Lung allocation for transplant: The European perspective

Are Martin Holm¹,² | Franz Immer³ | Christian Benden³,⁴

¹Department of Respiratory Medicine, Oslo University Hospital, Oslo, Norway
²Institute for Clinical Medicine, University of Oslo, Oslo, Norway
³Swisstransplant, Berne, Switzerland
⁴University of Zurich Medical Faculty, Zürich, Switzerland

Abstract
Since the first successful lung transplants in humans were done in the 1980s, lung transplantation has become an established treatment for end-stage pulmonary disease. Because the access to transplantable organs is limited and unpredictable, rules that guide the allocation of lungs for transplants have emerged. Such rules are governed not only by medical and bioethical necessities, but also by local traditions, legislation, and practical circumstances. Therefore, there may be significant differences between the organ allocation practices in various parts of the world. In this brief communication, the European perspective on lung allocation is presented, also adding a very brief description of other parts of the world.

KEYWORDS
health care policy, lung transplantation, organ allocation

1 | THE HISTORY OF LUNG TRANSPLANTATION IN EUROPE

The surgical technique of transplanting lungs was developed already in 1947 by Dr Demikhov in Russia using dogs.¹ When researchers in Switzerland developed the first calcineurin inhibitor in the late seventies,² human organ transplants on a larger scale became possible, and the first successful lung transplantation in humans was performed in Toronto in 1983.¹ Later, the development of a viable system for ex vivo lung perfusion by Dr Stig Steen in Sweden in 2001, and the introduction of donation after circulatory death (DCD) has increased the donor pool substantially in many countries.³ In 2017, 2210 LTx was performed in Europe (compared to 2478 in the USA),⁴ and an overview over number of donated organs per million inhabitant (PMI), number of lung transplants PMI and whether there is an "opt-in" or an "opt-out" system for organ donation in selected countries is shown in Table 1.

2 | EUROPEAN LUNG ALLOCATION SYSTEMS

The original lung allocation in Europe was based on the existing system for abdominal transplantations, paired with the competent surgeons’ estimation of the medical needs and possibilities of each singular case. However, as the transplantation gradually became an established treatment, expectations emerged that the limited supply of available organs should be shared according to predictable and justifiable principles. As in the USA, the overarching principle in Europe is to ensure optimal matching of organs and to consider medical acuity and recipient longevity. Over time, acknowledging the different national legislations and cultures,⁵ several different schemes have evolved in the different European countries. Compared to the USA, in many European countries, there may be higher expectations of a universal provision of health care with equal access for all citizens, and this may also be reflected in the selection and allocation rules. The degree to which the transplanting surgeon has kept some of the original influence over individual allocation decisions, is variable.

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2.1 | Eurotransplant: the European LAS

The Eurotransplant (ET) network was founded in 1967 and today consists of Austria, Belgium, Croatia, Germany, Hungary, Luxembourg, the Netherlands, and Slovenia, serving a total population of around 136 million people. Until 2007, the lung allocation in ET was based on national allocation according to acuity and/or time on wait-list. Additionally, there was a category termed “High Urgency.” It was defined by medical criteria and granted supranational priority. In 2007, an adapted version of the LAS was introduced, called the Eurotransplant LAS (ET LAS). There are some differences between the ET LAS and the LAS in the USA, for instance in that the ET LAS includes information about extra corporal life support. In ET, the LAS is used to determine supranational priority, defined by a LAS > 50. An important twist is that the patient with a score over 50 only gets the organ if the organ exchange balance of the patient’s country is positive with the country of the donating center. In other words, the ET LAS is “less geographic” than the US LAS in that no local allocation is made in cases with LAS > 50, but still national organ exchange balance trumps acuity. While Germany and the Netherlands use the LAS to determine the entire national allocation (ie, also for cases with LAS < 50), with no geographic boundaries within the country, the other ET countries allocate recipients with a LAS < 50 by so-called “centre decision,” which is based on clinical judgment with a varying degree of written criteria. Extended criteria organs are allocated independently of the ET LAS by so-called rescue allocation, granting the organ to the first center expressing interest. In Germany, such organs amount to about a third of the total number of organs, and these may be allocated at the accepting center’s discretion.

2.2 | National allocation systems: France, UK, Switzerland, and others

Some countries in Europe have rejected the use of a scoring system for allocation of organs, and instead introduced other ways to organize priority. In France (67 million inhabitants), there are 11 LTx centers, each supplied with organs from a geographically defined area. In 2007, definitions of acuity which granted the right to national priority were introduced, based on rather straightforward clinical criteria, as recently reviewed. A comparable system defining high urgency recipients has been operating in Spain (46 million inhabitants) since at least 1998. There are eight centers for LTx in Spain. Similarly, after considering an introduction of the LAS, criteria based rules for national allocation of organs were introduced in the UK (63 million inhabitants) in 2017. Although introduced surprisingly late, the UK system is underpinned by detailed guidelines for patient selection, acuity assessment and donor matching, which take into account factors including

### TABLE 1  Organ donation, lung transplantation, and organ donation systems in selected countries

| Country            | Utilized deceased organ donors (PMI) | Lung transplants (PMI) | Organ donation systema | Allocation system                                      |
|--------------------|--------------------------------------|------------------------|------------------------|--------------------------------------------------------|
| United Kingdom     | 24.31                                | 2.84                   | Opt-inb                | Supraregional by criteria of urgency15                 |
| Germany            | 11.6                                 | 4.56                   | Opt-in                 | Eurotransplant; Supraregional and local by LAS10       |
| The Netherlands*   | 15.18                                | 4.35                   | Opt-in                 | Eurotransplant; Supraregional and local by LAS6        |
| Belgium            | 29.91                                | 10.09                  | Opt-in                 | Eurotransplant; Supraregional by LAS, local by center decision5 |
| France             | 28.85                                | 5.86                   | Opt-out                | Supraregional by criteria of urgency12,13              |
| Italy              | 24.72                                | 2.43                   | Opt-out                | Variable9                                              |
| Spain              | 48.3                                 | 7.95                   | Opt-out                | Supraregional by criteria of urgency14                 |
| Sweden             | 19.1                                 | 7.4                    | Opt-out                | Scandiatransplant, Supranational by center discretion, max3/year18 |
| Switzerland        | 18.59                                | 4.94                   | Opt-in                 | National by criteria (federal law)17                   |
| Poland             | 13.07                                | 1.13                   | Opt-out                | Not known to us                                        |
| USA                | 32.81                                | 7.84                   | Opt-in                 | Regional by LAS                                        |
| Canada*            | 21.91                                | 9.51                   | Opt-in                 | Regional, by center discretion20                       |
| Australia          | 22.34                                | 8.95                   | Opt-in                 | Supraregional by criteria of urgency21                 |
| Japan              | 0.75                                 | 0.56                   | Opt-in                 | Not known, often directed living donation23            |
| South Korea        | 10.1                                 | 1.82                   | Opt-in                 | Supraregional by criteria of urgency22                 |

Note: All data are for 2018 except * which are for 2017. Data are based on the Global Observatory on Donation and Transplantation (GODT) data, produced by the WHO-ONT collaboration.

Abbreviation: PMI: per million inhabitant.

The organ donation system is termed “Opt-in” for systems that require explicit donor consent, and “Opt-out” for systems that apply presumed or deemed consent. Neither term is necessarily accurate, as additional factors may apply.

In the United Kingdom, Wales has an “Opt-out” system.

In Spain, there is no official Opt-out registry, according to Arshad et al.
donor and recipient size and even include an appendix of donor acceptability criteria. The system provides an impressively detailed algorithm by which organs are granted to named super-urgent and urgently listed patients and thereafter to non-urgent patients at each of the six UK transplant centers, where individual recipient selection remains at the discretion of the center. Simultaneously, a detailed guide for patient selection criteria were issued in the UK. This is particularly commendable, considering the low level of transparency ensuing the vague or even absent written statements for listing criteria and donor acceptability criteria in most other regions of the world. In Switzerland (8.5 million inhabitants), there is national allocation based on waiting time at the two centers for LTx. Here, a federal law introduced in 2007 regulates the prioritized national allocation according to a specific algorithm, which, for instance, specifies and “urgent” status for an intubated and ventilated patient. Based on the estimated medical benefit, LTx centers can accept or refuse an organ offer. In Italy, the European LAS was introduced for allocation at one center in 2016, while other centers allocate according to clinical judgment.

2.3 | Scandiatransplant: collaboration, no score

The Nordic countries collaborate through Scandiatransplant (totally about 27 million inhabitants). Here, national allocation is based on center judgment at each of the six-member centers, located in five countries. A unique feature in this region is that since 2009, each center may nominate a limited number of highly urgent recipients (currently 3/yr/center) for supranational priority.

2.4 | International organ exchange across Europe

In Europe, international organ exchange aims for the optimal distribution of donor organs by offering them to a suitable transplant candidate in another country if there is no suitable transplant candidate on the national waiting-list of the donor’s country. The European Union (EU) passed the necessary legislation in 2010. Nowadays, most European countries already participate in cross-border organ exchange either through bilateral agreements and/or broader alliances such as ET, but organ exchange across such defined areas do occur.

2.5 | Canada, Australia, Latin America, South Korea, Japan

Although beyond the scope of this review, a brief mentioning of centers outside Europe and the United States may be appropriate at this point, as most of these centers may bear resemblance to some European system. In Canada, there is regional allocation with local allocation at the four lung transplant centers and no systematic national organ exchange. This is similar to the UK system before 2017. The lack of national allocation is presumably partly due to the vast geographic distances in the central and western parts of the country. In the east, language may play a role. In Australia, there is local allocation at the four LTx centers, with some degree of national organ exchange based on clinical criteria, somewhat similar to the French system. There are organ exchange collaborations between Argentina and Paraguay, but the LTx is still in rapid development in Latin America, and defined rules for allocation are not yet known to us. In Asia, there is national allocation based on medical acuity in South Korea. In Japan, a large number of LTx are performed with living donors, often tied to directed allocation. Allocation rules for other Asian countries are not known to us.

3 | DIFFERENCES BETWEEN THE USA AND EUROPE

Although the total number of LTx performed is comparable in the USA and Europe, there are significant differences regarding patients’ selection and organ allocation. Simplified, it might be said that in the USA, there is a high potential mobility for the patients between various transplant centers, where the only limitation for patient flexibility seems to be financial, while in Europe, nationality and language may hinder such mobility. Conversely, in the USA, there are no formalized rules for organ sharing across defined areas; all organs are allocated locally first. In contrast, many European countries participate in organ sharing collaborations of some sort, as mentioned, increasing the mobility of organs.

3.1 | Strengths and limitations of scoring systems

Since the introduction of the LAS in the USA in 2005, the use of scoring systems for allocation has been discussed at many European centers. While it was introduced for high urgency organ exchange in ET and for all regular allocation in Germany and in The Netherlands, it was rejected in France, UK, Scandiatransplant, and elsewhere. The LAS in both Eurotransplant and in the USA is thought to represent an objective numeric expression of acuity (ie, risk of death within a year if no transplant occurs), and, to a lesser degree, benefit (ie, chance of survival for one year after transplant). As such, it is reproducible and accountable and avoids the unfortunate effects of allocation based on time on wait-list. It may possibly also reduce the risk of opaque, center, or physician based decisions. However, the LAS is based on a calculation that may be difficult to understand. It also implies some ethical choices that are not immediately evident. For instance, the LAS adds extra weight to acuity and does not include information of survival >1 year. This is presumably a response to the mandate from the US government to reduce wait-list deaths, but may come at the cost of long-term survival after LTx, which may be shorter in the most urgent patients. It is also a purely utilitarian model, aiming at optimizing survival benefit (ie, the relationship between lifetime lost if not transplanted and lifetime won if transplanted) while not considering factors such as life years lost (which would favor the young) or resource use (which possibly would favor the less acutely
ill) or quality of life. Finally, it has been criticized for not predicting acuity very well and for being hard to update, although there is an appeal system both in the USA and in Eurotransplant. Finally, while the LAS is a highly specific system for allocation, expressed at the level of decimals, paradoxically, there are often no clear criteria for recipient selection at the single centers, except for the very widely defined patient selection criteria published in the ISHLT consensus document in 2015. The suitability of a scoring system for organ allocation may therefore depend on what system it is supposed to replace; and in Europe, different regions have found different solutions, a typical European approach probably also emphasizing its cultural and political heterogeneity.

4 | FUTURE DIRECTIONS

Although the number of lung transplants performed may have peaked in the wealthier countries of Europe, growth may still be expected in some regions, such as Eastern and South-Eastern Europe. These countries may wish to seek collaboration within existing organ exchange organizations, such as ET and Scandiatransplant. The ensuing increase in number of countries and the greater heterogeneity between collaborating countries (both regarding health care systems, and more general issues such as culture and language) may pose challenges to the established organizations regarding transparency and efficiency of the allocation systems.

The authors are unable to predict the future of lung allocation rules in Europe, but it seems reasonable to assume that increased immigration as seen over recent years may affect the view on the European allocation rules, both by increasing the numbers of persons in need and by changing the spectrum of primary diagnosis, with many of the migrants originating from areas of the world with very different circumstances for health care. Furthermore, the use of nationality to define eligibility may be increasingly challenged.

REFERENCES

1. Venuta F, Van Raemdonck D. History of lung transplantation. J Thorac Dis. 2017;9(12):5458-5471.
2. Azzi JR, Sayegh MH, Mallat SG. Calcineurin inhibitors: 40 years later, can’t live without. J Immunol. 2013;191(12):5785-5791.
3. Steen S, Sjöberg T, Pierre LJ, Eriksson L, Algotssson L. Transplantation of lungs from a non-heart-beating donor. Lancet. 2001;357(9259):825-829.
4. http://www.transplant-observatory.org/summary/. last accessed April 01; 2020.
5. The Fix for the American Health Care System can be Found in Europe. The Economist. August 10; 2017.
6. https://www.eurotransplant.org/cms/index.php?page=cooperation_brief. last accessed April 01; 2020.
7. Smits JM, Nossent GD, Vries ED, et al. Evaluation of the lung allocation score in highly urgent and urgent lung transplant candidates in eurotransplant. J Heart Lung Transplant. 2011;30(1):22-28.
8. Smits JM, Nossent G, Evrard P, et al. Lung allocation score: the Eurotransplant model versus the revised US model - a cross-sectional study. Transpl Int. 2018;31(8):930-937.
9. https://www.eurotransplant.org/wp-content/uploads/2020/01/H6-ETHAS.pdf. last accessed April 01, 2020.
10. Gottlieb J, Greer M, Sommerwerck U, et al. Introduction of the lung allocation score in Germany. Am J Transplant. 2014;14(6):1318-1327.
11. Gottlieb J, Smits J, Schramm R, et al. Lung transplantation in Germany since the introduction of the lung allocation score. Dtsch Arztebl Int. 2017;114(11):179-185.
12. Roussel A, Sage E, Massard G, et al. Impact of donor, recipient and matching on survival after high emergency lung transplantation in France. Eur Respir J. 2019;54(5):1900096.
13. Holm AM, Gottlieb J. Saving those who can’t wait. Eur Respir J. 2019;54(5):1901668.
14. Román A, Calvo V, Ussetti P, et al. Urgent lung transplantation in Spain. Transplant Proc. 2005;37(9):3987-3990.
15. http://odt.nhs.uk/pdf/lung_allocation_policy.pdf. last accessed April 01, 2020.
16. http://odt.nhs.uk/pdf/lung_selection_policy.pdf. last accessed April 01, 2020.
17. https://www.admin.ch/opc/de/classified-compilation/20062074/index.html, last accessed April 01, 2020.
18. Auråén H, Schultz HHL, Hämäinnen P, et al. Urgent lung allocation system in the Scandiatransplant countries. J Heart Lung Transplant. 2018;37(12):1403-1409.
19. https://www.eurotransplant.org/about-eurotransplant/internatio nal-organ-exchange/. last accessed April 01, 2020.
20. https://www.cst-transplant.ca/cgi/page.cgi/transplant-programs opos.html, last accessed April 01, 2020.
21. https://www.tsanz.com.au/TSANZ_Clinical_Guidelines_Versio n1.3%5B698%5D.pdf, last accessed April 01, 2020.
22. Haam SJ, Lee DY, Paik HC. An overview of lung transplantation in Korea. Transplant Proc. 2008;40(8):2620-2622.
23. Date H. Current status and problems of lung transplantation in Japan. J Thorac Dis. 2016;8(Suppl 8):S63-636.
24. https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf, last accessed April 01, 2020.
25. Banga A, Mohanka M, Mullins J, et al. Incidence and variables associated with 30-day mortality after lung transplantation. Clin Transplant. 2019;33(2):e13468.
26. Russo MJ, Iribarne A, Hong KN, et al. High lung allocation score is associated with increased morbidity and mortality following transplantation. Chest. 2010;137(3):651-657.
27. Weill D, Benden C, Corris PA, et al. A consensus document for the selection of lung transplant candidates: 2014– an update from the pulmonary transplantation council of the international society for heart and lung transplantation. J Heart Lung Transplant. 2015;34(1):1-15.
28. https://ec.europa.eu/eurostat/statistics-explained/index.php/Migration_and_migrant_population_statistics, last accessed April 01, 2020.
29. Arshad A, Anderson B, Sharif A. Comparison of organ donation and transplantation rates between opt-in and opt-out systems. Kidney Int. 2019;95:1453-1460.

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