

Heart transplantation and left ventricular assist systems: not too early, not too late

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This article refers to ‘Screening for heart transplantation and left ventricular assist system: results from the ScrEEning for advanced Heart Failure treatment (SEE-HF) study’ by L.H. Lund *et al.*, published in this issue on pages 152–160.

Although heart transplantation (HT) and the implantation of a left ventricular assist device (LVAD) both provide clear benefits with respect to the natural history of advanced heart failure (HF), with 1-year survival rates of around 80–90%,^{1, 2} many have had the impression that these advanced therapies are often underused – not just because of short supply or cost, but because of short demand, i.e. failure to refer suitable patients. This notion is supported by the fact that the frequency with which these therapies are employed varies not only from country to country³ (*Figure 1*) but also among different regions of the same country, even when no causative significant differences in supply or cost are to be expected. For example, among the 17 Spanish autonomous communities, those two with the lowest HT rates do not have their own HT programmes (HT patients are referred to other communities), which suggests that the low rates may in part be due to a tendency to overlook the possibility of HT.⁴ Of course, it is also true that, for a number of reasons, including the subjectivity of many partial criteria of advanced HF, it is often difficult to detect whether a ‘stable HF’ patient is eligible for HT or LVAD implantation.

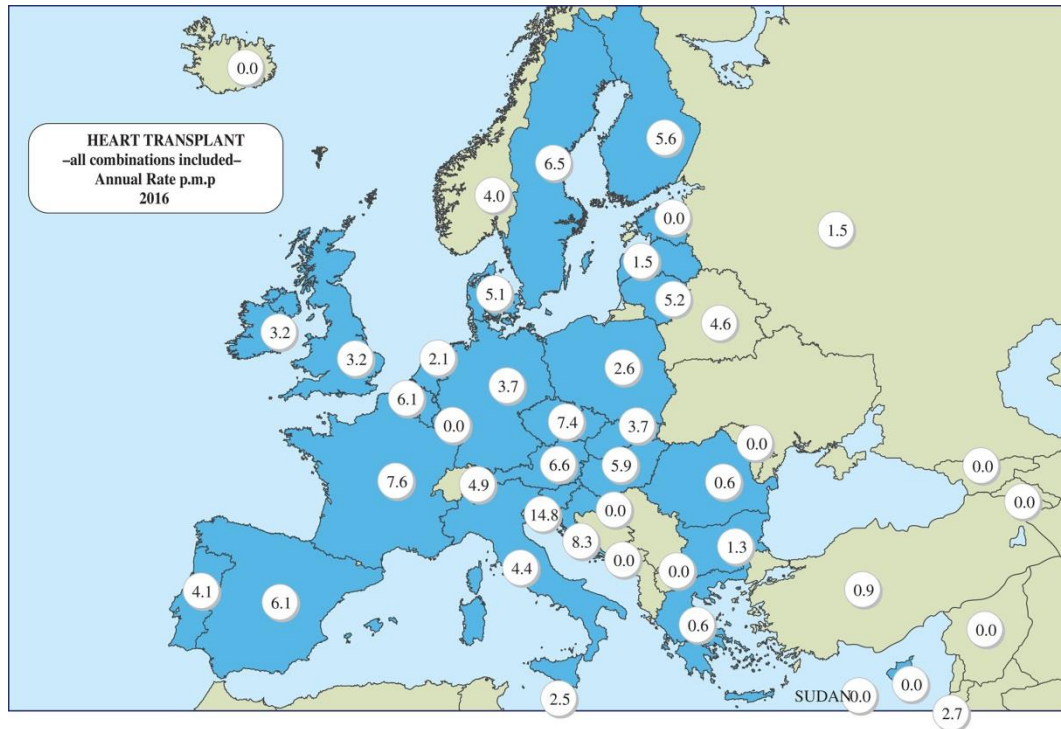


Figure 1. Heart transplantation rates in Europe in 2016 (patients per million population) according to the Global Observatory on Donation and Transplantation.³ ‘The data and information presented here are published in order to promote transparency in transplantation activities. They are the most reliable facts available to date to “Global Observatory on Donation and Transplantation” knowledge.’

In this issue of the Journal, Lund and colleagues report the results of the ScREENing for advanced Heart Failure treatment (SEE-HF),⁵ a multicentre study in which a two-stage screening protocol was applied to patients with a cardiac resynchronization therapy (CRT) or implantable cardioverter defibrillator (ICD) device to detect those who were eligible for HT or LVAD implantation. Eight centres in seven European countries participated, all of which had an LVAD programme and six of the eight an HT programme. The criterion for passage from stage 1 to stage 2 of the screening protocol was that the patient was stable under optimal medical management, have New York Heart Association (NYHA) class III–IV HF symptoms and an ejection fraction (EF) $\leq 40\%$, and consent to undergo stage 2, i.e. further detailed work-up for eligibility for HT and LVAD in accordance with the latest American and European guidelines.^{6–9} Patients meeting eligibility criteria were offered listing for HT or implantation of an LVAD. No randomization, blinding or control group were used.

Of 1722 screened patients, 121 (7%) fulfilled the medical criteria, 99 of whom consented to further work-up (5.7%). For 23 of the 99 (23%) HT or LVAD implantation was indicated without any contraindication, but the indicated intervention (listing for HT or LVAD implantation) was accepted by only 11 of these 23, i.e. 11% of those who had accepted further work-up (three more were listed for HT or received an LVAD despite a guideline-based contraindication).

Although analysis of the results was limited by the unexpectedly small sample size (recruitment having been slow and consequently having been terminated before the desired sample size was reached), the authors of this innovative study are to be congratulated, for it has confirmed that active screening can find candidates for HT or LVAD implantation to whom these therapies would not otherwise have been offered at so early a date. In the present study, HT or LVAD implantation were offered to almost one-quarter of the patients who progressed to stage 2 screening, i.e. the consenting stable patients who had reduced EF and NYHA class III–IV

symptoms as well as an implanted ICD or CRT. Although the yield of the first stage of the screening process was only 7% (as was to be expected, as many patients have an ICD or CRT to correct heart conditions that do not involve advanced HF), it would nevertheless seem amply to justify the relatively small effort of screening for reduced EF and NYHA class III–IV, given the high yield of the second stage and the clear prognostic benefit of HT and LVAD implantation.^{1, 2}

It would not seem to be reasonable to require stage 2 screening to be carried out in an ordinary CRT/ICD clinic. Rather, stage 2 screening should probably be performed in dedicated advanced HF units by cardiologists with specific training in the care of advanced HF patients, such as those who since 2008 have been recognized by the American Board of Medical Specialties as having the secondary subspecialty of Advanced HF and Transplant Cardiology^{10, 11} or the Heart Failure Association of the European Society of Cardiology HF curriculum,¹² which is a programme designed to last 2 years, and in the second year possible to choose between four different modules of which one is specific for HT and mechanical circulatory support. The development in some countries of quality standards that define units of advanced HF is an important step forward to improve the quality of care of these patients.^{13, 14} A possible collateral advantage of screening for HT and LVAD candidates might be the reinforcement of procedures for referral to such units from centres that lack them.^{13, 15, 16}

The reason for wishing to perform HT or LVAD implantation as soon as advancing HF makes the patient a candidate is of course that the patient's condition may otherwise deteriorate so quickly (i.e. end-organ damage, particularly liver, kidney or lung) that these therapies become contraindicated. It should not be forgotten that the contrary can also occur: it is not unknown for a patient listed for HT to improve to the point of having to be removed from the list. Also, the condition of a patient for whom HT or LVAD implantation is indicated may, over time, evolve to make the other therapy more suitable; and an LVAD implanted as a bridge to transplant may eventually be seen as the more appropriate destination therapy, or vice versa.^{6, 17} Thus, screening for HT and LVAD implantation candidates should certainly not determine subsequent therapy irrevocably. Lund *et al.* have nevertheless shown convincingly that such screening definitely has a place in the future care of HF patients. It is to be hoped that, by promoting a vision of HT and LVAD implantation, not as interventions to be performed only *in extremis*, but as rather more routine procedures, it may also help overturn Lund *et al.*'s other crushing result: the rejection of these therapies by half the patients to whom they were offered.

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References

1. Lund LH, Edwards LB, Dipchand AI, Goldfarb S, Kucheryavaya AY, Levvey BJ, Meiser B, Rossano JW, Yusen RD, Stehlik J; International Society for Heart and Lung Transplantation. The Registry of the International Society for Heart and Lung Transplantation: Thirty-third Adult Heart Transplantation Report-2016; Focus Theme: Primary Diagnostic Indications for Transplant. *J Heart Lung Transplant* 2016;35:1158–1169.
2. Gustafsson F, Rogers JG. Left ventricular assist device therapy in advanced heart failure: patient selection and outcomes. *Eur J Heart Fail* 2017;19:595–602.
3. Global Observatory on Donation and Transplantation. International figures on donation and transplantation 2016. *Newsletter Transplant* 2017;22(1). [Accessed: 20 September 2017]. Available from: <http://www.transplant-observatory.org/download/newsletter-2017/>.
4. Organizacion Nacional de Trasplantes. Memoria Trasplante Cardiaco 2016. [Accessed: 20 September 2017]. Available from: <http://www.ont.es/infesp/Memorias/Memoria%20Coraz%C3%B3n.pdf>.
5. Lund LH, Trochu J-N, Meyns B, Caliskan K, Shaw S, Schimitto JD, Schibilsky D, Damme L, Heatley J, Gustafsson F. Screening for heart transplantation and left ventricular assist system: results from the ScREEning for advanced Heart Failure treatment (SEE-HF) study. *Eur J Heart Fail* 2017;doi:<https://doi.org/10.1002/ejhf.975>. [Epub ahead of print]
6. Peura JL, Colvin-Adams M, Francis GS, Grady KL, Hoffman TM, Jessup M, John R, Kiernan MS, Mitchell JE, O'Connell JB, Pagani FD, Petty M, Ravichandran R, Rogers JG, Semigran

- MJ, Toole JM; American Heart Association Heart Failure and Transplantation Committee of the Council on Clinical Cardiology, Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, Council on Cardiovascular Disease in the Young, Council on Cardiovascular Nursing, Council on Cardiovascular Radiology and Intervention, and Council on Cardiovascular Surgery and Anesthesia. Recommendations for the use of mechanical circulatory support: device strategies and patient selection: a scientific statement from the American Heart Association. *Circulation* 2012;126:2648–2667.
7. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K, Falk V, Filippatos G, Fonseca C, Gomez-Sanchez MA, Jaarsma T, Køber L, Lip GY, Maggioni AP, Parkhomenko A, Pieske BM, Popescu BA, Rønnevik PK, Rutten FH, Schwitter J, Seferovic P, Stepinska J, Trindade PT, Voors AA, Zannad F, Zeiher A; ESC Committee for Practice Guidelines. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2012;14:803–869.
 8. Feldman D, Pamboukian SV, Teuteberg JJ, Birks E, Lietz K, Moore SA, Morgan JA, Arabia F, Bauman ME, Buchholz HW, Deng M, Dickstein ML, El-Banayosy A, Elliot T, Goldstein DJ, Grady KL, Jones K, Hryniewicz K, John R, Kaan A, Kusne S, Loebe M, Massicotte MP, Moazami N, Mohacsi P, Mooney M, Nelson T, Pagani F, Perry W, Potapov EV, Eduardo Rame J, Russell SD, Sorensen EN, Sun B, Strueber M, Mangi AA, Petty MG, Rogers J; International Society for Heart and Lung Transplantation. The 2013 International Society for Heart and Lung Transplantation Guidelines for mechanical circulatory support: executive summary. *J Heart Lung Transplant* 2013;32:157–187.
 9. Mehra MR, Canter CE, Hannan MM, Semigran MJ, Uber PA, Baran DA, Danziger-Isakov L, Kirklin JK, Kirk R, Kushwaha SS, Lund LH, Potena L, Ross HJ, Taylor DO, Verschuuren EA, Zuckermann A; International Society for Heart Lung Transplantation (ISHLT) Infectious Diseases Council; International Society for Heart Lung Transplantation (ISHLT) Pediatric Transplantation Council; International Society for Heart Lung Transplantation (ISHLT) Heart Failure and Transplantation Council. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: a 10-year update. *J Heart Lung Transplant* 2016;35:1–23.
 10. Francis GS, Greenberg BH, Hsu DT, Jaski BE, Jessup M, LeWinter MM, Pagani FD, Piña IL, Semigran MJ, Walsh MN, Wiener DH, Yancy CW Jr. ACCF/AHA/ACP/HFSA/ISHLT 2010 clinical competence statement on management of patients with advanced heart failure and cardiac transplant: a report of the ACCF/AHA/ACP Task Force on Clinical Competence and Training. *Circulation* 2010;122:644–672.
 11. Jessup M, Drazner MH, Book W, Cleveland JC, Jr., Dauber I, Farkas S, Ginwalla M, Katz JN, Kirkwood P, Kittleson MM, Marine JE, Mather P, Morris AA, Polk DM, Sakr A, Schlendorf KH, Vorovich EE. 2017 ACC/AHA/HFSA/ISHLT/ACP Advanced Training Statement on Advanced Heart Failure and Transplant Cardiology (Revision of the ACCF/AHA/ACP/HFSA/ISHLT 2010 Clinical Competence Statement on Management of Patients With Advanced Heart Failure and Cardiac Transplant): A Report of the ACC Competency Management Committee. *J Am Coll Cardiol* 2017;69:2977–3001.
 12. McDonagh TA, Gardner RS, Lainscak M, Nielsen OW, Parissis J, Filippatos G, Anker SD. Heart Failure Association of the European Society of Cardiology specialist heart failure curriculum. *Eur J Heart Fail* 2014;16:151–162.
 13. Anguita Sanchez M, Lambert Rodriguez JL, Bover Freire R, Comin Colet J, Crespo Leiro MG, Gonzalez Vilchez F, Manito Lorite N, Segovia Cubero J, Ruiz Mateas F, Elola Somoza FJ, Íñiguez Romo A. Classification and quality standards of heart failure units: scientific consensus of the Spanish Society of Cardiology. *Rev Esp Cardiol (English Edn)* 2016;69:940–950.
 14. Westenbrink BD, Brugts JJ, McDonagh TA, Filippatos G, Ruschitzka F, van Laake LW. Heart failure specialization in Europe. *Eur J Heart Fail* 2016;18:347–349.
 15. McDonagh TA, Blue L, Clark AL, Dahlstrom U, Ekman I, Lainscak M, McDonald K, Ryder M, Strömberg A, Jaarsma T; European Society of Cardiology Heart Failure Association Committee on Patient Care. European Society of Cardiology Heart Failure Association Standards for delivering heart failure care. *Eur J Heart Fail* 2011;13:235–241.
 16. Aspromonte N, Gulizia MM, Di Lenarda A, Mortara A, Battistoni I, De Maria R, Gabriele M, Iacoviello M, Navazio A, Pini D, Di Tano G, Marini M, Ricci RP, Alunni G, Radini D, Metra M, Romeo F. ANMCO/SIC Consensus Document: cardiology networks for outpatient heart failure care. *Eur Heart J Suppl* 2017;19(Suppl D):D89–D101.
 17. Steffen RJ, Blackstone EH, Smedira NG, Soltesz EG, Hoercher KJ, Thuita L, Starling RC, Mountis M, Moazami N. Optimal timing of heart transplant after HeartMate II left ventricular assist device implantation. *Ann Thorac Surg* 2017;104:1569–1576.