Review Article on Extracorporeal Life Support in Thoracic Surgery

Extracorporeal life support as a bridge to lung transplantation: a narrative review

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Background and Objective: The utilization of extracorporeal life support (ECLS) as a bridge to lung transplantation (LTx) has rapidly expanded over recent years in highly urgent patients even though the reported outcomes in current literature are still divergent. The aim of our narrative review was to provide a comprehensive picture on the peri and post-operative outcomes of patients bridged to LTx with this device from the most updated literature in the field.

Methods: The literature about ECLS bridge to LTx was searched on PubMed using a formal strategy. We focused our research on studies published between 2015 and 2022 and in English language. Abstracts, case reports, conference presentations, editorials, expert opinions and review articles were excluded.

Key Content and Findings: ECLS has emerged as a valid tool to bridge critically ill patients to LTx. Some issues, like the selection of candidates and the post-operative outcomes, are still matter of debate in the current reported series. We analyzed 14 papers published in the last seven years and with at least 20 patients to provide an updated overview on this topic. We found that, in highly experienced centers, ECLS can be used as a good strategy to allow critically ill patients to remain eligible to LTx with satisfying post-operative outcomes.

Conclusions: Specific scores and algorithms should be implemented to improve the selection process of candidates who could benefit more from ECLS as a bridge to LTx. Ambulatory/awake ECLS strategies should be always preferred to enroll patients in active rehabilitation programs awaiting LTx, improving short and long-term outcomes and increasing the success of LTx.

Keywords: Extracorporeal life support (ECLS); extracorporeal membrane oxygenation (ECMO); bridge to lung transplantation; outcomes; survival

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Introduction

The expression "bridge to lung transplantation" refers to different strategies to support critically ill patients with an acute decompensation until the organs are available (1). The utilization of extracorporeal devices to bridge a patient to lung transplantation (LTx) is necessary when the use of pre transplant mechanical ventilation is not sufficient to support patients with end-stage irreversible respiratory failure awaiting LTx.

The first experience with extracorporeal membrane oxygenation (ECMO) as a bridge to LTx was reported in 1978 but unfortunately the recipient died 18 days after transplantation because of bronchial anastomotic complication (2). The following clinical experience with extracorporeal life support (ECLS), reported between 1980s and 1990s, showed bad outcomes with high mortality and complication rates (3). In most recent years the use of ECLS as bridge to LTx has rapidly expanded, becoming an important tool in an increasing number of specialized centers with satisfying results, especially in a context of urgency-based allocation system. The paucity of donors and the long waiting time on the list has raised increasingly interest in bridging strategies for patients with end-stage lung disease awaiting transplantation (4).

According to the last International Society of Heart and Lung Transplantation (ISHLT) guidelines, the use of ECLS as a bridge to LTx is recommended in case of: oxygen saturation less than 90% with high flow non-invasive oxygenation devices, hemodynamic instability, use of positive pressure ventilation which could determine lung injuries and secondary organ dysfunction, and inability to perform adequate physical therapy with current support (5). On the other hand, uncontrolled sepsis, older age, lack of center experience with bridging devices could be predictors of negative outcomes (5). In this context, the selection of the candidate who can derive the greatest benefit from ECLS strategies is one of the main issues, indeed highly urgent patients are actually the ones who would benefit most from this support but at the same time they might be considered in clinical conditions which are too severe for these devices.

In general, ECLS as a bridge to LTx is recommended in patients already evaluated as candidates for LTx and preferably in awake conditions to allow liberation from mechanical ventilation and active participation in physical therapy (5,6). Any patient with refractory hypoxemia and hypercapnia and right ventricular failure, despite optimal ventilatory and medical management, is a potential candidate for ECLS. It is important to say that the need for ECLS should be anticipated to place it electively rather than emergently and the placement of this support is determined by patient's condition; if the patient is not an adequate candidate for LTx and has irreversible organ damage ECLS should be avoided, if the patient is already on the waiting list, without any absolute contraindication, ECLS placement should be considered. In more challenging situations, ECLS should be used as a bridge to decision.

In most recent years, the role of ECLS has also been extensively investigated as a bridge to lung re-transplantation (ReTx) (7) keeping in mind the risk factors, such as recipient age, inter-transplant interval, primary graft dysfunction as transplant indication and type of ECLS, before bridging these patients on ECLS to ReTx.

The aim of this paper is to provide a comprehensive review of the most updated literature on short- and long- term outcomes of patients bridged to LTx with extracorporeal mechanical support devices. We present this article in accordance with the Narrative Review reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-22-1163/rc).

Methods

We performed a literature search using on PubMed between May 2022 and July 2022. We combined the terms "ECMO", "ECLS", "bridge", "lung", "transplantation" as MeSH terms.

In addition to a narrative review, we provided a collection of the most updated literature on this topic. After the research using the keywords mentioned above, we identified as eligible studies those published in the last seven years [2015–2022] to provide the most updated overview on current evidences on this topic. All the selected publications were limited to human subjects and were in English language. In order for studies to be deemed eligible for inclusion, at least 20 patients had to be included. Abstracts, case reports, conference presentations, editorials, review articles were excluded. In order to avoid bias, we also decided not to considered studies on ECLS as a bridge to lung re-transplantation, to a multiorgan transplantation. Two investigators (Faccioli E, Inci I) independently reviewed each article. Discrepancies between the two reviewers were resolved by discussion and consensus. The search strategy summary is reported in *Table 1*.

After the selection according to inclusion and exclusion criteria, 14 studies were included in this review.

Results

Circuit and cannulation: basic principles

ECLS devices can replace the function of both heart and lungs. Talking about ECMO, the basic circuit consists of a centrifugal pump, coupled with a hollow fiber membrane oxygenator and oxygen blender and a heparin-coated circuit. ECMO functions share the same principles of cardiopulmonary bypass (CPB), however CPB is typically employed for hours during cardiac surgery, ECMO is designed to support circulation for longer duration so it can be considered as a good strategy to bridge a patient to

Table 1 The search strategy summary

Items	Specification
Date of search	1 May 2022–1 July 2022
Databases and other sources searched	PubMed
Search terms used	"ECMO AND bridge AND lung AND transplantation", "ECLS AND bridge AND lung AND transplantation"
Timeframe	2015–2022
Inclusion and exclusion criteria	All the studies on ECLS bridge to lung transplantation in English language, with at least 20 patients and published between 2015 and 2022 were included. Abstract, case reports, conference presentations, editorials, expert opinions and review articles were excluded. Studies on ECLS bridge to lung retransplantation or multi-organ transplantation were also excluded
Selection process	EF independently selected and reviewed all initial articles, with additional review by II. Final article inclusion was determined by all the authors

ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation.

LTx in patients in whom invasive mechanical ventilation is insufficient to maintain an adequate gas exchange. The available configurations to bridge a patient to LTx are:

(I) Venovenous (VV): traditionally the preferred cannulation involves the insertion of a drainage cannula into the inferior vena cava (IVC) through a femoral vein and a placement of a reinfusion cannula into the superior vena cava (SVC) via the jugular vein;

(II) Venoarterial (VA): for those patients awaiting LTx with an associated hemodynamic failure (for example patients with pulmonary hypertension and right heart dysfunction), the VA configuration is necessary. This configuration involves the cannulation of femoral vein and femoral artery. In some cases, when this configuration does not provide sufficient oxygenation to cerebral and coronary vasculature, a more complex configuration, such as veno-venoarterial (VVA) ECMO is required. This hybrid configuration can return oxygenated blood to both femoral artery and internal jugular vein.

Different bridging strategies

Different ECLS modalities can be used as a bridge to LTx depending to the type of physiologic impairment, the patient's need and the availability of the device in different time periods and in centers. The best configuration is chosen considering different parameters such as partial pressure of carbon dioxide (PCO_2), ratio of partial pressure of oxygen to inspired oxygen fraction and pH (8).

VV ECMO

VV ECMO is the most common configuration used to bridge a patient to LTx. It is generally utilized in patients with refractory respiratory failure who are not able to provide adequate gas exchange despite the maximal ventilatory support. It requires the placement of peripheral catheters: the most common strategy provides that deoxygenated blood is drained from the femoral vein while the oxygenated blood is returned to femoral, jugular or subclavian vein. This configuration provides oxygenation primarily, without the advantages of a VA ECMO, in fact the oxygenated blood goes to the right side of the heart and needs to be pumped to the left side to go to the lungs and to the whole body. For this reason, as a bridging strategy, VV ECMO can only be used in patients without significant hemodynamic impairment, but just with hypercapnic respiratory failure (low flow) or with hypoxia (full flow).

Recently, the jugular cannulation with single-site multi-lumen venous cannula is becoming more and more popular especially as it allows the patients to ambulate (9). This cannula removes blood from a proximal and distal port in the superior and inferior vena cava; after the oxygenation the blood is reinfused and returns to the body through a port oriented towards the tricuspid valve.

VA ECMO

VA ECMO configuration is used for hemodynamic support

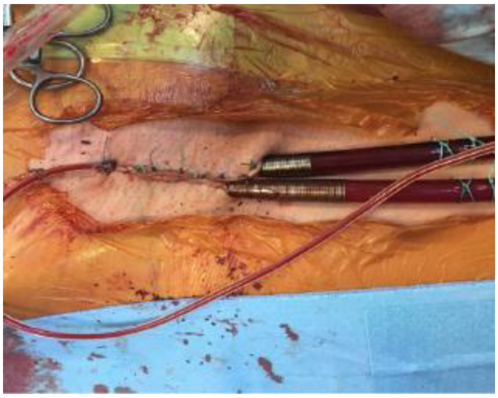

Figure 1 Veno-arterial ECMO with peripheral cannulation and additional cannula for distal reperfusion of the leg. ECMO, extracorporeal membrane oxygenation.

with or without respiratory failure. VA ECMO can replace the functions of both lungs and heart totally or partially. In this case the deoxygenated blood is drained from a vein (outflow) while the oxygenated is reinfused through an artery (inflow), bypassing the pulmonary circulation and unloading it. The standard approach is femoro-femoral with a placement of an additional distal perfusion cannula to prevent limb ischemia (*Figure 1*).

Even though the general principles of gas exchange and blood flow are the same as CPB there are some important differences: in CPB the superior and inferior vena cavae are occluded by the cannulas so all the venous return (except the coronary sinus) goes through the circuit. For this reason, because of a total stagnation of blood in the pulmonary circulation and in some heart chambers, a fully anticoagulation is required. Again, in VA ECMO the flow is generally maintained at about 80% of venous return, so 20% passes through the heart and the lungs and this allows to avoid stagnant flow and clotting. One of the complications which may occur in the VA ECMO setting, especially if the lung function is very poor, is the Harlequin or red feet-blue head syndrome: the systemic blood gases will reflect the mixture of cardiac and extracorporeal flow, resulting in lower oxygenation proximal to the site of mixing. In femoral artery access the mixing takes place in the mid aorta so the upper body is perfused by the blood from the left ventricle resulting in differential circulation with the lower body perfused by fully saturated blood and the upper part with desaturated blood. The management of this situation is to perfuse some of the post-oxygenator blood in the right atrium with an infusion cannula in the jugular vein.

Veno-arteriovenous (VAV) ECMO

In some patients bridged to LTx, VA-ECMO alone may not be sufficient to both oxygenate and assist the hemodynamic state. In fact, in some cases of severe pulmonary dysfunction associated to hemodynamic instability a VA ECMO could not be able to provide adequate upper body oxygenation. If patients with peripheral VA ECMO have inadequate oxygenation of coronary arteries and cerebral vasculature, a hybrid configuration which returns oxygenated blood both in the femoral artery and in jugular vein may be necessary. This configuration, known as VAV ECMO, is quite complex and could limit mobilisation.

Addition of an arterial line to venovenous ECMO

An additional arterial cannula (upgrading) can be added to a VV ECMO by configuring a VVA ECMO in case of a severe right heart dysfunction, providing both respiratory and circulatory support. In this case, blood is drained from veins, oxygenated and returned to the right atrium and a central artery. In case of bridging, if the patient's conditions improve, this configuration allows a switch from VA to VV facilitating ambulation and rehabilitation.

Extracorporeal carbon dioxide removal (ECCO$_2$-R)

The ECCO$_2$-R is an established treatment option in case of acute severe hypercapnic respiratory failure. This device allows to support conventional ventilation adjusting respiratory acidosis consequent to tidal volume reduction in protective ventilation setting. As a bridge to LTx, it is useful to correct isolated hypercapnic failure in chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF) or exacerbation in pulmonary fibrosis patients (10) allowing a more protective ventilation and avoiding in some cases intubation and mechanical ventilation. It also can be used in intubated patients with hypercapnic failure to correct acidosis. Techniques for ECCO$_2$-R include (I) pumpless arterio-venous circuits, (II) low-flow venous circuits based on the technology of continuous renal replacement therapy (III) venovenous circuits based on extracorporeal membrane oxygenation technology.

The indication of ECLS as a bridge to LTx needs to be accurately evaluated day by day and according to patients' conditions the bridging modality can be upgraded or downgraded. For example, an upgrade from VV to VA is mandatory in case of hemodynamic instability or from ECCO2-R to VV ECMO in case of worsening of hypoxia

Table 2 Different ECLS configuration as a bridge to LTx

ECLS configuration	Cannulation	Support provided	Patient conditions
VV ECMO	Peripheral (double lumen cannula in the SVC via the jugular or subclavian vein or single lumen cannula in the femoral vein or jugular and femoral vein)	Respiratory	Hypoxemia
VA ECMO	Peripheral (femoral vessels; jugular/subclavian vein and subclavian artery)	Respiratory + circulatory	Hypoxemia with hemodynamic instability
VAV ECMO	Same as VA ECMO + additional cannula in the jugular vein	Respiratory + circulatory	Hypoxemia + severe right heart dysfunction (in case of inadequate oxygenation of the upper body)
VVA ECMO	Same as VV ECMO + additional cannula in the subclavian artery	Respiratory + circulatory	Hypoxemia + severe right heart dysfunction
$ECCO_2$-R	Peripheral (veno-venous or veno-arterial)	Respiratory	Hypercapnia

ECLS, extracorporeal life support; LTx, lung transplantation; VV, veno-venous; VA, veno-arterial; VAV, veno-arteriovenous; VVA, veno-venoarterial; ECMO, extracorporeal membrane oxygenation; $ECCO_2$-R, extracorporeal carbon dioxide removal; SVC, superior vena cava.

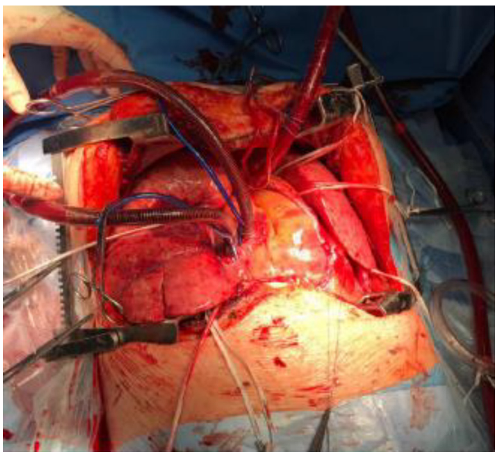

Figure 2 Veno-arterial ECMO with central cannulation (bicaval configuration). ECMO, extracorporeal membrane oxygenation.

and hypercapnia.

Table 2 summarizes the different ECLS configurations as bridge to LTx with the kind of support provided.

Generally, all the patients bridged to LTx with an ECLS device need its prolongation also in the intra-operative setting. For example, a patient with a peripheral VV ECMO could be maintained with this configuration or switched to a peripheral VA during the transplantation, especially in case of necessity of hemodynamic stabilization. The preferred intra-operative ECLS strategy during LTx is the central VA ECMO with the cannulation of aorta and right atrium (*Figure 2*). This strategy was historically reserved for more complex or unstable patients but in most recent time it has been applied preemptively in every case in some centers especially for its protective role on ischemia-reperfusion injury (11,12). Again, in some centers for the subgroup of patients with primitive pulmonary hypertension and with supra-systemic pulmonary arterial pressure, peripheral VA ECMO is installed before the induction of general anesthesia to prevent hemodynamic deterioration (11).

Selection of the adequate candidate

One of the most important issues is the selection of the adequate candidate who might benefit most from ECLS as a bridge: the main indication is the rapid pulmonary deterioration in a potential candidate who had already been evaluated for LTx with refractory hypoxemia and/or hypercapnia despite optimal medical strategies (5,8).

First of all, it is established that the success of bridge to LTx is mainly due to center experience with ECLS and LTx (5,8,11); the selection of the proper candidate is usually made by a multidisciplinary team composed by surgeons, anesthesiologists, ECLS specialists and pulmonologists.

Some absolute and relative contraindications for the use of ECLS as bridge to LTx are presented in *Table 3* (11).

In general, since a patient who would require an ECLS device as a bridge to LTx is exposed to a significantly impaired long-term survival compared to other patients, the selection of the adequate candidate is a crucial point.

Table 3 Absolute and relative contraindications for ECLS as a bridge to LTx

Absolute contraindications	Relative contraindications
Irreversible multiorgan damage (other than lungs)	Older age (>65 y)
Refractory bacteriemia or septic shock	Acute kidney injury requiring renal replacement
Severe obstructive vascular disease	High vasopressor requirement
Contraindication to systemic anticoagulation	Obesity (BMI >30 kg/m^2)
Ineligibility to lung transplantation	High predictive prolonged necessity of MV

ECLS, extracorporeal life support; LTx, lung transplantation; y, years; BMI, body mass index; MV, mechanical ventilation.

Patients with extra-pulmonary organ dysfunction may still be considered eligible for ECLS as a bridge to LTx only if the dysfunction is potentially reversible (pulmonary hypertension, early renal of liver impairment). Again, all the factors which could limit the donor matching, prolonging the time of ECLS as a bridge, such as immunological sensitization, small chest size, and the need of multiorgan transplant are important in the selection of patients (13,14).

The investigation of predictors of outcomes in these patients is mandatory but a consensus on which factors might help clinicians to better select the proper candidate has not been achieved yet.

In recent times, several scores have been widely investigated as predictors of mortality in patients with ECMO for cardiac or acute respiratory failure (15-20) but no available scores exist to predict mortality in patients with ECLS as a bridge to LTx. To best of our knowledge, only the STABLE score (21) is a validated tool to predict in-hospital mortality in ECMO bridged patients to LTx. This is an easily calculable novel pretransplant risk model for patients supported with ECMO before transplantation which accounts 6 variables (age, days on waiting list, dialysis on waiting list, transplant center volume, mechanical ventilation, total bilirubin) with a maximum of 24 possible risk points which were highly associated with post-transplant in-hospital mortality. Unfortunately, STABLE Score has some limitations: firstly, it considers only ECMO and not other devices, secondly it is tailored only on adults and ultimately it could not be representative of the European reality as it is created on United Network for Organ Sharing (UNOS) database. In most recent years, the role of ECLS has also been extensively investigated as a bridge to lung re-transplantation: in this case the selection of recipients is a crucial point as the overall survival is significantly worse compared to patients ECLS-bridged to first time LTx (7).

Another important aspect to consider, talking about the selection of the adequate candidate for ECLS as a bridge to LTx, is the awake or ambulatory setting. During "awake ECLS" patients breathe spontaneously without ventilatory support. The possibility of awake support depends on several factors, in particular it is indicated in case of ability to protect airways, low dose or no vasoactive requirement and no need for high PEEP. On the other side, it is not indicated if the patient is hemodynamically unstable or under deep sedation, in case of active bleeding or brain injury. In case of awake ECLS the cannulation can be performed without intubation or in some cases the patient can be intubated and extubated in a second moment, after the insertion of the cannulas. This ECLS configuration has some advantages such as the possibility to perform physical activity maintaining adequate muscle mass and spontaneous breathing reducing the risk of ventilator-associated pneumonia. The main drawbacks are the risk of cannulas dislocation and also the increase in oxygen consumption and CO_2 production.

The decision to initiate awake ECLS as a bridge to LTx should always be performed by multidisciplinary teams and in highly experienced centers (22).

ECLS related complications

ECLS bridge related complications do not substantially differ from those reported for extracorporeal mechanical support. They depend on the type of cannulation technique (VA or VV) and strategy. The most common complications include bleeding, infections and renal failure while less common ones are embolism, stroke, and limb ischemia (4).

Bleeding, the most common complication related to the extracorporeal support, is due to both continuous anticoagulation and platelets dysfunction. Meticulous surgical technique, platelet counts greater than 50,000/mm^3

and maintaining the target activated clotting time (ACT) reduce the likelihood of bleeding. Intervention is mandatory when a major bleeding occurs. Systemic thromboembolism is reported in 15% (23) while rates of deep venous thrombosis may be higher and associated with femoral cannulation. Anticoagulation and vigilant observation for signs of clot in the circuit successfully prevent thromboembolism in most patients. A sudden change in the pressure gradient could suggest thrombus development. Again, the risk of bleeding could be increased by a variety of complications which can occur during cannulation (such as hemorrhage, arterial dissection or perforation) and also by heparin-induced thrombocytopenia which can occur in patients on ECLS. All these complications related to bleeding could lead to a high blood transfusion requirement which can impact on antibody sensitization influencing pre- and post-transplant outcomes. Generally, better outcomes are reported if the duration of ECLS bridge is short (13).

It has to be specified that complications which can occur during cannulation for bridging to LTx could be more difficult to manage and potentially life-threating because the patient is also affected by an end-stage pulmonary disease with an acute failure and these complications may strongly affect the surgical outcomes.

Outcomes of ECLS as a bridge to LTx

In the field of LTx, mechanical ventilation (MV) has been historically considered the traditional bridging strategy while the use of ECLS devices was once considered a contraindication to LTx (24). In most recent times, especially because of the improvement in technical aspects and in center's expertise, the use of ECLS as a bridging strategy to LTx has been widely accepted and its use has gradually increased over the last decade, trying to promote as much as possible awake bridging strategies (6). However, until now, only few papers and with small number of patients and divergent reported results have been published on this topic (25,26).

In order to get an updated overview on clinical outcomes of ECLS bridged patients to LTx, we performed research including the most recent published articles on this topic (*Table 4*). Only studies published in the last seven years [2015–2022] and in English language were considered. We otherwise excluded those with less than 20 patients or those which considered ECLS bridge to re-transplantation or multi organ transplantation, not allowing to extract data only for patients bridged to first time LTx. Fourteen papers were finally included.

The majority of these studies were heterogeneous, composed by a mixture of intubated and extubated/ambulatory patients, with different outcomes considered. This made the analysis difficult, so we paid attention not to overinterpret any of these results but only presenting them with the different limitations.

The first consideration concerns the configuration used as a bridge to LTx: VV ECMO is the most common, except in two studies (34,36). VV ECMO is generally the preferred strategy in case of hypercapnic failure; in recent times, since the increasing experience with the placement of dual-lumen cannulas, this configuration was extended in many centers to hypercapnic patients with concomitant moderate hypoxemia (37) while in case of severe hypoxemia, when a higher flow is required, the conventional dual-cannula VV ECMO configuration is the preferred. On the other hand, as already said above, VA ECMO as a bridge to LTx is generally reserved in most critical patients with associated hemodynamic instability: this was also evidenced by the study of Xia *et al.* (34) in which they reported a higher in-hospital mortality (4% *vs.* 0%) and a lower 3-year survival (83.3% *vs.* 97.4%) in patients bridged with VA ECMO compared to those with VV ECMO.

The other important speculation concerns the widespread tendency, among published study, to promote awake ECLS as much as possible to start physiotherapy and a rehabilitation program as soon as possible. The percentage of awake/ambulatory ECMO among the different studies ranges between 23% (27,29) and 84.5% (34). Only in the study published by Ko *et al.* (30) all the patients were simultaneously mechanically ventilated while on ECMO, so we can assume that nobody was awake.

Generally, as the center's experience with bridging strategies increases, also the percentage of awake bridged patients increases trying to start ECLS bridge before noninvasive ventilation fails and when tolerance of physical therapy is not entirely lost (6). This tendency has also been established in the last ISHLT guidelines (5) where it is stated that, after the initiation of ECLS as bridge to LTx, candidates should be preferably awake and mobilized. This evidence is also supported by the fact that the highest in-hospital mortality among the studies considered in this review was reported by Ko *et al.* (30). These authors have shown that LTx after bridging with ECMO leads to acceptable patient outcomes compared to unbridged ones but it should be noted that they had not awake ECLS patients, so we can suppose that it may affect also the short-

Table 4 Main studies on published on ECLS bridge to LTx

Author, year, country	No. of patients	ECLS configuration	Median ECLS bridge duration (d)	Awake/ ambulant ECLS bridge	Successful bridge to LTx	In-hospital mortality	1-y survival	3-y survival
Inci, 2015 (27), Switzerland (Europe)	30	VV ECMO: 38% VA ECMO: 15% Other: 27%	21	23%	87%	NR	68%	53%
Tipograf, 2019 (28), USA (America)	121	VV ECMO: 52% VA ECMO: 43% VAV ECMO: 2.5% Other: 2.4%	12	68%	59%	9% (*)	88% (*)	83% (*)
Biscotti, 2017 (6), USA (America)	72	VV ECMO: 62.5% VA ECMO: 31.9% VAV ECMO: 4.2% Other: 1.4%	12	69.4%	55.6%	7.5% (*)	90.3% (*)	NR
Hakim, 2018 (29), USA (America)	30	VV ECMO: 80% VA ECMO: 16.7% VAV ECMO: 3.3%	8	23 %	87%	8% (*)	85% (*)	80% (*)
Ko, 2020 (30), South Korea (Asia)	27	VV ECMO: 89% VA ECMO: 3.6% VAV ECMO: 7.4%	11	0%	100%	25.9%	NR	NR
Ius, 2018 (31), Germany (Europe)	68	VV ECMO: 74% VA ECMO: 37%	9	84%	100%	15%	79%	NR
Oh, 2021 (32), South Korea (Asia)	78	VV ECMO: 85% VA ECMO: 15%	13	75.6%	52.6%	NR	73.2% (*)	70.6% (*)
Sef, 2022 (33), UK (Europe)	21	VV ECMO: 100%	8	62%	100%	NR	66.7%	NR
Xia, 2021 (34), USA (America)	58	VV ECMO: 46.5% VA ECMO: 53.4%	12	84.5%	78%	0% VV (*) 4% VA (*)	NR	94.7% VV (*) 83.3% VA (*)
Kim, 2021 (35), South Korea (Asia)	64	VV ECMO: 97% VA ECMO: 3%	NR	39.1%	100%	NR	76% (awake) 46.2% (not awake)	NR
Kukreja, 2020 (36), USA (America)	62	VV ECMO: 45% VA ECMO: 55%	9.5	45% (*)	68%	10% (*)	97% (*)	NR
Hashimoto, 2018 (37), Canada (America)	34	VV ECMO: 100%	12	44.1%	100%	NR	73.1% (iVV) 90.0% (iVA)	NR
Banga, 2017 (38), USA (America)	25	VV ECMO: 84% VA ECMO: 16%	7	64%	60%	0% (*)	93% (*)	NR
Hoetzenecker, 2018 (39), Austria (Europe)	60	VV ECMO: 43% VA ECMO: 10% Other: 47%	10	37%	100%	11%	76%	68%

*, on successfully bridged patients. ECLS, extracorporeal life support; LTx, lung transplantation; d, days; y, years; VV, venovenous; ECMO, extracorporeal membrane oxygenation; VA, venoarterial; VAV, veno-arteriovenous; NR, not reported; iVV, intra-operative VV ECMO; iVA, intra-operative VA ECMO.

term survival. One of the possible explanations of this finding is the median age of their population (58 years) which is quite high and may have impact the general pre-transplant conditions of their recipients. On the other hand, Xia *et al.* (34) reported the higher percentage of awake ECMO bridge and consensually the lowest in-hospital mortality (0% VV ECMO and 4% VA ECMO).

Concerning long-term outcomes, 1-y survival rate ranges between 46.2% (35) and 97% (36) while 3-y survival from 53% (27) to 94.7% (34). The high variability in survival outcomes could be influenced by institutional difference in cannulation and devices utilized, the different composition of the waiting list among the centers, the severity of post-transplant complications and the center's volume and expertise. Interestingly, the highest 3-y survival was reported by Xia *et al.* (34), the group with the highest percentage of awake bridged patients. In the most recent years, awake strategies demonstrated significantly better survival at 6 months with shorter post-operative length of stay (40). The awake strategy can reduce complications related to prolonged intubation and ventilation improving mobilization and also due to the smaller and light weight devices recently utilized.

Conclusions

The most updated evidences on ECLS confirm that these extracorporeal mechanical support devices can be successfully used to bridge the sickest patients to LTx. A wide variety of configurations are available and need to be individualized on patients' condition.

The selection of the proper candidate is one of the most crucial aspects in this setting: each patient should be discussed by a multidisciplinary transplant team with high expertise in ECLS strategies to implement bridging strategies to LTx.

Awake ECLS strategy should be promoted as much as possible, avoiding mechanical ventilation and allowing daily rehabilitation, to improve short- and long-term outcomes.

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Footnote

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