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# Are mechanical circulatory supports the forgotten aspect in the implementation of therapies for heart failure?

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Heart failure (HF) is a frequent and severe condition. It is estimated that one in four patients will die within a year following hospitalization for acute decompensation, with significant variations across age strata. A recent study reported that the 1-year mortality following hospitalization for HF was 9%, 14%, and 18% for patients under 55, between 55–64, and 65–74 years, respectively.<sup>1</sup> Higher values are found when older and unselected patients are included.<sup>2</sup>

Another rather recent worrisome finding is the increase in the incidence of HF among younger individuals due to a rise in ischaemic heart disease, especially among men aged 36–50 years in Europe.<sup>3</sup> Although younger than 50 years, this population will experience a 25% readmission rate for HF, and 75% for all causes with a mortality exceeding 10% at 2 years.<sup>3</sup> Consistent data show an increasing incidence of cardiogenic shock following myocardial infarction among the young, along with an associated increase in mortality from ischaemic cardiogenic shock within this same demographic.<sup>4</sup> Moreover, epidemiological data confirm that mortality due to HF among young individuals is generally on the rise in North America, even as the availability of treatments and devices continues to increase.<sup>5</sup> This subgroup of young patients who develop acute coronary syndrome followed by severe cardiac dysfunction and HF is an obvious target for treatment with long-term mechanical circulatory support (MCS) and heart transplantation.

The treatment for HF with reduced ejection fraction relies on four therapeutic classes including beta-blockers, renin–angiotensin system inhibitors, mineralocorticoid receptor antagonists (MRAs), and sodium–glucose cotransporter 2 inhibitors (SGLT2i), each with a class I recommendation.<sup>6</sup> Meta-analyses of randomized clinical trials demonstrate that the implementation of these four classes could reduce all-cause mortality by 61%, with an estimated increase in survival of 5 years for a patient who would be 70 years old.<sup>7</sup> However, tolerance of HF treatments is poor, with

discontinuation rates ranging from 23% (SGLT2i) to 42% (MRAs) at 1 year according to a multinational observational study.<sup>8</sup> This intolerance is a sign of advanced HF, and the more risk factors patients have, the higher the likelihood of treatment intolerance becomes.<sup>9</sup> In these populations with advanced disease, significant myocardial fibrosis makes hormonal therapies ineffective and intolerable, necessitating invasive mechanical therapies based on Laplace's law to reduce left ventricular intraluminal pressure.<sup>10</sup>

For selected patients suffering from advanced HF, transplantation is recommended as class I, and long-term MCS are recommended as class IIa for bridge to decision or transplantation or as destination therapies in the 2021 European Society of Cardiology (ESC) HF guidelines and as class I in the 2022 American Heart Association/American College of Cardiology/Heart Failure Society of America guidelines.<sup>6,11</sup> These recommendations are supported by the excellent long-term results of the latest generations of centrifugal pumps, with a survival rate of over 56% at 5 years in randomized trials and registries, corresponding to an absolute 22% reduction in all-cause mortality at 5 years between axial and centrifugal pumps.<sup>12,13</sup> With the number of heart transplants per country limited by the availability of grafts, optimizing the care of patients with advanced HF primarily relies on the implementation of long-term MCS. However, data evaluating the evolution of practices in Europe are scarce.

To assess the implementation of left ventricular assist devices (LVADs) following the 2021 ESC HF guidelines<sup>6</sup> and the dissemination of long-term results from the MOMENTUM 3 trial,<sup>13</sup> we analysed market data reflecting the sales of long-term MCS systems across various countries from 2018 to 2023. These data serve as a reliable proxy for MCS implantation rates. Our focus was on European nations that reported a minimum of 30 MCS implantations in 2018. It is worth noting that over 98% of implanted MCS devices were LVADs.

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We observed an eight-fold variation in LVAD use per capita across European countries ranging from 1.1 to 8.7 implantations per million inhabitants (IPMI) in the United Kingdom (UK) and Germany, respectively (Figure 1). Countries can be schematically divided into three groups according to the rate of implantations: (1) high-implantation countries including Germany and the Czech Republic with rates between 7 and 8 IPMI; (2) intermediate-rate countries between 4 and 6 IPMI including the Netherlands, Austria, Belgium, and Switzerland; and (3) low-implantation countries with rates between 1 and 3 IPMI including Poland, Italy, Sweden, France, and the UK. The number of implantations does not appear to be explained solely by device reimbursement (online supplementary Table Appendix S1.). Indeed, although LVADs are fully reimbursed in countries with high implantation rates, we note that some countries with full reimbursement implant very few (France and Italy, for example).

The trend in the number of implantations between 2018 and 2023, including the period of the COVID-19 pandemic, exhibited significant variations across countries. The COVID period was associated with a reduction in the number of implantations in the majority of European countries.<sup>14</sup> Focusing on Germany and France, which led in implant numbers in 2018, there was a general downward trend in implantations from 2018 to 2022. However, Germany experienced a reversal, concluding with a modest reduction of 13%, in contrast to France, where the decline persisted, culminating in a 42% decrease.

Countries were divided into three groups according to the change in implantation rate over the 2018–2023 period: (1) countries with a significant decrease, experiencing more than a 25% reduction in activity including France (–42%), the UK (–40%), Sweden (–31%), and Switzerland (–29%); (2) stable countries with a change of <25% including Germany (–13%), Belgium (–9%), Austria (–4%), and Italy (8%); and (3) countries with a significant increase (>25%) including the Netherlands (27%), Poland (67%), the Czech Republic (105%), and Spain (122%). The change in the number of implantations between 2018 and 2023 appears to be independent of a country's implantation rate, with countries exhibiting intermediate implantation rates demonstrating all three possible trends in evolution. It is important to acknowledge that a low baseline implantation rate results in greater variability in percentage calculations.

These data highlight the significant disparity in the rate of LVAD implantation in Europe, the highly variable impact of the COVID-19 pandemic on implantation activity, and a very variable evolutionary trend from one country to another between 2018 and 2023. A presentation of the LVAD per millions of inhabitants/HF prevalence ratio would be useful to describe LVAD utilization, but reliable data on the prevalence of HF in Europe are limited by the absence of a universal definition of HF before 2021 and the unavailability of reliable national statistics or registries.<sup>15,16</sup>

The estimated median survival of patients on intravenous inotropes being less than 1 year, and the median survival of ambulatory patients with advanced HF being less than 2 years, the use of LVAD in these patients is justified in order to improve survival outcomes.<sup>10</sup> In the context of a stable number of heart

transplants and a persistent shortage of grafts in Europe, the lack of global implementation of LVAD or even a significant reduction in the number of implantations in some countries raises questions.

Several factors may account for this inertia: (i) improvement in pharmacological therapies; (ii) insufficient and late referral; (iii) gaps in the evidence of efficacy of MCS in ambulatory advanced HF patients; (iv) changes in the criteria for heart graft allocation, placing LVAD recipients at a disadvantage; and (v) insufficient acceptance of LVAD by patients and medical teams.

The improvement in HF therapies is real and constant. However, the increase in mortality among young patients and the residual mortality reaching 10% and 20% within a year following hospitalization makes this hypothesis unlikely to explain the lack of implementation.

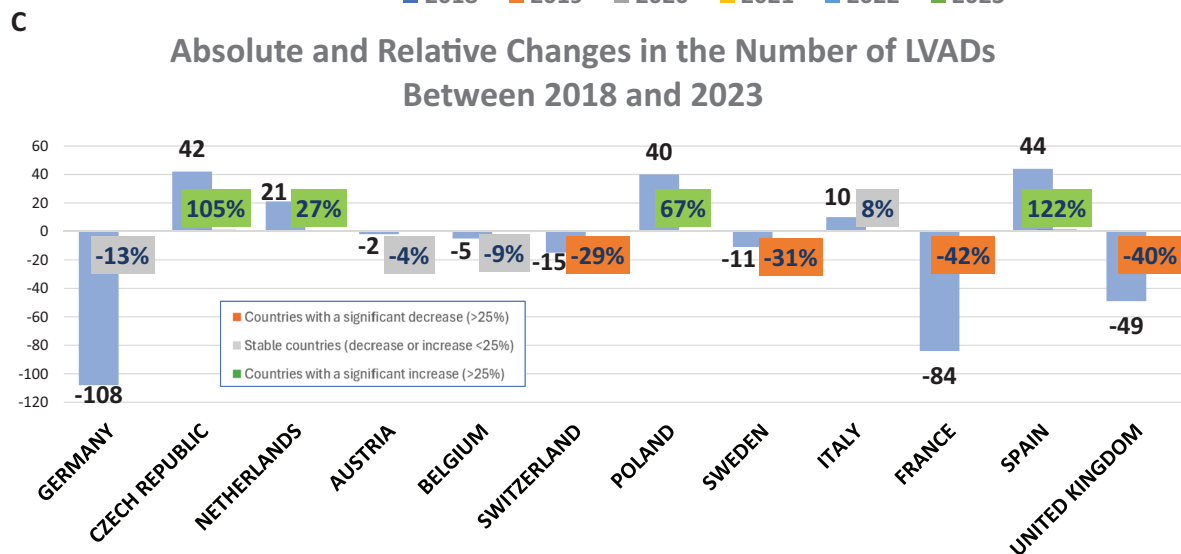
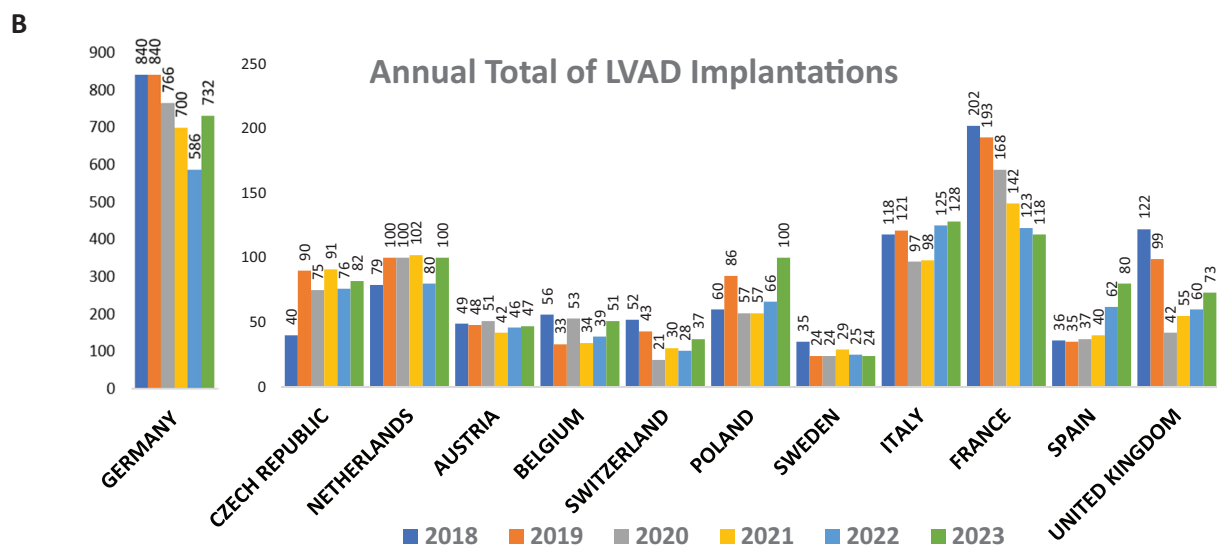
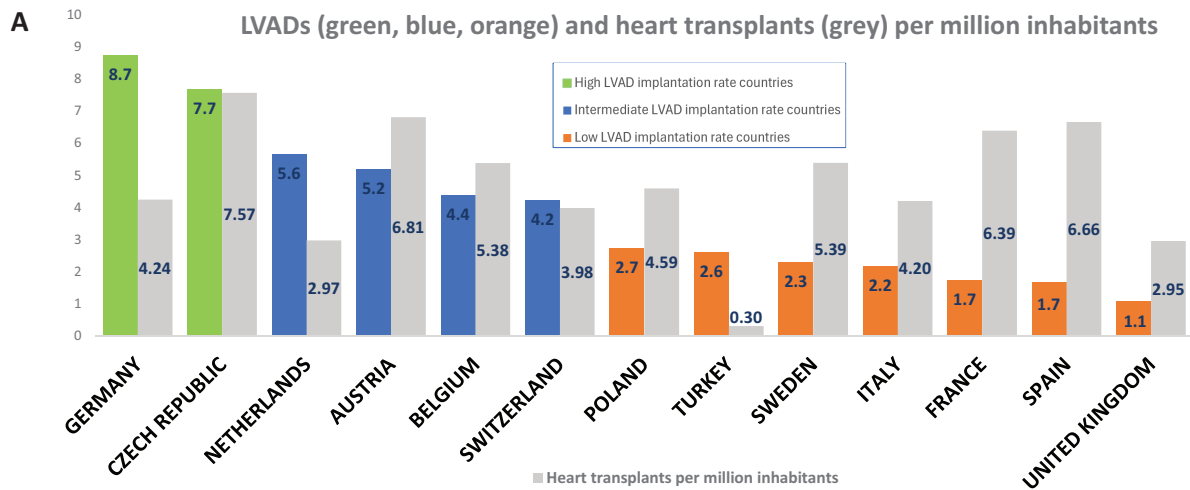
The challenges of referral, likely exacerbated by the COVID crisis, are a probable explanation for our results. Special attention to the structuring of the network, and the education of patients and cardiologists to the definition of advanced HF, is necessary to improve referral and the number of patients who could benefit from LVAD.

As emphasized in the latest HF guidelines,<sup>6</sup> the optimal timing for MCS implantation in non-inotrope-dependent advanced HF patients is a subject of debate. Randomized studies are currently underway to specify the place of an earlier LVAD implantation in ambulatory advanced HF patients (AMBU-VAD trial, NCT04768322).

Given the favourable survival of patients supported by LVAD, graft allocation systems in France and in the United States have reduced access to transplantation for patients with supports.<sup>17,18</sup> This was associated with a significant decrease in the number of patients implanted with an LVAD before listing or after registration,<sup>19</sup> without reducing mortality on the list nor improving the post-transplant prognosis of isolated heart grafts.<sup>20</sup> It appears necessary to better define the role of LVAD in the treatment of advanced HF to increase the overall survival of patients. Unfortunately, we currently lack information on the relative use of LVADs according to different strategies (bridge to transplant/recovery/candidacy or destination therapy) by country in Europe.

The acceptability of the device by patients and cardiologists remains probably one of the obstacles to its use. Although the new generation of LVADs has significantly reduced the risk of thromboembolic complications, improving survival and prognosis, the persistence of the percutaneous power cable makes acceptance difficult and is associated with a continued risk of infection.

In conclusion, despite the increase in HF mortality among young people and the improvement in MCS, we do not assist to an increase in their use and a decrease in implantations is even observed in most countries. Structuring the network, educating practitioners on referral criteria, and redefining the place of LVADs in access to transplantation are necessary to reduce mortality among young patients suffering from advanced HF.



**Figure 1** Trends in left ventricular assist device (LVAD) implantation in Europe from 2018 to 2023. (A) LVADs (2023) and heart transplants (2022) per million inhabitants by country. (B) Annual total of LVAD implantations by country from 2018 to 2023. (C) Absolute and relative changes in the number of LVAD implantations by country from 2018 to 2023.

## Supplementary Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

**Conflict of interest:** G.B. has received personal fees from Abbott, AstraZeneca, Boehringer Ingelheim and Novartis, outside the submitted work. All other authors have nothing to disclose.

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