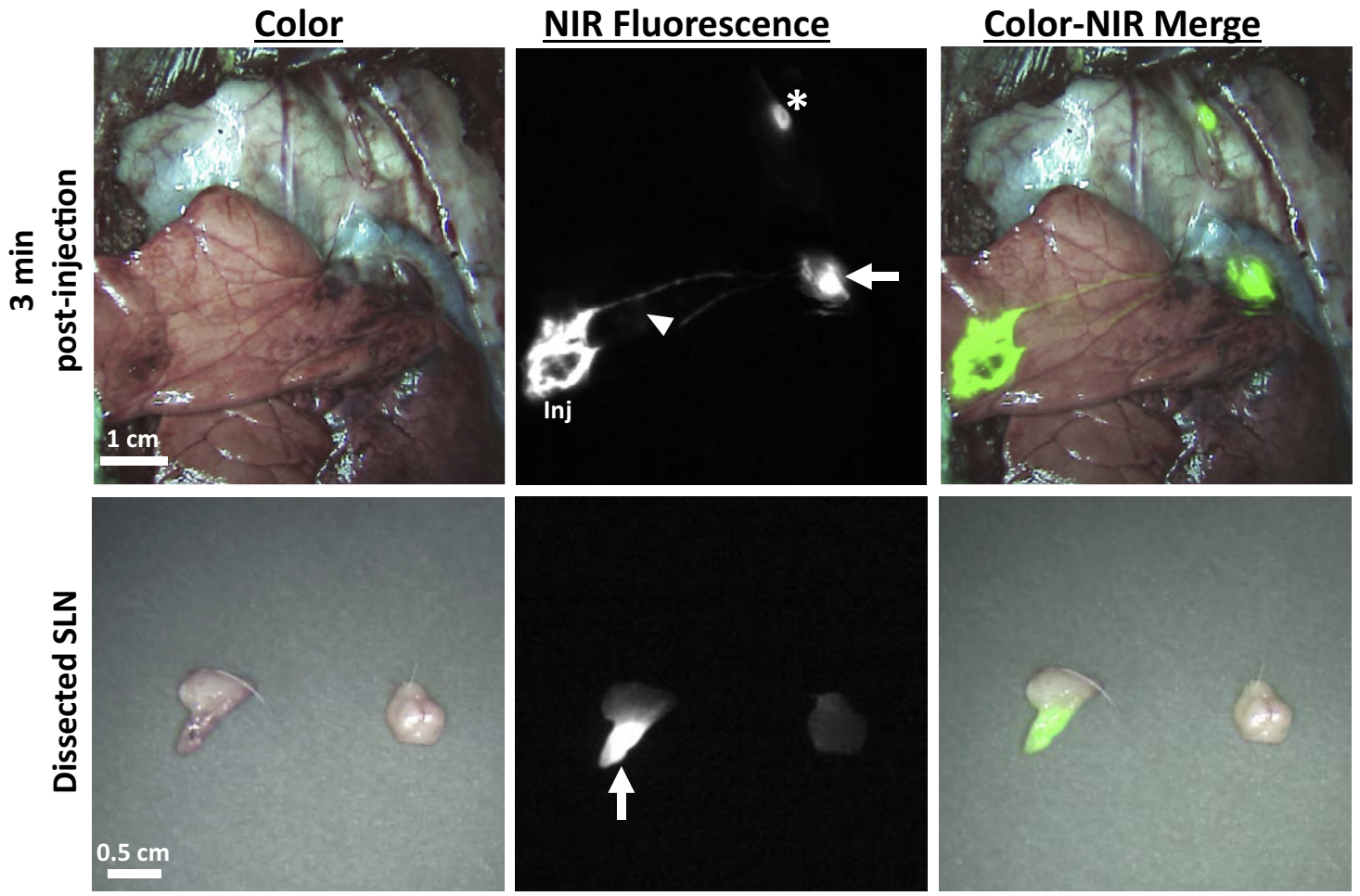
Patients with known or suspected stage I NSCLC were enrolled in a prospective pilot trial for lesion localization and SLN mapping via NB-guided NIR marking. Successful localization, SLN detection rates, histopathologic status of SLN versus overall nodes, and concordance to initial clinical stage were measured. Ex vivo confirmation of NIR+ SLNs and adverse events were recorded.

NB-guided NIR lesion localization and SLN identification was safe and feasible. This minimally invasive image-guided technique may permit the accurate localization and nodal staging of early stage lung cancers.

Sentinel lymph node with near-infrared fluorescent in NSCLC – Boston group study



Sentinel lymph node
Near-infrared fluorescent in NSCLC



Sentinel lymph node with near-infrared fluorescent in NSCLC – Boston group study

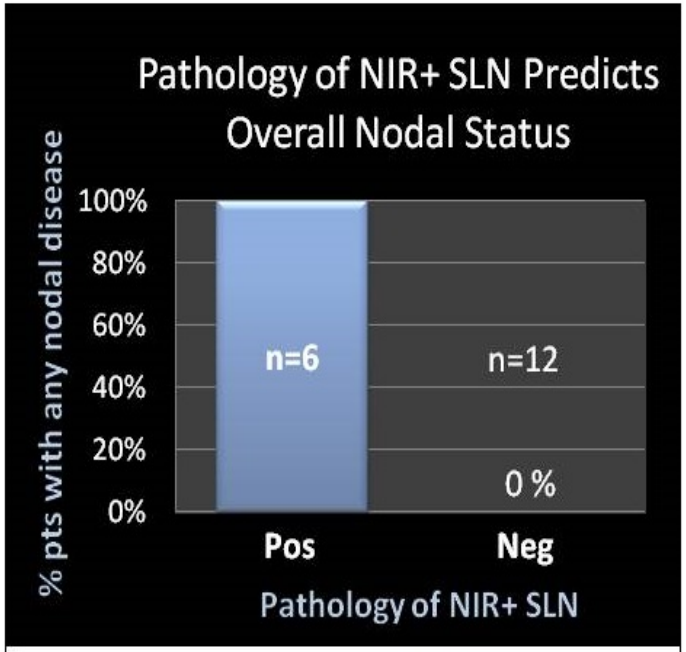


Fig. NIR+ SLNs were identified in 18 subjects. In the 12 subjects with SLNs negative for histopathologic evidence of disease, none had disease in any other LNs removed, suggesting there were no false negative cases. Disease was identified in the SLNS of 6 subjects, 4 of which went on to demonstrate disease in other LNs.

Drainage pleural

Combien de drain?… 1

Tohoku J Exp Med. 2014;232(1):55-61.
Postoperative drainage with one chest tube is appropriate for pulmonary lobectomy: a randomized trial.
Tanaka M, Sagawa M, Usuda K, Machida Y, Ueno M, Motono N, Sakuma T.

To expand postoperative residual lungs after pulmonary lobectomy, thoracic drainage with two chest tubes has been recommended. Several studies recently demonstrated that postoperative drainage with one chest tube (PD1) was as safe as that with two chest tubes (PD2). However, most of the patients in those studies underwent lobectomy by standard thoracotomy. Although the number of pulmonary lobectomies by video-assisted thoracic surgery (VATS) has been increasing in recent years, there have been no reports that compared PD1 with PD2 after pulmonary lobectomy, including that by VATS. To elucidate whether postoperative management with PD1 is as safe as that with PD2, we conducted a randomized controlled trial.

In conclusion, since PD1 has advantages in saving cost and time and in low risk of transcutaneous infection, PD1 is appropriate after pulmonary lobectomy by VATS and by open thoracotomy.

Drainage pleural

On l'enlève quand?

Eur J Cardiothorac Surg. 2014 Feb;45(2):241-6.

Early chest tube removal after video-assisted thoracic surgery lobectomy with serous fluid production up to 500 ml/day.

Bjerregaard LS, Jensen K, Petersen RH, Hansen HJ.

In fast-track pulmonary resections, we removed chest tubes after video-assisted thoracic surgery (VATS) lobectomy with serous fluid production up to 500 ml/day. Subsequently, we evaluated the frequency of recurrent pleural effusions requiring reintervention.

Data from 622 consecutive patients undergoing VATS lobectomy from January 2009 to December 2011 were registered prospectively in an institutional database. Data included age, gender, lobe(s) resected, bleeding and duration of surgery. Follow-up was 30 days from discharge. All complications requiring pleurocentesis or reinsertion of a chest tube, and all readmissions were registered. Twenty-three patients were excluded due to missing data, in-hospital mortality and loss to follow-up, leaving 599 for final analysis. Our primary outcome was the number of patients requiring reintervention due to recurrent pleural effusion. Secondary outcomes included time of chest tube removal and time to discharge. The incidence of recurrent pleural effusions requiring reintervention was compared between three groups according to the postoperative day (POD) of chest tube removal (Day 0-1, 2-3 and ≥4, respectively) using Fisher's exact test.

Our findings suggest that chest tube removal after VATS lobectomy is safe despite volumes of serous fluid production up to 500 ml/day. The proportion of patients who developed pleural effusion necessitating reintervention was low (2.8%), and a complication of the reintervention was seen in only 1 patient.

Drainage pleural

Combien de drain?… ZERO

Eur J Cardiothorac Surg. 2013 Aug;44(2):225-9; discussion 229.
Omitting chest tube drainage after thoracoscopic major lung resection.
Ueda K, Hayashi M, Tanaka T, Hamano K.

Absorbable mesh and fibrin glue applied to prevent alveolar air leakage contribute to reducing the length of chest tube drainage, length of hospitalization and the rate of pulmonary complications. This study investigated the feasibility of omitting chest tube drainage in selected patients undergoing thoracoscopic major lung resection.
Intraoperative air leakages were sealed with fibrin glue and absorbable mesh in patients undergoing thoracoscopic major lung resection. The chest tube was removed just after tracheal extubation if no air leakages were detected in a suction-induced air leakage test, which is an original technique to confirm pneumostasis. Patients with bleeding tendency or extensive thoracic adhesions were excluded.

The refined strategy for pneumostasis allowed the omission of chest tube drainage in the majority of patients undergoing thoracoscopic major lung resection without increasing the risk of adverse events, which may contribute to a fast-track surgery.

Anesthésie

Péridurale ou bloc paravertébral, c'est utile?

J Cardiothorac Vasc Anesth. 2012 Feb;26(1):78-82.
Thoracic epidural or paravertebral catheter for analgesia after lung resection: is the outcome different?
Elsayed H, McKevith J, McShane J, Scawn N.

The aim of this study was to determine whether thoracic epidural analgesia (TEA) or a paravertebral catheter block (PVB) with morphine patient-controlled analgesia influenced outcome in patients undergoing thoracotomy for lung resection.
The study population consisted of 1,592 patients who had undergone thoracotomy for lung resection between May 2000 and April 2008.

Paravertebral catheter analgesia with morphine patient-controlled analgesia seems as effective as thoracic epidural for reducing the risk of postoperative complications. The authors additionally found that paravertebral catheter use is associated with a shorter hospital stay and may be a better form of analgesia for fast-track thoracic surgery.

Fast track in thoracic surgery

Rapport d'expérience…

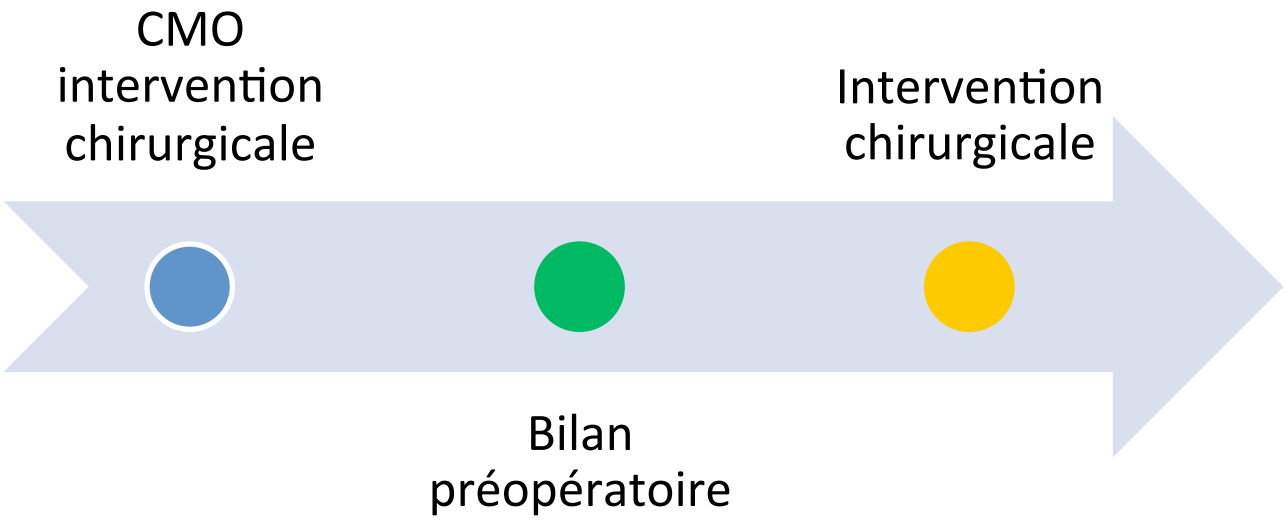
Eur J Cardiothorac Surg. 2009 Aug;36(2):383-91; discussion 391-2.
Fast-track rehabilitation for lung cancer lobectomy: a five-year experience.
Das-Neves-Pereira JC, Bagan P, Coimbra-Israel AP, Grimaillof-Junior A, Cesar-Lopez G, Milanez-de-Campos JR, Riquet M, Biscegli-Jatene F.

Fast-track rehabilitation is a group of simple measures that reduces morbidity, postoperative complication and accelerates postoperative rehabilitation reducing hospital stay. It can be applied to lung cancer lobectomy. Fast-track rehabilitation cornerstones are: minimally invasive surgical techniques using video-assisted and muscle sparring incisions, normovolemia, normothermia, good oxygenation, euglicemia, no unnecessary antibiotics, epidural patient-controlled analgesia, systemic opiods-free analgesia, early ambulation and oral feeding. Our objective is to describe a five-year experience with fast-track rehabilitation A retrospective non-controlled study including 109 consecutive patients submitted to fast-track rehabilitation in the postoperative care of lung cancer lobectomy was performed. Only collaborative patients who could receive double-lumen intubation, epidural catheters with patient-controlled analgesia, who had Karnofsky index of 100, previous normal feeding and ambulation, absence of morbid obesity, diabetes or asthma, were eligible. Postoperative oral feeding and aggressive ambulation started as soon as possible.

Fast-track rehabilitation for lung cancer lobectomies can be safely performed in a selected group of patients if a motivated multidisciplinary group of professionals is available and seems to reduce postoperative complication and hospital stay.

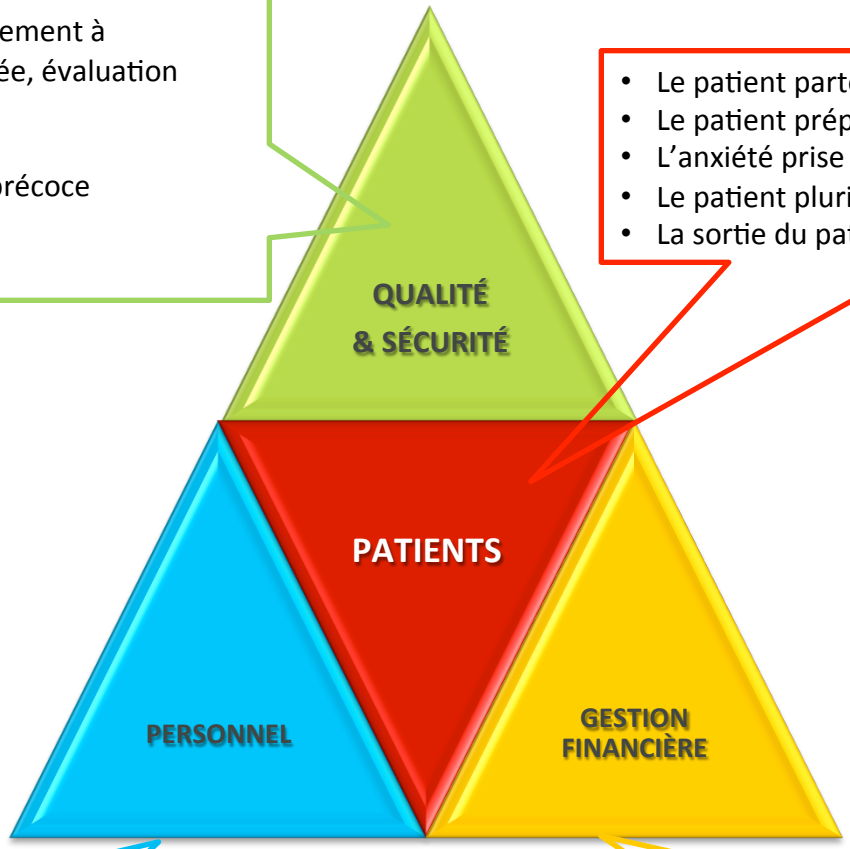
Itinéraire

Un patient dans un mouvement dès le premier contact…



Objectifs

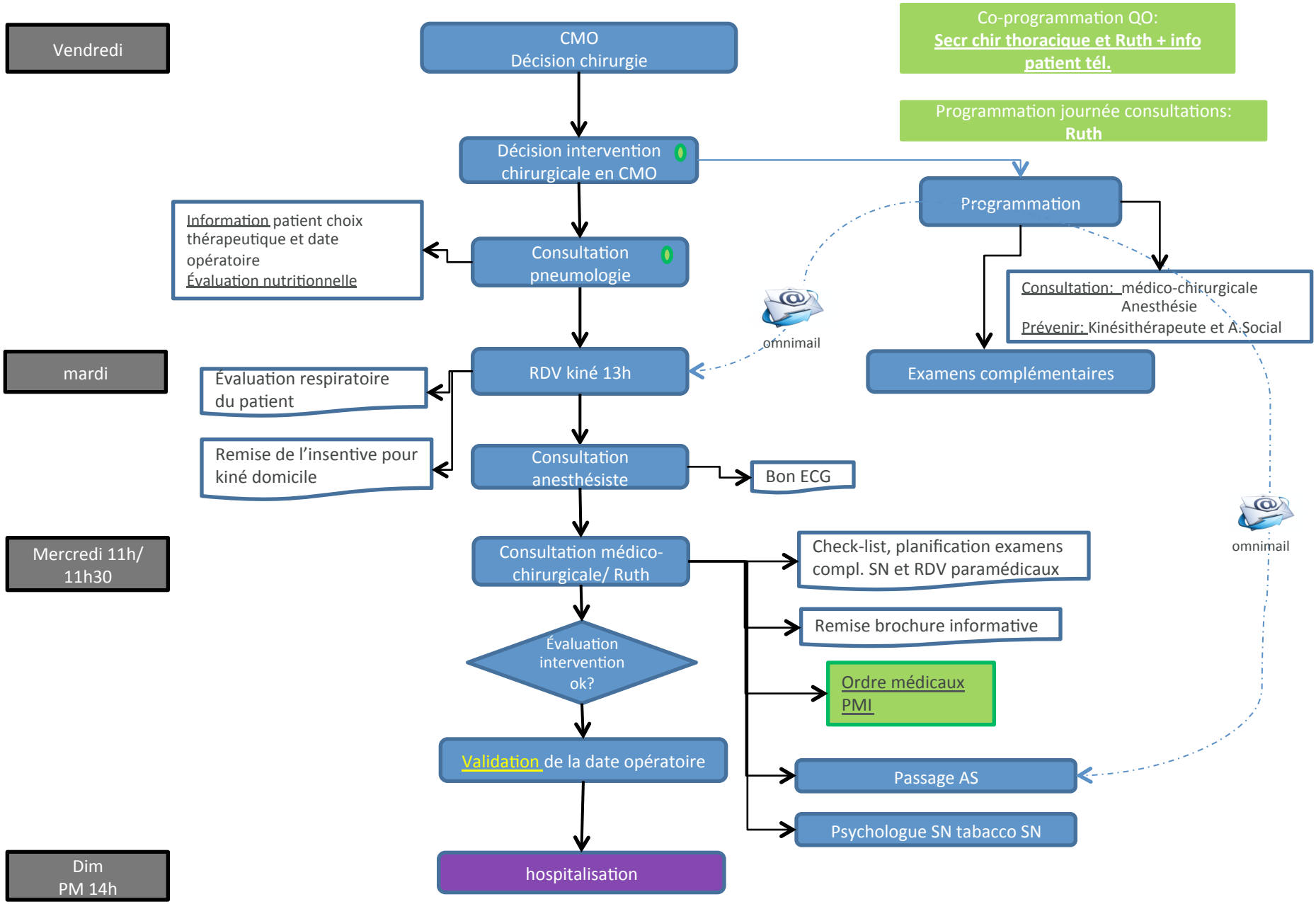
- Le délai court entre le choix thérapeutique et l'intervention
- Les patients conditionnés physiquement à l'intervention (dénutrirons détectée, évaluation anesthésiste)
- Réconciliation médicamenteuse
- Gestion de la douleur efficace et précoce
- La rééducation immédiate



- Le patient partenaire de son rétablissement
- Le patient préparé à son intervention
- L'anxiété prise en charge
- Le patient pluri-consulte rapidement
- La sortie du patient est anticipée

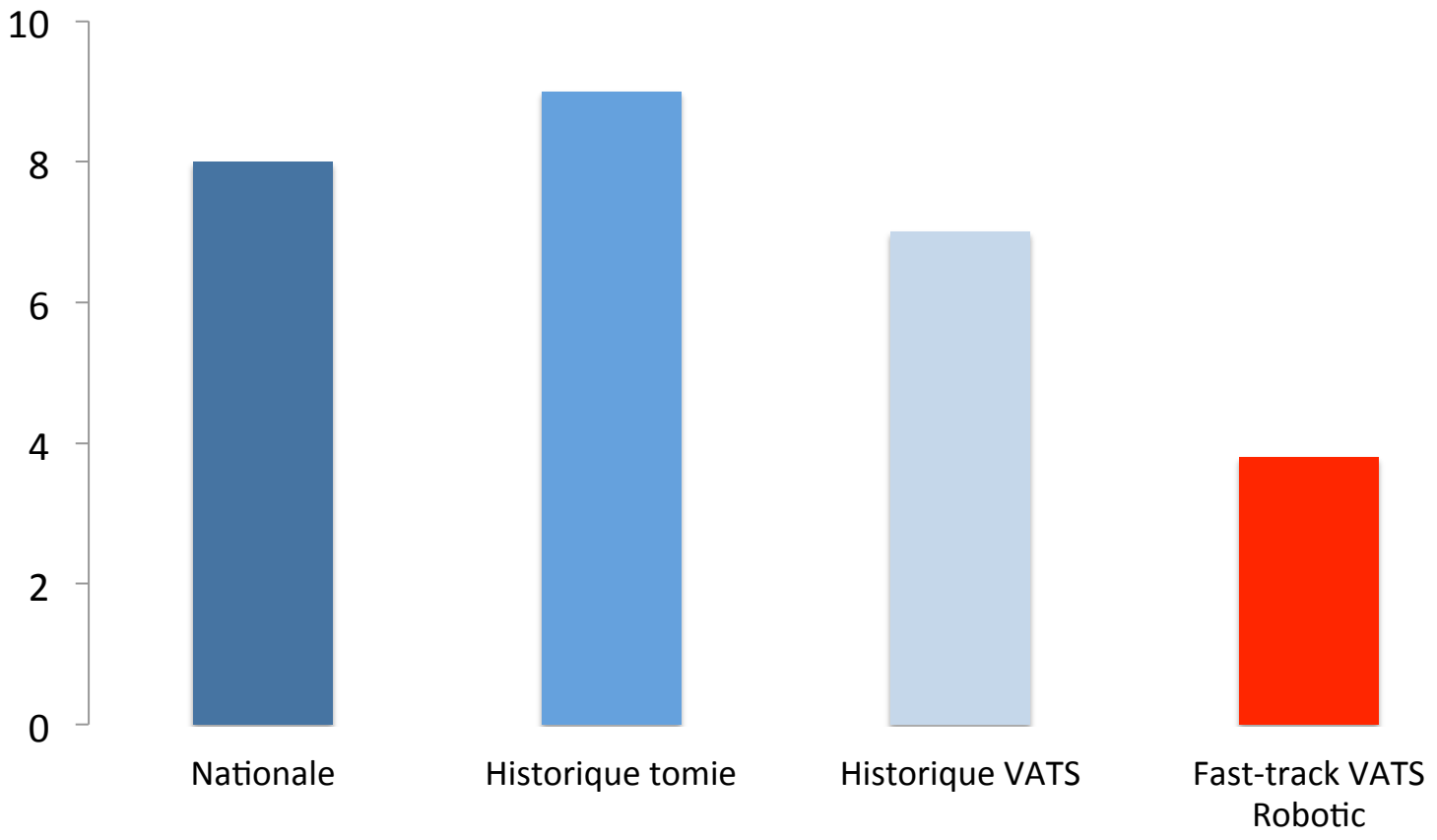
- Chaque métier sait ce qu'il doit faire et quand
- Tous les patients connus par l'équipe
- Transmissions des informations claires basée sur les objectifs a atteindre

- Diminuer la durée moyenne de séjour


Vendredi
CMO
Décision chirurgie
Co-programmation QO:
Secr chir thoracique et Ruth + info patient tél.
Programmation journée consultations:
Ruth
Décision intervention chirurgicale en CMO
Programmation
Information patient choix thérapeutique et date opératoire
Évaluation nutritionnelle
Consultation pneumologie
omnimail
Consultation: médico-chirurgicale
Anesthésie
Prévenir: Kinésithérapeute et A.Social
mardi
RDV kiné 13h
Examens complémentaires
Évaluation respiratoire du patient
Remise de l'insentive pour kiné domicile
Consultation anesthésiste
Bon ECG
omnimail
Mercredi 11h/ 11h30
Consultation médico-chirurgicale/ Ruth
Check-list, planification examens compl. SN et RDV paramédicaux
Remise brochure informative
Évaluation intervention ok?
Ordre médicaux PMI
Validation de la date opératoire
Passage AS
Psychologue SN tabacco SN
Dim PM 14h
hospitalisation

Itinéraire

Nos résultats…



Conclusions

- Le fastrack est une sur la constitution de parcourt de soins basés sur *l'evidence base medicine* qui réduit le stress physique et psychique lié à l'intervention.
- C'est une vision intégrée et interdisciplinaire de la prise en charge du patient.
- Cette démarche diminue la durée du séjour hospitalier, les coûts généraux et pourrait raisonnablement avoir un impact sur la morbi-mortalité (cf chirurgie digestive et cardiaque).

Conclusions

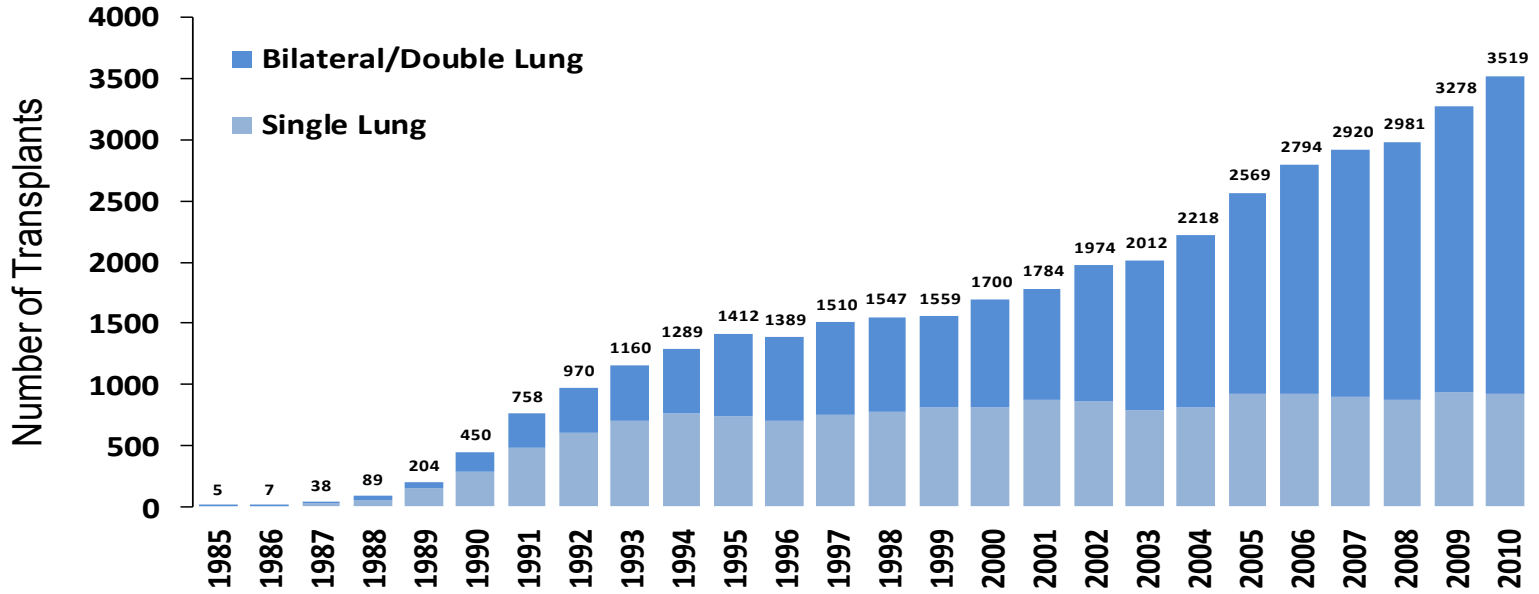
- L'avenir de la Chirurgie Thoracique est donc l'intégration des différents métiers dans des missions communes définies autour et avec le patient pour chaque pathologie.
- L'organisation des hôpitaux doit être revue fondamentalement et organisée en "trajets de soins" plutôt qu'en services médicaux et paramédicaux.

En transplantation pulmonaire, on peut encore avancer?

The shortage of donor lungs

- According to the *Thirtieth Adult Lung and Heart-Lung Transplant Report 2013*, from the Registry of the International Society for Heart and Lung Transplantation, lung transplantation (LTx) is a therapy that is being performed worldwide, with numbers increasing every year.

Yusen, J Heart Lung Transplant, 2013



The shortage of donor lungs

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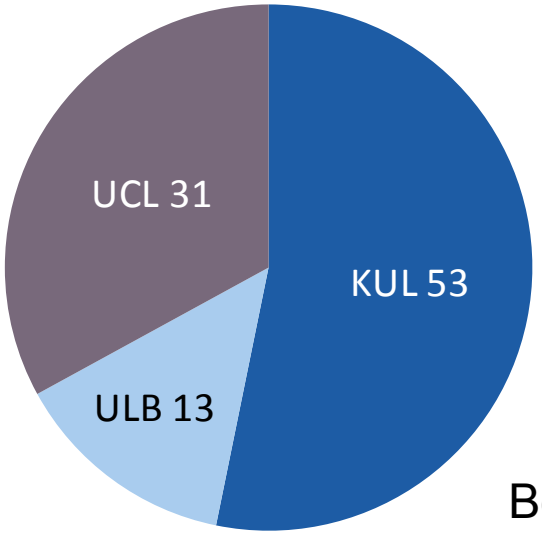
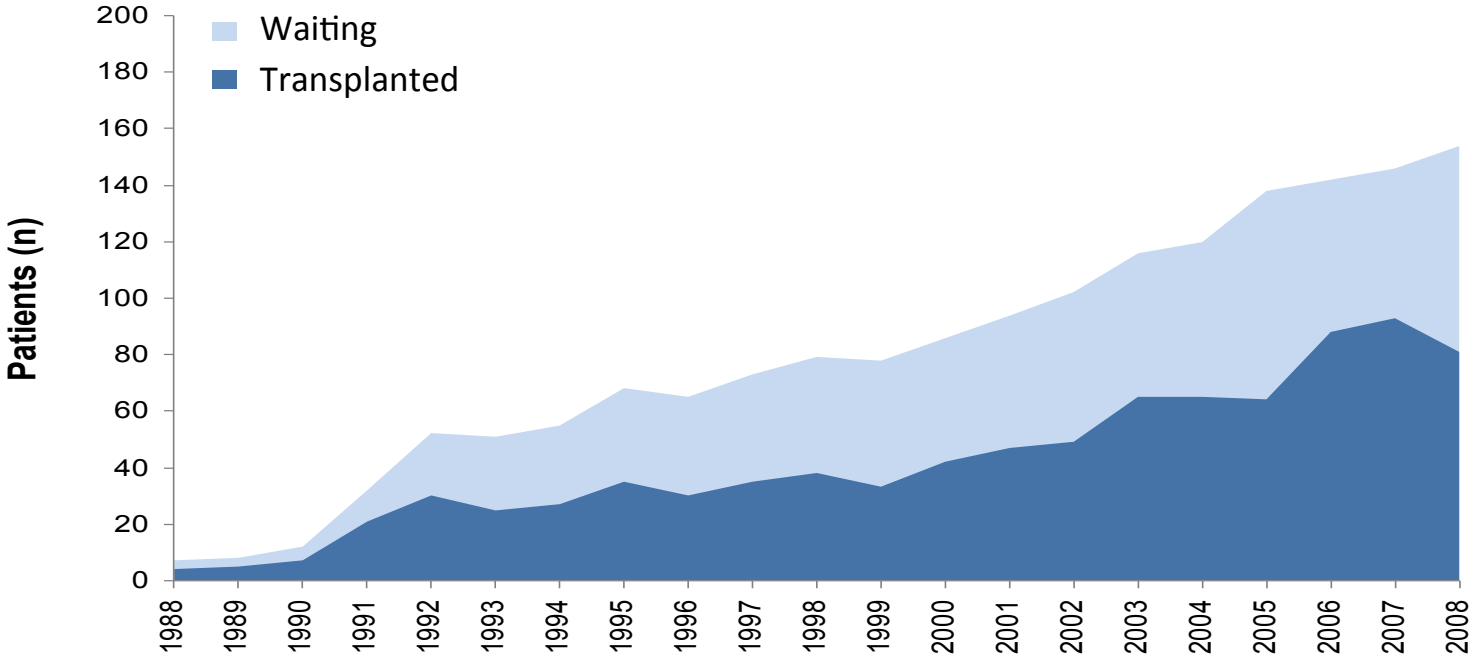


Belgium, 2013

The shortage of donor lungs

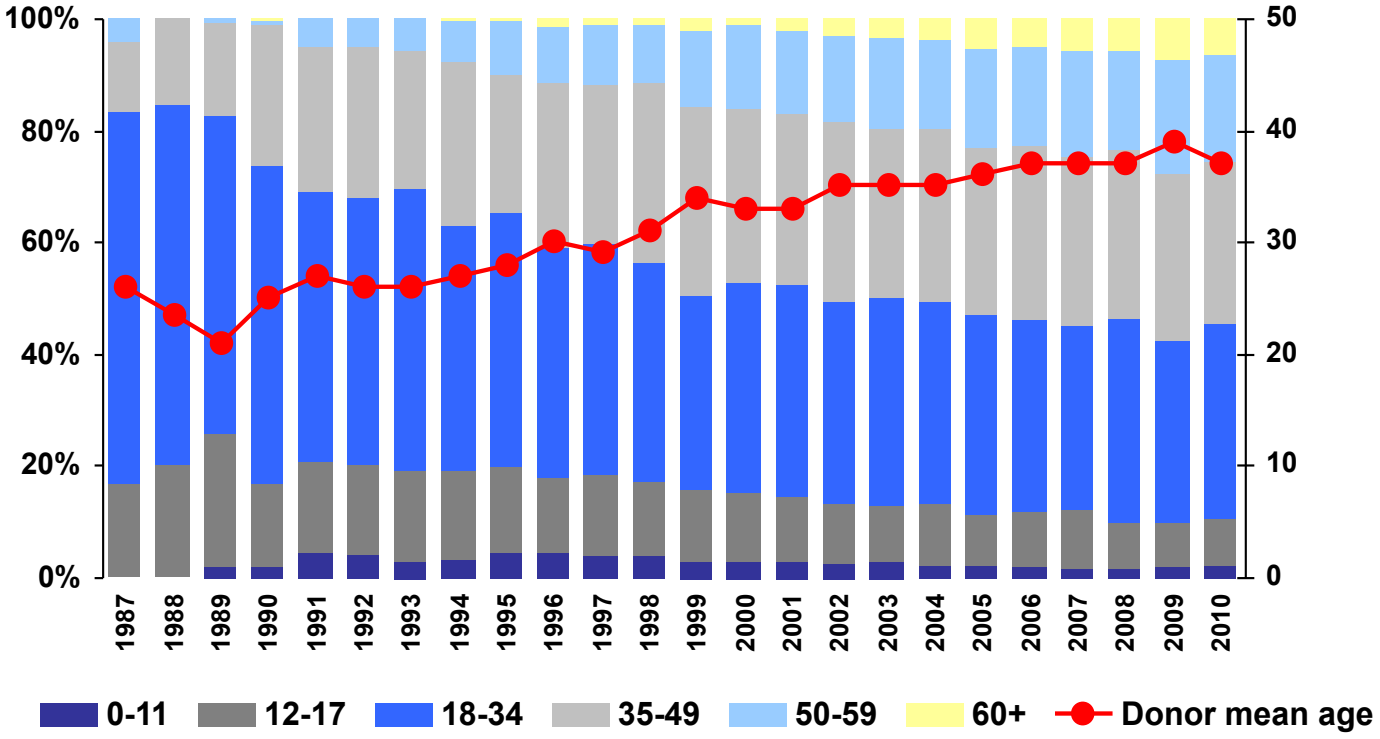
- Nevertheless, the amount of lungs suitable for transplantation has not followed this trend and this equation generates considerable waitlist mortality (15,4 per 100 wait-list years in the US form 2010 to 2012).

Valapour, Am J Transplant, 2013



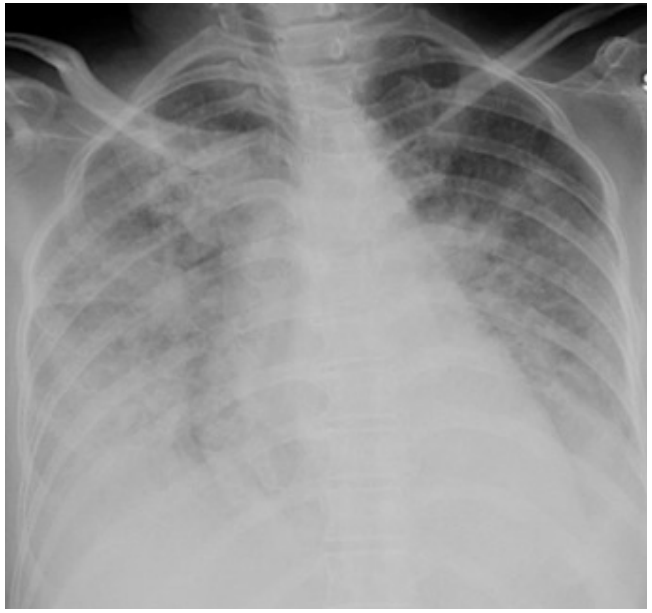
The shortage of donor lungs

- The mean age of lung donor increases with decreasing in relative organ quality (ET: From 21 in 1989 to 39 in 2009).



The shortage of donor lungs

- Donor lungs are subjected to several injurious mechanisms during the brain death/organ donation process (such as ventilator-acquired pneumonia, neurogenic and hydrostatic pulmonary edema, barotrauma). Thus, it is not surprising that the majority of donor lungs are not utilized for transplantation (39% ET 2012, 22% in the US 2012).



Strategies for lung donor pool expansion Ideal donor

- Ideal donor:
  - <55 year-old,
  - <20 pack-year smoking history,
  - no chest trauma,
  - clear chest X-ray,
  - central P/F >300,
  - absence of purulent secretions and organisms on gram stain of respiratory samples.

Pierre, J Thorac Cardiovasc Surg, 2002

- This scenario is known to correspond to less than half of the donors utilized for transplantation.

Strategies for lung donor pool expansion Extended criteria donor

- Several studies addressing the use of extended criteria donors
- A review study summarized the findings of 10 studies ranging from 1993 to 2010, bringing the best evidence up to date.
  - Although no clear differences in mid or long-term survival were observed, 4 of these studies revealed worse early outcomes (such as 30- and 90-day mortality, ICU and hospital stay and gas exchange at ICU arrival).

Schiavon, Interact Cardiovasc Thorac Surg, 2012

- Recently, the Hannover group has shown an interesting algorithm proposing allocation of extended criteria donor lungs to lower-risk recipients. Results were encouraging and deserve further analysis.

Sommer, J Heart Lung Transplant, 2013

Strategies for lung donor pool expansion Controlled DCD donor

- The first successful LTx was performed from DCD (Hardy - 1963)
- the concept of using controlled DCD lungs has been clinically revisited by D'Alessandro in 1995.

D'Alessandro, Transplantation,1995

- Series of studies have followed, reporting an increasing international experience and highlighting the potential of DCD to partially address the shortage of donor lungs… But…

Cypel,J Heart Lung Transplant, 2009
Erasmus, Transplantation, 2010
Love RB, Am J Transplant, 2012
Mason, Ann Thorac Surg 2012
De Oliveira, J Thorac Cardiovasc Surg, 2010
Levvey, Am J Transplant, 2012
Puri, Ann Thorac Surg, 2009

- Nevertheless, caution is still observed in the transplant community as there are a series of specific injuries that the DCD lung is prone to, specially during the interval from withdrawal of life sustaining therapies to pulmonary artery flush.

Strategies for lung donor pool expansion Uncontrolled DCD donor

- Another potential source of lungs comes from the use of uncontrolled DCDs (Maastricht categories I and II).

- The group of Madrid has explored this peculiar pool, reporting the experience with 29 cases.

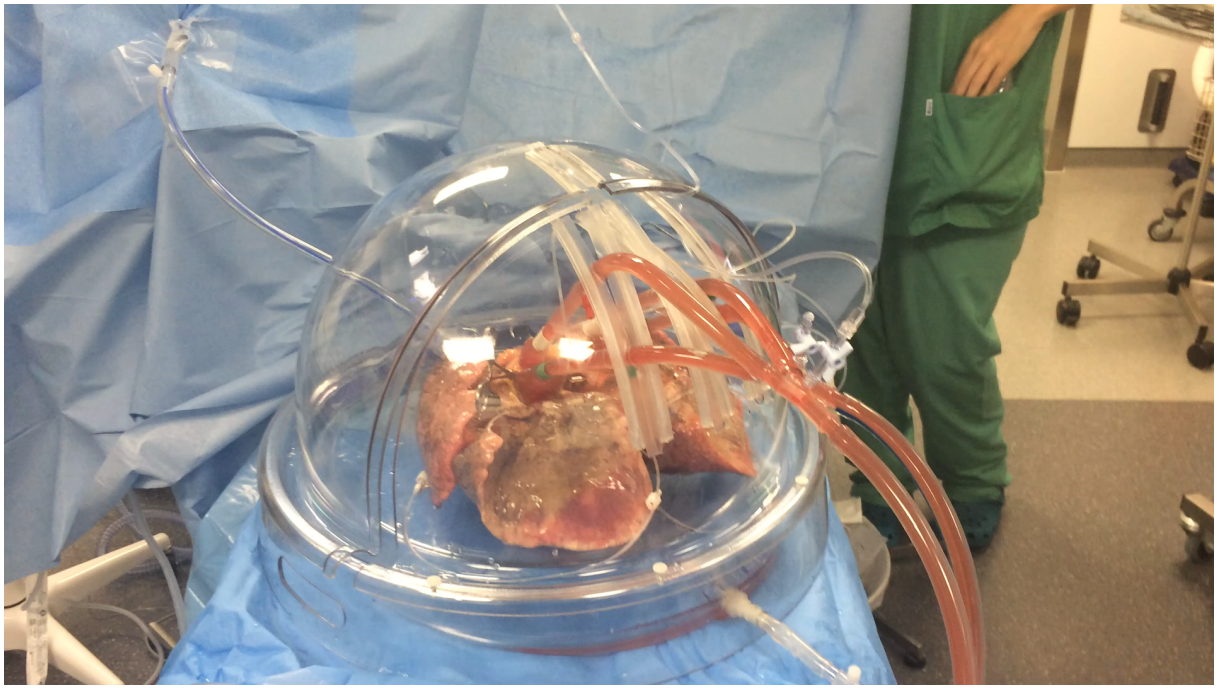
  Ninety-day and 1-year mortality were 22% and 32% respectively, with higher rates of primary graft dysfunction (PGD) 2-3 than expected.

de Antonio, J Heart Lung Transplant, 2007

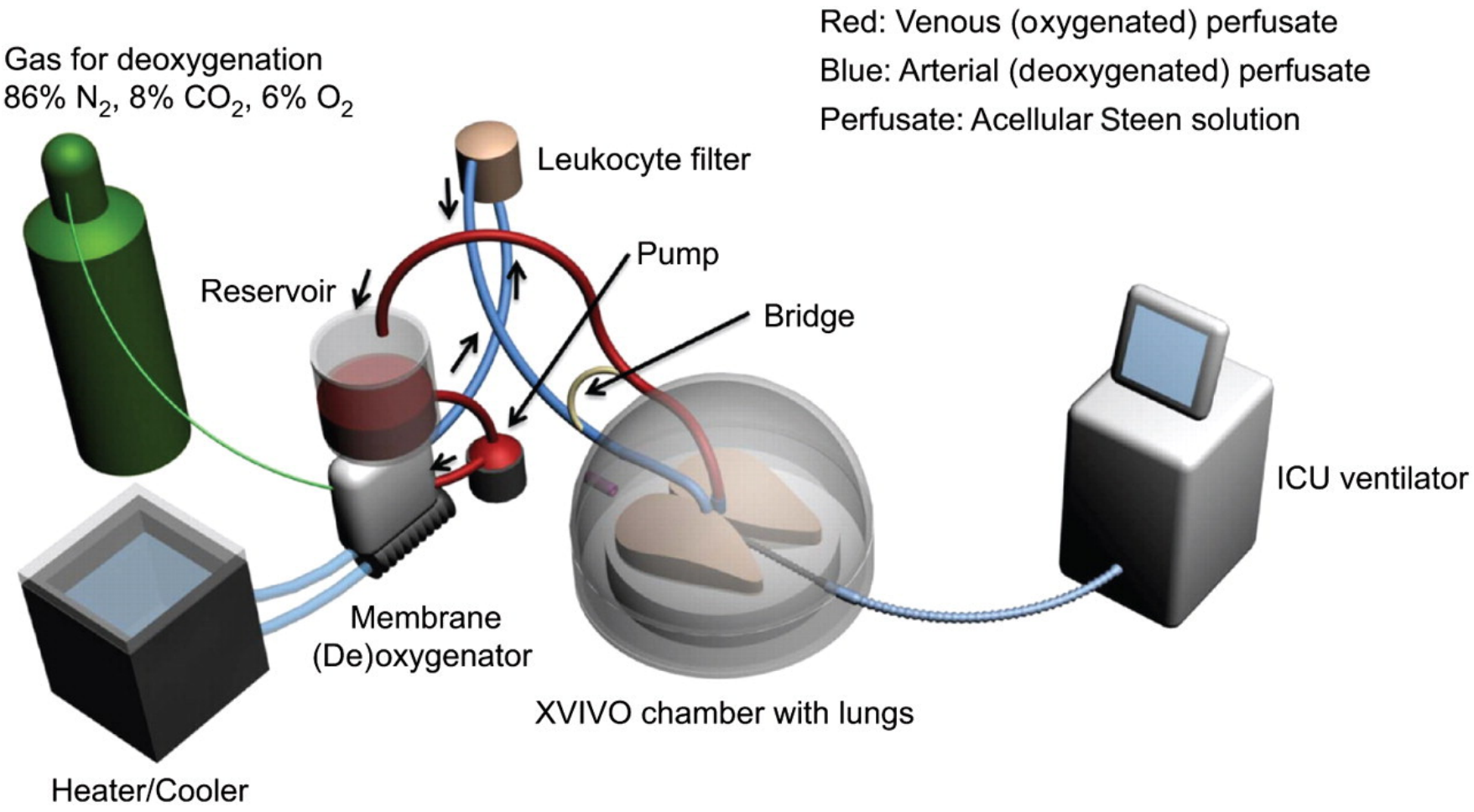
Strategies for lung donor pool expansion Ex vivo lung perfusion

- Clinical EVLP was shown to safely increase the donor pool by preserving high-risk donor lungs with similar outcomes to standard criteria donor lungs.

Cypel M, N Engl J Med, 2011



EVLP


Red: Venous (oxygenated) perfusate
Blue: Arterial (deoxygenated) perfusate
Perfusate: Acellular Steen solution
Gas for deoxygenation
86% N_2, 8% CO_2, 6% O_2
Leukocyte filter
Pump
Reservoir
Bridge
ICU ventilator
Membrane
(De)oxygenator
XVIVO chamber with lungs
Heater/Cooler

EVLP – Philosophies…

- Evaluation – Extending donor pool
- Improving quality – Reconditionning
- Prolong perfusion and/or transport time
- Research

EVLP – Philosophies…

- Evaluation – Extending donor pool
- Improving quality – Reconditionning
- Prolong perfusion and/or transport time
- Research

EVLP Evaluation – Extending donor pool

- Evaluation of poor prognostic donor…
  - DCD donor — Elgharably, Thorac Surg Clin, 2015
  - Circulatory death — Bozso, Can Respir J, 2014
  - Extending criteria donor — Bozso, Transpl Int, 2014
  - Hanging victim — Bennett, Ann Thorac Surg, 2014
  - Infected or suspicion of infection — Boffini, Transpl Int, 2014
- Evaluation of in vivo inevaluable donor…
  - Maastricht 2 — Suzuki, Am J Transplant, 2014
  - High-pressure pneumoplegia — Patil, J Thorac Cardiovasc Surg, 2014
  - ECMO — García Sáez, Eur J Cardiothorac Surg, 2014
- Evaluation for prognosing…
  - Perfusate protein expression during EVLP can differentiate lungs with good outcome from lungs PGD3 after transplantation. — Machuca, Ann Surg. 2014

EVLP Evaluation – Extending donor pool

Transplant Proc. 2013 Sep;45(7):2624-6.

Ex vivo lung perfusion increases the pool of lung grafts: analysis of its potential and real impact on a lung transplant program.

Boffini, Ricci, Barbero, Bonato, Ribezzo, Mancuso, Attisani, Simonato, Magistroni, Mansouri, Solidoro, Baldi, Pasero, Amoroso, Rinaldi.

BACKGROUND:

Among the strategies to increase the number of lung transplants, ex vivo lung perfusion (EVLP) represents a novel technique to expand the donor pool.

METHODS:

Data from donors referred to our center were retrospectively analyzed to identify grafts that could potentially be potentially reconditioned by EVLP and for comparison with those obtained by clinical application of EVLP program in our center.

RESULTS:

Among 75 rejected lungs, 23 organs have been identified as potentially treatable with EVLP with a hypothetic increase of lung transplant activity of 53%. After the introduction of the EVLP program in our center, lung transplantation with reconditioned grafts was performed in 7 (23%) patients with a 30% increase in transplant procedures.

CONCLUSION:

Although less than expected, EVLP increased the number of lungs suitable for transplantation.

EVLP – Philosophies…

- Evaluation – Extending donor pool
- Improving quality – Reconditionning
- Prolong perfusion and/or transport time
- Research

EVLP Improving quality – Reconditioning

- Improve function…
  - EVLP alone — Cypel, Thorac Surg Clin, 2015
  - Plasmin administration — Motoyama, J Heart Lung Transplant, 2014
  - Hydrogen preconditioning — Noda, Transplantation, 2014
- Treating…
  - Aspiration with intrabronchial surfactant instillation — Inci, J Surg Res, 2013
  - Acute pulmonary embolism with urokinase — Inci, Ann Thorac Surg, 2014
  - Reducing microbial load by high-dose empirical AB — Andreasson, J Heart Lung Transplant, 2014
  - Inflammation by mechanical removal of dendritic cell-generating non-classical monocytes — Stone, J Heart Lung Transplant, 2014
- Surgical act…
  - LVRS - Lobectomy — Nosotti, Transplant Proc, 2014

Worldwide experience with clinical EVLP Results

- Toronto conducted a nonrandomized clinical trial to assess the feasibility of EVLP selecting high-risk donor lungs for this modality of preservation.
  - 23 donor lungs were submitted to EVLP,
  - 20 being ultimately transplanted (15 bilateral/5 unilateral),
  - PGD grade 2 or 3 at 72 hours: 15% of the EVLP group and 30% of the contemporary no EVLP controls (116 cases), with no significant difference,
  - Time on mechanical ventilation, ECLS requirement, ICU stay, hospital stay and 30-day mortality were not different.

Cypel M, N Engl J Med, 2011

  - This experience was recently updated…
  - with a total of 50 lung transplants from 58 EVLPs (86% yield),
  - PGD 3 at 72 hours was recorded in 2% EVLP vs. 8.5% control (P=0.14),
  - Again, time on mechanical ventilation, ECLS requirement, ICU stay, hospital stay and 30-day mortality were not different,
  - 1-year survivals: 87% for EVLP group vs. 86% for the standard group.

Cypel, J Thorac Cardiovasc Surg, 2012

Worldwide experience with clinical EVLP Results

- Vienna reported their experience…
  - 13 clinical EVLPs which rendered 9 double-lung transplants (69% yield),
  - Early outcomes - days on mechanical ventilation, ICU stay, hospital stay and 30-day mortality were comparable to 119 contemporary conventional preservation transplants,
  - Interestingly, all the four declined cases developed massive pulmonary edema and were recovered from donors with trauma history.

Aigner, Am J Transplant, 2012

- The groups from Toronto, Vienna and Paris presented their clinical EVLP experience at the 2013 ISHLT meeting.
- A total of 125 clinical EVLPs were performed with an 82.5% yield,
- Incidence of PGD3 at 72 hours was 5% and the 12-month mortality was 12%.

Cypel, Journal of Heart and Lung Transplantation 2013

Worldwide experience with clinical EVLP Results

- The NOVEL Lung trial is an FDA mandated multicenter clinical trial (NOVEL Lung Trial) studying EVLP for marginal donors.
- The initial report included 31 patients that received EVLP lungs. Early outcomes such as PGD, length on mechanical ventilation, ICU stay, hospital stay and 30-day mortality were similar to 31 non-EVLP controls.

Sanchez, J Heart Lung Transplant, 2013

- At the 2014 ISHLT meeting, the trial results were updated to 76 EVLPs rendering 42 lung transplants (55% conversion rate). In comparison with 42 contemporary controls, early outcomes and 1-year survival were not different.

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EVLP – Philosophies…

- Evaluation – Extending donor pool
- Improving quality – Reconditionning
- Prolong perfusion and/or transport time
- Research

EVLP Prolong perfusion and/or transport time

Am J Transplant. 2014 Oct;14(10):2412-6.

Combined liver and lung transplantation with extended normothermic lung preservation in a patient with end-stage emphysema complicated by drug-induced acute liver failure.

Ceulemans, Monbaliu, Verslype, van der Merwe , Laleman , Vos , Neyrinck, Van Veer, De Leyn , Nevens , Pirenne , Verleden , Van Raemdonck .

Isolated lung transplantation (LuTx) and liver transplantation are established treatments for irreversible lung and liver failure. Combined liver and lung transplantation (cLiLuTx) is a less common, but approved therapy of combined organ failure, mostly applied in patients suffering from progressive cystic fibrosis and advanced liver disease. We report a patient who was listed for LuTx due to end-stage chronic obstructive pulmonary disease and who developed drug-induced acute hepatic failure. The only therapeutic option was hyper-urgent cLiLuTx. To correct the poor coagulation in order to reduce the per-operative risk of bleeding, the liver was transplanted first. In anticipation of the longer lung preservation time, cold flushed lungs were preserved on a portable lung perfusion device for ex vivo normothermic perfusion for 11 h 15 min, transplanted sequentially off-pump, and reperfused after a total ex vivo time of 13 h 32 min and 16 h for the first and second lung, respectively. Ten months later, the patient is doing well and no rejection occurred. Normothermic ex vivo lung perfusion may help to prolong preservation time, facilitating long-distance transport and combined organ transplantation..

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Eur J Cardiothorac Surg. 2014 Mar;45(3):e54-60.

Successful prolonged ex vivo lung perfusion for graft preservation in rats.

Noda, Shigemura, Tanaka, Bhama, D'Cunha, Luketich, Bermudez.

Ex vivo lung perfusion (EVLP) strategies represent a new frontier in lung transplantation technology, and there have been many clinical studies of EVLP in lung transplantation. The establishment of a reliable EVLP model in small animals is crucial to facilitating translational research using an EVLP strategy. The main objective of this study was to develop a reproducible rat EVLP (R-EVLP) model that enables prolonged evaluation of the explanted lung during EVLP and successful transplantation after EVLP.

The donor heart-lung blocks were procured with cold low-potassium dextran solution and immersed in the solution for 1 h at 4 °C. And then, the heart-lung blocks were flushed retrogradely and warmed up to 37 °C in a circuit perfused antegradely with acellular perfusate. The perfusate was deoxygenated with a gas mixture (6% O2, 8% CO2, 86% N2). The perfusion flow was maintained at 20% of the entire cardiac output. At 37 °C, the lungs were mechanically ventilated and perfusion continued for 4 h. Every hour, the perfused lung was evaluated for gas exchange, dynamic lung compliance (Cdyn) and pulmonary vascular resistance (PVR).

R-EVLP was performed for 4 h. Pulmonary oxygenation ability (pO2/pCO2) was stable for 4 h during EVLP. It was noted that Cdyn and PVR were also stable. After 4 h of EVLP,

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EVLP Research

World J Exp Med. 2014 May 20;4(2):7-15.

Animal models of ex vivo lung perfusion as a platform for transplantation research.

Nelson, Bobba, Ghadiali, Hayes, Black, Whitson.

Ex vivo lung perfusion (EVLP) is a powerful experimental model for isolated lung research. EVLP allows for the lungs to be manipulated and characterized in an external environment so that the effect of specific ventilation/perfusion variables can be studied independent of other confounding physiologic contributions. At the same time, EVLP allows for normal organ level function and real-time monitoring of pulmonary physiology and mechanics. As a result, this technique provides unique advantages over in vivo and in vitro models. Small and large animal models of EVLP have been developed and each of these models has their strengths and weaknesses. In this manuscript, we provide insight into the relative strengths of each model and describe how the development of advanced EVLP protocols is leading to a novel experimental platform that can be used to answer critical questions in pulmonary physiology and transplant medicine.

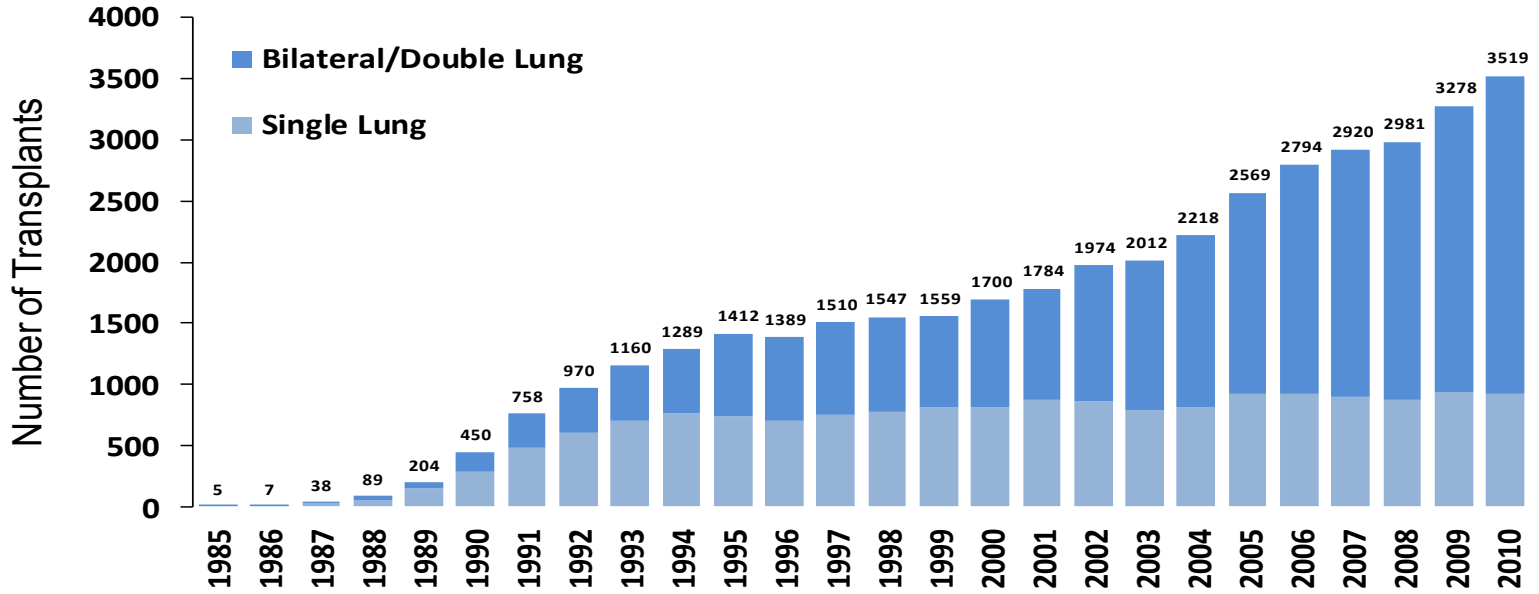
Conclusions

- The use of EVLP…
  - allows an objective assessment of high-risk donor lungs.
  - autorize treatment, reconditionning of suposed non-transplantable lungs.
  - permits when these lungs are transplanted, acceptable rates of primary graft dysfunction, with an early and mid-term outcomes similar to those with conventionally selected and transplanted lungs.
  - permits to explore new source of donors (DCD donor, circulatory death, extending criteria donor, hanging victim, infected organs, ECMO…).
  - help to prolong preservation time, facilitating long-distance transport and combined organ transplantation.
  - leads to experimental platform that can be used to answer questions in pulmonary physiology and transplant medicine.

The shortage of donor lungs

- According to the *Thirtieth Adult Lung and Heart-Lung Transplant Report 2013*, from the Registry of the International Society for Heart and Lung Transplantation, lung transplantation (LTx) is a therapy that is being performed worldwide, with numbers increasing every year.

Yusen, J Heart Lung Transplant, 2013



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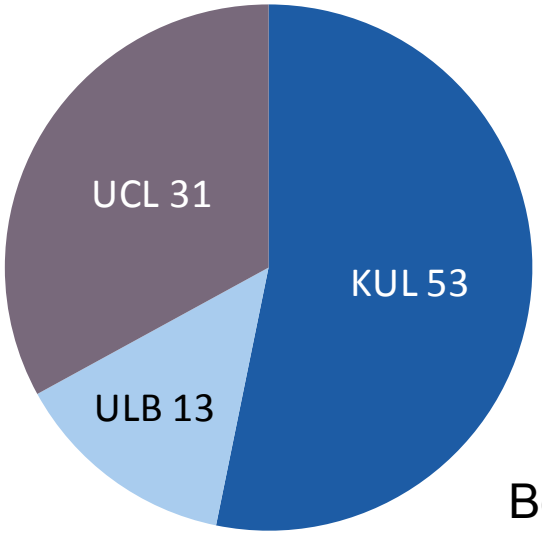
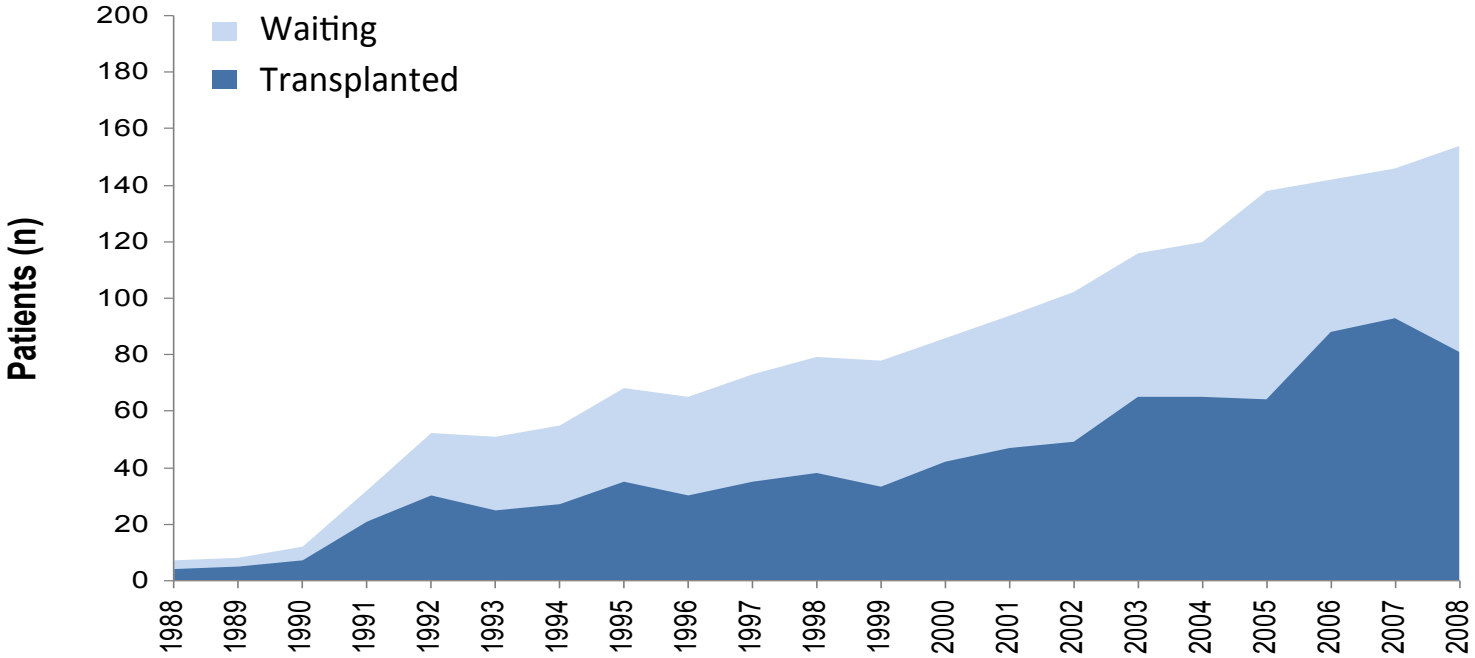


Belgium, 2013

The shortage of donor lungs

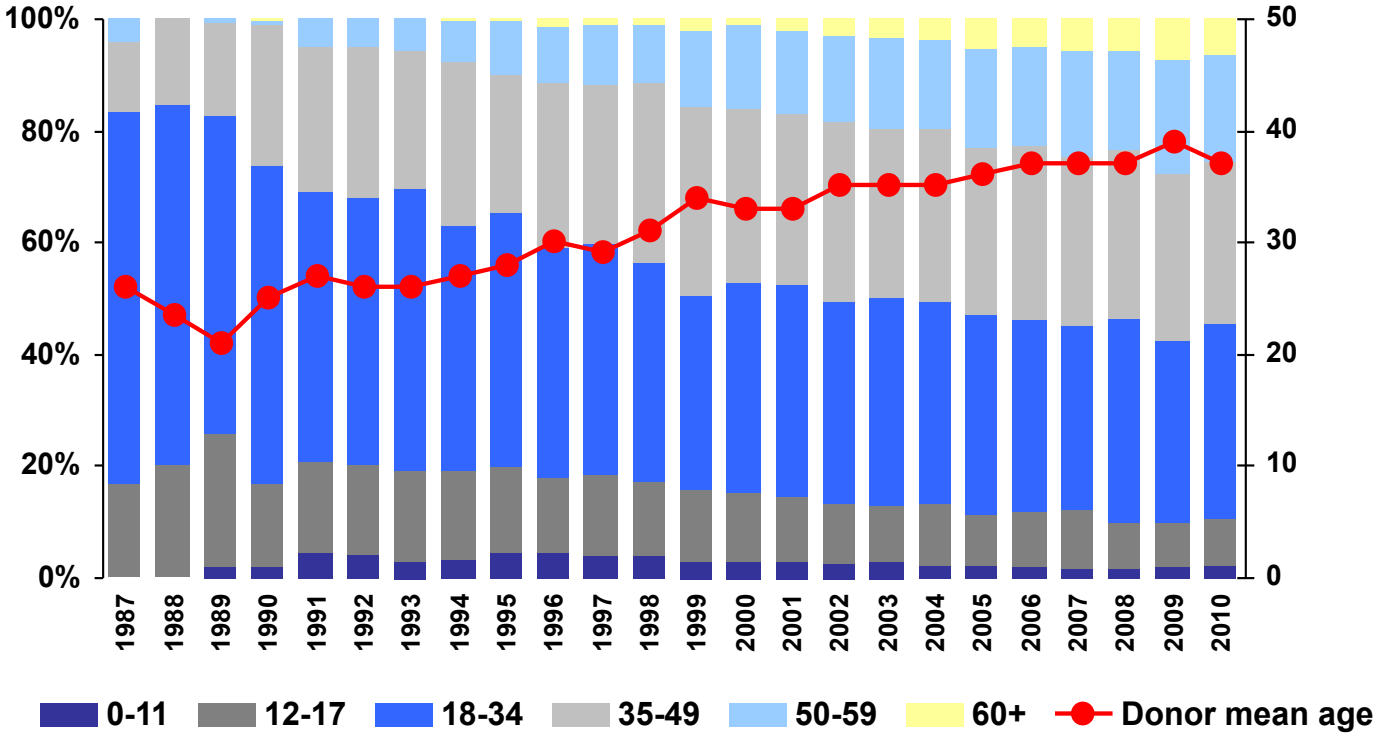
- Nevertheless, the amount of lungs suitable for transplantation has not followed this trend and this equation generates considerable waitlist mortality (15,4 per 100 wait-list years in the US form 2010 to 2012).

Valapour, Am J Transplant, 2013



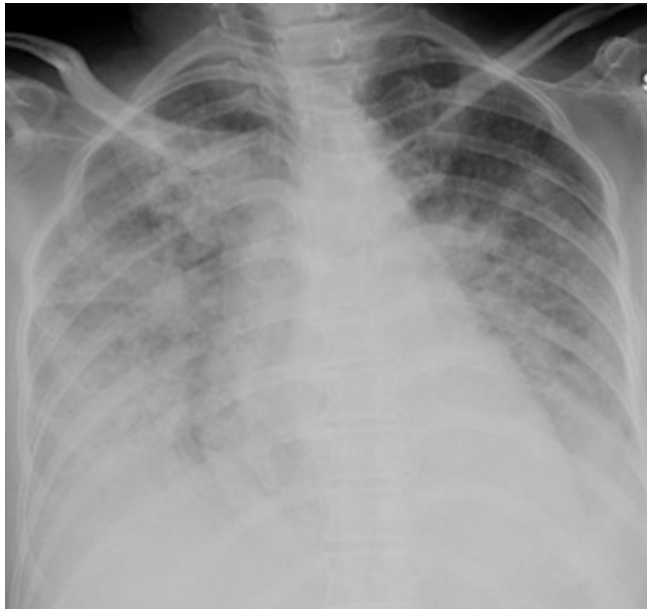
The shortage of donor lungs

- The mean age of lung donor increases with decreasing in relative organ quality (ET: From 21 in 1989 to 39 in 2009).



The shortage of donor lungs

- Donor lungs are subjected to several injurious mechanisms during the brain death/organ donation process (such as ventilator-acquired pneumonia, neurogenic and hydrostatic pulmonary edema, barotrauma). Thus, it is not surprising that the majority of donor lungs are not utilized for transplantation (39% ET 2012, 22% in the US 2012).



Strategies for lung donor pool expansion Ideal donor

- Ideal donor:
  - <55 year-old,
  - <20 pack-year smoking history,
  - no chest trauma,
  - clear chest X-ray,
  - central P/F >300,
  - absence of purulent secretions and organisms on gram stain of respiratory samples.

Pierre, J Thorac Cardiovasc Surg, 2002

- This scenario is known to correspond to less than half of the donors utilized for transplantation.

Strategies for lung donor pool expansion Extended criteria donor

- Several studies addressing the use of extended criteria donors
- A review study summarized the findings of 10 studies ranging from 1993 to 2010, bringing the best evidence up to date.
  - Although no clear differences in mid or long-term survival were observed, 4 of these studies revealed worse early outcomes (such as 30- and 90-day mortality, ICU and hospital stay and gas exchange at ICU arrival).

Schiavon, Interact Cardiovasc Thorac Surg, 2012

- Recently, the Hannover group has shown an interesting algorithm proposing allocation of extended criteria donor lungs to lower-risk recipients. Results were encouraging and deserve further analysis.

Sommer, J Heart Lung Transplant, 2013

Strategies for lung donor pool expansion Controlled DCD donor

- The first successful LTx was performed from DCD (Hardy - 1963)
- the concept of using controlled DCD lungs has been clinically revisited by D'Alessandro in 1995.

D'Alessandro, Transplantation,1995

- Series of studies have followed, reporting an increasing international experience and highlighting the potential of DCD to partially address the shortage of donor lungs… But…

Cypel,J Heart Lung Transplant, 2009
Erasmus, Transplantation, 2010
Love RB, Am J Transplant, 2012
Mason, Ann Thorac Surg 2012
De Oliveira, J Thorac Cardiovasc Surg, 2010
Levvey, Am J Transplant, 2012
Puri, Ann Thorac Surg, 2009

- Nevertheless, caution is still observed in the transplant community as there are a series of specific injuries that the DCD lung is prone to, specially during the interval from withdrawal of life sustaining therapies to pulmonary artery flush.

Strategies for lung donor pool expansion Uncontrolled DCD donor

- Another potential source of lungs comes from the use of uncontrolled DCDs (Maastricht categories I and II).

- The group of Madrid has explored this peculiar pool, reporting the experience with 29 cases.

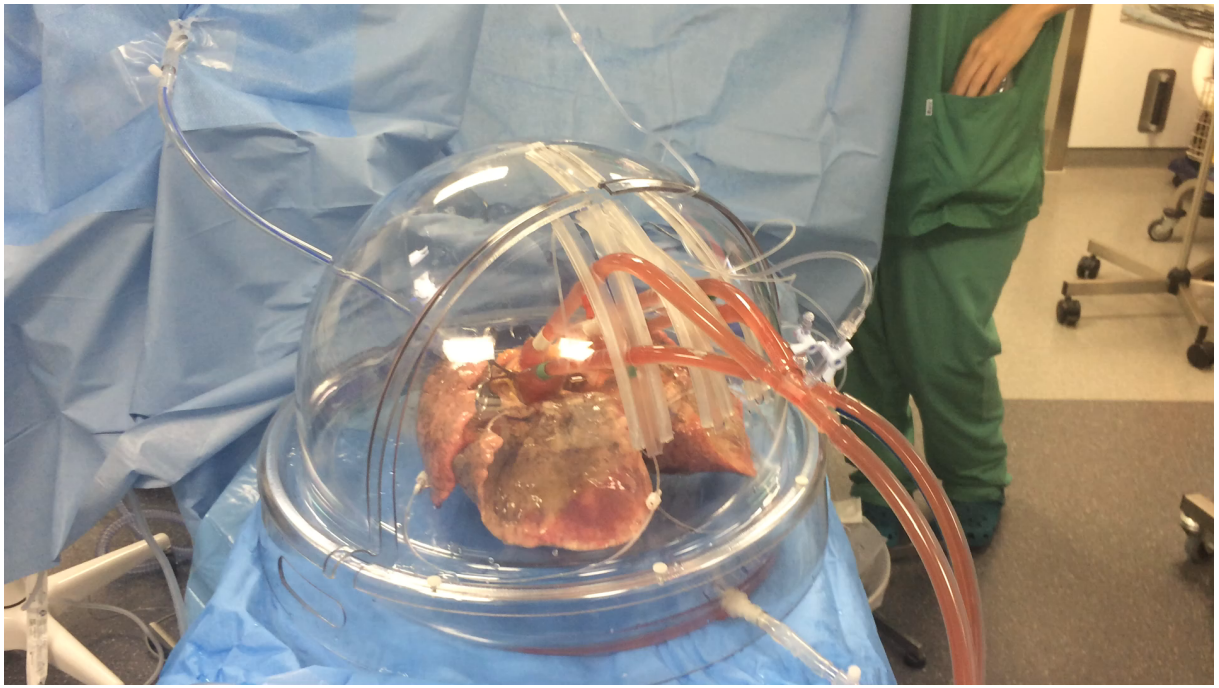
  Ninety-day and 1-year mortality were 22% and 32% respectively, with higher rates of primary graft dysfunction (PGD) 2-3 than expected.

de Antonio, J Heart Lung Transplant, 2007

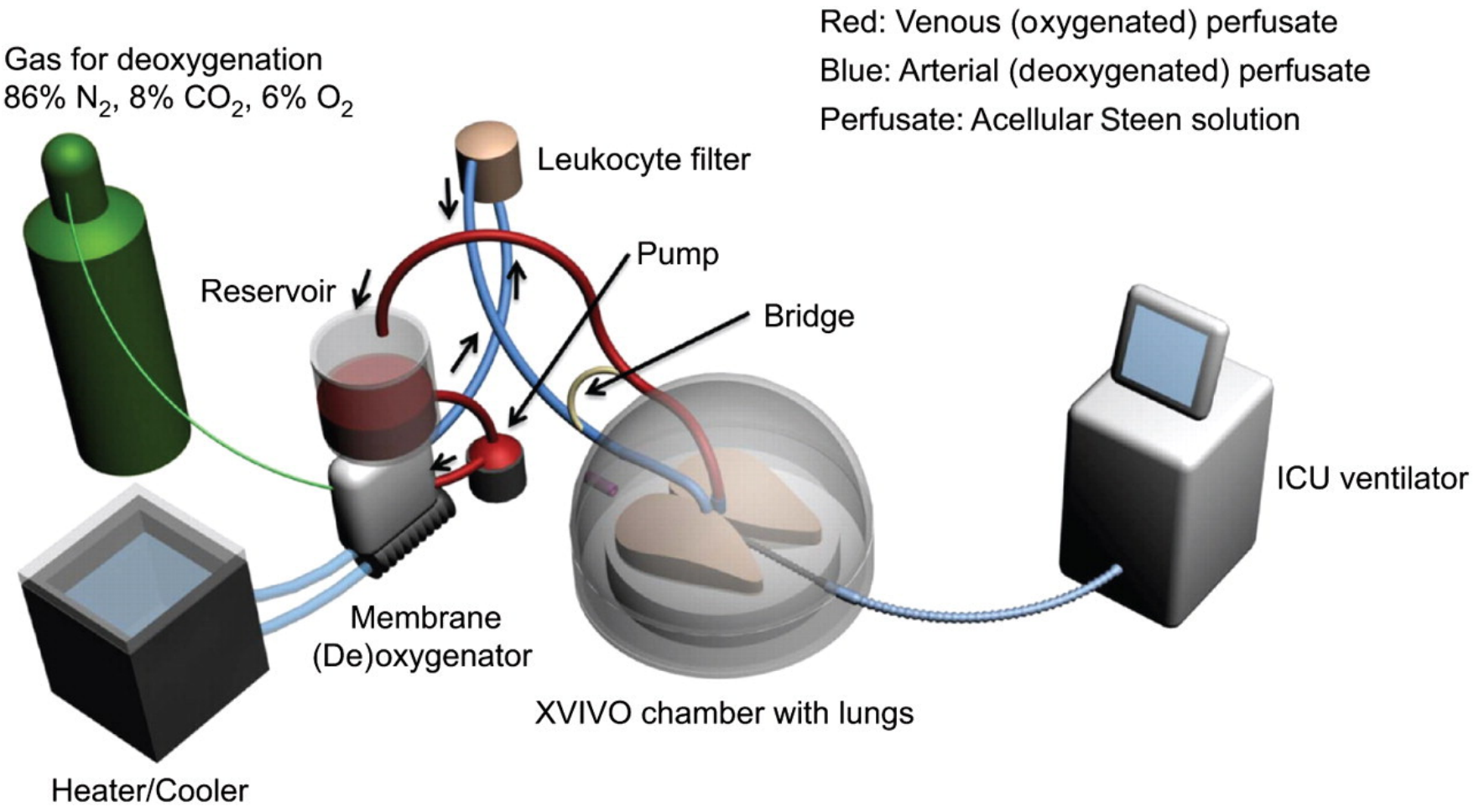
Strategies for lung donor pool expansion Ex vivo lung perfusion

- Clinical EVLP was shown to safely increase the donor pool by preserving high-risk donor lungs with similar outcomes to standard criteria donor lungs.

Cypel M, N Engl J Med, 2011



EVLP


Red: Venous (oxygenated) perfusate
Blue: Arterial (deoxygenated) perfusate
Perfusate: Acellular Steen solution
Gas for deoxygenation
86% N_2, 8% CO_2, 6% O_2
Leukocyte filter
Pump
Reservoir
Bridge
ICU ventilator
Membrane
(De)oxygenator
XVIVO chamber with lungs
Heater/Cooler

EVLP – Philosophies…

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EVLP Evaluation – Extending donor pool

- Evaluation of poor prognostic donor…
  - DCD donor — Elgharably, Thorac Surg Clin, 2015
  - Circulatory death — Bozso, Can Respir J, 2014
  - Extending criteria donor — Bozso, Transpl Int, 2014
  - Hanging victim — Bennett, Ann Thorac Surg, 2014
  - Infected or suspicion of infection — Boffini, Transpl Int, 2014
- Evaluation of in vivo inevaluable donor…
  - Maastricht 2 — Suzuki, Am J Transplant, 2014
  - High-pressure pneumoplegia — Patil, J Thorac Cardiovasc Surg, 2014
  - ECMO — García Sáez, Eur J Cardiothorac Surg, 2014
- Evaluation for prognosing…
  - Perfusate protein expression during EVLP can differentiate lungs with good outcome from lungs PGD3 after transplantation. — Machuca, Ann Surg. 2014

EVLP Evaluation – Extending donor pool

Transplant Proc. 2013 Sep;45(7):2624-6.

Ex vivo lung perfusion increases the pool of lung grafts: analysis of its potential and real impact on a lung transplant program.

Boffini, Ricci, Barbero, Bonato, Ribezzo, Mancuso, Attisani, Simonato, Magistroni, Mansouri, Solidoro, Baldi, Pasero, Amoroso, Rinaldi.

BACKGROUND:

Among the strategies to increase the number of lung transplants, ex vivo lung perfusion (EVLP) represents a novel technique to expand the donor pool.

METHODS:

Data from donors referred to our center were retrospectively analyzed to identify grafts that could potentially be potentially reconditioned by EVLP and for comparison with those obtained by clinical application of EVLP program in our center.

RESULTS:

Among 75 rejected lungs, 23 organs have been identified as potentially treatable with EVLP with a hypothetic increase of lung transplant activity of 53%. After the introduction of the EVLP program in our center, lung transplantation with reconditioned grafts was performed in 7 (23%) patients with a 30% increase in transplant procedures.

CONCLUSION:

Although less than expected, EVLP increased the number of lungs suitable for transplantation.

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- Improving quality – Reconditionning
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EVLP Improving quality – Reconditioning

- Improve function…
  - EVLP alone — Cypel, Thorac Surg Clin, 2015
  - Plasmin administration — Motoyama, J Heart Lung Transplant, 2014
  - Hydrogen preconditioning — Noda, Transplantation, 2014
- Treating…
  - Aspiration with intrabronchial surfactant instillation — Inci, J Surg Res, 2013
  - Acute pulmonary embolism with urokinase — Inci, Ann Thorac Surg, 2014
  - Reducing microbial load by high-dose empirical AB — Andreasson, J Heart Lung Transplant, 2014
  - Inflammation by mechanical removal of dendritic cell-generating non-classical monocytes — Stone, J Heart Lung Transplant, 2014
- Surgical act…
  - LVRS - Lobectomy — Nosotti, Transplant Proc, 2014

Worldwide experience with clinical EVLP Results

- Toronto conducted a nonrandomized clinical trial to assess the feasibility of EVLP selecting high-risk donor lungs for this modality of preservation.
  - 23 donor lungs were submitted to EVLP,
  - 20 being ultimately transplanted (15 bilateral/5 unilateral),
  - PGD grade 2 or 3 at 72 hours: 15% of the EVLP group and 30% of the contemporary no EVLP controls (116 cases), with no significant difference,
  - Time on mechanical ventilation, ECLS requirement, ICU stay, hospital stay and 30-day mortality were not different.

Cypel M, N Engl J Med, 2011

  - This experience was recently updated…
  - with a total of 50 lung transplants from 58 EVLPs (86% yield),
  - PGD 3 at 72 hours was recorded in 2% EVLP vs. 8.5% control (P=0.14),
  - Again, time on mechanical ventilation, ECLS requirement, ICU stay, hospital stay and 30-day mortality were not different,
  - 1-year survivals: 87% for EVLP group vs. 86% for the standard group.

Cypel, J Thorac Cardiovasc Surg, 2012

Worldwide experience with clinical EVLP Results

- Vienna reported their experience…
  - 13 clinical EVLPs which rendered 9 double-lung transplants (69% yield),
  - Early outcomes - days on mechanical ventilation, ICU stay, hospital stay and 30-day mortality were comparable to 119 contemporary conventional preservation transplants,
  - Interestingly, all the four declined cases developed massive pulmonary edema and were recovered from donors with trauma history.

Aigner, Am J Transplant, 2012

- The groups from Toronto, Vienna and Paris presented their clinical EVLP experience at the 2013 ISHLT meeting.
- A total of 125 clinical EVLPs were performed with an 82.5% yield,
- Incidence of PGD3 at 72 hours was 5% and the 12-month mortality was 12%.

Cypel, Journal of Heart and Lung Transplantation 2013

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