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Role of ECMO in Transplant Recipient

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Extracorporeal life support (ECLS) for heart/lung in a patient in cardiorespiratory failure is a highly specialized technique which needs careful patient selection, resources, infrastructure and interdisciplinary expertise much like a transplant program. The aim of this editorial is to outline the scope of Extracorporeal membrane oxygenator (ECMO) in preoperative bridging and perioperative management of sick patients with organ failure awaiting transplant as well as post-transplant. The attempt is to collate data of international and national experience for reference.

ECMO is a validated tool as a bridge to heart or lung transplant if the patients decompensate while awaiting a transplant. The method, timing of initiation and end objectives of ECMO in these patients is not the same as that for conventional patients with sudden onset heart lung failure.

Of greater challenge is the role of ECMO in liver transplant recipient perioperatively as it is definitely not a bridge to liver transplant. However, with careful selection and in ideal candidates ECMO can be used to stabilize a patient with liver failure or chronic liver disease who may otherwise be deemed too sick to transplant.

Heart transplant

Patients with heart failure listed for transplant when they decompensate would need some mechanical support to maintain circulation. They could be candidates for a Ventricular assist device(LVAD orBIVAD). ECMO as first line of intervention for such patients before decision to VAD or transplant, allows to stabilize patient [1,2]. This bridge to bridge for patients of INTERMACS 1 category pre VAD helps to downgrade the disease on the INTERMACS scale [2].

Bridge to heart transplant– Since the turn of the century VA ECMO has been increasingly (From 22% to 40%) utilised in heart transplant candidates who present with cardiac failure prior to transplant from. The outcomes however, of these patients, are poor as compared to those not requiring a bridge. Thus, awake ECMO prior to VAD insertion is probably the most effective way of stabilizing a patient prior to heart transplant [3].

ECMO is most useful in patients who are difficult to wean off CPB intra operatively or post-transplant- primary graft rejection; poor RV function post op; borderline donor.

Role of ECMO in lung transplant (1)

Awake ECMO as an alternative to mechanical ventilation as bridge to lung transplant helps to prevent the evils of intubation like risk of ventilator associated pneumoniae or deconditioning of respiratory muscles as it allows for active physiotherapy. A recent study showed patients bridged with awake ECMO spent less day's post operatively in hospital. Awake ECMO is keeping a patient awake and mobile on ECMO. May be initiated without intubation or under anesthesia and intubation then patient is extubated once ECMO targets are met. The latter is more common as most patients are unstable at initiation and cannulation.

However, the outcomes of patients bridged to transplant (mechanical/ECMO) had poor outcomes compared to those needing no support preoperatively. The longest run on ECMO for lung failure has been 107 days prior to transplant. There is a prototype developed and tested on sheep by Robert Bartlett and team of an implantable, total artificial lung (TAL) that could function for 3-6 months would allow more patients to undergo successful lung transplantation, just as the ventricular assist device has been applied to cardiac failure and transplantation. The TAL (Total artificial lung or Biolung) is close to completion.

ECMO is preferred method of cardiopulmonary support intraoperatively and post operatively in case of hemodynamic instability or primary graft failure during lung transplant. A Veno-arterial-venous (VAV) configuration hybrid ECMO is preferred in these patients to ensure hemodynamic support and oxygen rich blood returning to right ventricle to ensure healing of transplanted lungs.

Role of ECMO in liver Transplant

ECMO for liver failure is the trickiest as it goes against the principles of patient selection for extracorporeal life support use. Traditionally ECMO is used to support the heart or lung or both in an otherwise fit patient with reversible heart/lung failure.

Multiple organ involvement is common in liver disease. Most CLD patients have more than one accompanying systemic affectations such as Hepatorenal syndrome, Hepatic encephalopathy (even coma) Coagulopathy (low platelets, high

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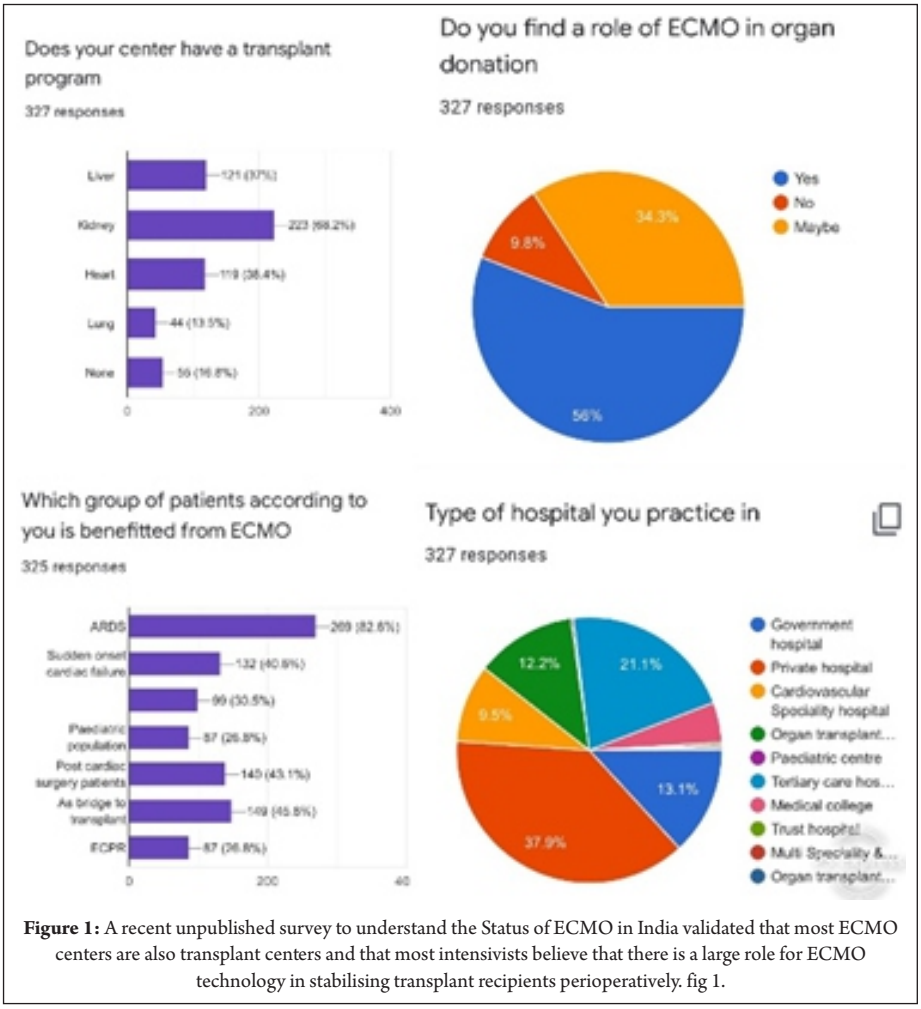

Figure 1: A recent unpublished survey to understand the Status of ECMO in India validated that most ECMO centers are also transplant centers and that most intensivists believe that there is a large role for ECMO technology in stabilising transplant recipients perioperatively. fig 1.

INR, low fibrinogen), G I bleed all of which are relative contraindications for use of ECMO.

The situations where ECMO has been considered in liver failure patients are

1. Acute liver failure
2. Hepatopulmonary syndrome
3. High cardiac risk perioperatively
4. Post-transplant ARDS
5. Post-transplant sepsis

Acute liver failure is a complex multiorgan involvement with extreme coagulopathy and encephalopathic features. However, it presents suddenly with varied etiologies in young otherwise fit individuals with no past premorbidities. Many extracorporeal therapies such as CRRT, Plasma exchange, MARS have been used in the past to keep these patients alive or bridge them to transplant while either deceased donor or live donor is worked up.

In case of severe circulatory collapse with rapidly escalating inotrope score or pulmonary complications due to fluid overload and VAP ECMO may help to stabilize a patient, who would otherwise be too sick to transplant. The largest reported series is from Kings hospital London where they salvaged two patients who presented with cardiogenic shock and ALF on ECMO without transplant. They bridged 5 patients deemed too sick to transplant of whom only one survived to hospital discharge [4].

The availability of bedside visco-elastic tests of coagulation and better ECMO machines, biolined tubing's and cannulas make it easier to avoid anticoagulation in these coagulopathic sick patients. Another advantage is that all other extracorporeal therapies can be added in series while maintaining hemodynamics with ECMO and alleviate the need of harmful doses of inotropes which can cause further end organ damage.

ECMO in Hepatopulmonary syndrome [5] - Hepatopulmonary syndrome (HPS) is triad of liver disease, intrapulmonary vascular dilatation, and abnormal gas exchange, and is found in 10–32% of patients with liver disease. Algorithm for the management of severe HPS consists of Trendelenburg position, inhaled nitric oxide, inhaled epoprostenol, IV methylene blue with or without inhaled vasodilators. Invasive techniques like embolization of lower lobar pulmonary vessels and ECMO are last resorts if all else fails.

Most reported cases of HPS and ECMO are in post liver transplant cases who had superadded ARDS or fluid overload complicating the hypoxia. There are case reports of ECMO used as bridge to liver transplant in an extremely hypoxemic cirrhotic HPS patient with ARDS [6].

Early liver transplant which helps the reversal of blood shunting in the lungs by hypoxic pulmonary vasoconstriction is the treatment of Hepatopulmonary syndrome [7].

There are concerns that ECMO in post liver transplant setting may potentially reverse of hypoxic pulmonary vasoconstrictive responses by flooding lungs with oxygen rich blood and delay the reversal of shunting. But this is a theoretical concern as there are reports of successful use of ECMO.

Perioperative ECMO use in high cardiac risk patients

Case report of liver transplant in a patient with severe mitral regurgitation, severe tricuspid regurgitation, left atrium and left ventricle enlargement, cardiac insufficiency, pulmonary arterial hypertension, and hypoxemia [8].

Veno-arterial ECMO as an intraoperative rescue option in case of Porto pulmonary hypertension recognized during liver transplantation has been reported by Martucci G, Burgio G, Lullo F et al [9].

An interesting case of ECMO as a bridge to lung transplantation in a patient with persistent severe porto-pulmonary arterial hypertension following liver transplantation has been reported by Wiklund L et al [10].

Post Liver transplant -

There are many occasions when a patient immediate post liver transplant presents with ARDS due to fluid overload massive transfusion, or with septic shock. This situation is difficult as decision to salvage these patients with ECMO is fraught with multitude of challenges.

Table 1: Studies on awake ECMO as a bridge to lung transplantation. "Successful bridge" defines the number of patients bridged with "awake ECMO" to lung transplantation without the need for intubation and mechanical ventilation.

Reference	Year	No.of Patients	Average bridge duration	Type of ECMO	Successful bridge
Olsson et al 14	2010	5	21	VA	04-May
Fuehner et al 15	2012	26	9	VV,VA	NA
Javidfar et al 16	2012	6	NA	VV,VA	NA
Hoopes et al 17	2013	18	11	VV VA Central	18/18
Croti et al 18	2013	10	28	VV,VA,AV	08-Oct
Lang et al 19	2014	5	21	AV , VV	05-May
Mohite et al 20	2015	7	89	VV,VA	NA
Inci et al 21	2015	6	NA	NA	06-Jun

Table 2: Transplant data summary for five years

Years	Kidney		Liver		Heart	Lung
	D	L	D	L		
2014	628	4884	325	1002	53	15
2015	984	5571	498	1118	118	51
2016	1261	5697	694	1060	216	73
2017	1169	6165	579	1264	237	106
2018	1164	6772	631	1314	241	191

The survival rate of patients with septic shock with or without ECMO is 25 % - 30 % (11). Post liver transplant patients on immunosuppressants are at high risk of line sepsis coagulopathy and bleeding and also fewer vascular access options making ECMO initiation and maintenance very challenging.

VV ECMO for ARDS / hypoxaemia post liver transplant is an acceptable option with at par survival rate albeit a higher risk of line sepsis.

ECMO In Transplant patients in Indian scenario Organ Donation statistics in India as per NOTO deceased donor organs used over past five years

The transplant scenario in India is improving with more donations per year and similarly the number of centres providing ECMO service and transport on ECMO is also on a rise. The heart and lung transplants are limited due to patient decompensation making them too sick to transplant. The Liver waiting list is long in spite of increase in donation rates which makes it imperative to accept every organ even if borderline and to keep these patients fit perioperatively by any means. This is where ECMO has its role.

Table 3. Demand versus supply

Organs	Waiting list (31/12/2018)	Transplants done
Kidney	12758	7936
Liver	4173	1945
Heart	425	241
Lung	75	191

Kumar L Dr1, Balakrishnan D2, Varghese R1 et al. reported a ofa 16-year-old boy with cirrhosis presented with HPS and a PaO2of 37 mm Hg on room air and underwent living donor liver transplant successfully managed onECMO for post-transplant hypoxaemia following very severe hepatopulmonary syndrome (12).

Sunder T, Ramesh T P, Kumar K M, Suresh M, Singh SP, Seth S. Lung transplant: The Indian experience and suggested guidelines mentions the problems faced by the lung transplant units in India include late referral, reluctance of physicians to refer cases due to lack of confidence in surgical outcomes, bed bound and sick patients who have developed myopathies and are therefore not very good surgical patients, ventilator dependence of patients, ventilator-associated pneumonia and graft dehiscence. There were 39 heart transplants with three bridge to transplants where two were bridged from a ventricular-assist device and one from an extracorporeal membrane oxygenator. They also have bridged one case on ECMO to lung transplant [12].

Paediatric cardiac transplants data shared by Dr Pankaj Bhosle and Sachin Patil in a poster at IACTACON 2019 accounts for ten heart transplants of which three received ECMO perioperatively. One was bridged on ECMO, one had failure to wean and one child had a large graft. All three made it to hospital discharge.

Summary

ECMO should be considered for patients who are considered too sick to transplant to improve their chances.

Awake ECMO is a promising alternative to mechanical ventilation in lung transplant patients.

HPS with refractory hypoxaemia especially due to super added insults of ARDS volume overload both pre, peri and post liver transplant has been widely documented with good results. ALF with MOF especially if immediate transplant is not an option and severe sepsis mostly post-operative have low one-year survival but ECMO still has potential as a rescue therapy.

Prophylactic perioperative ECMO in patients with cardiac conditions who may not tolerate the stress of liver transplant would help improve outcomes.

Conclusion

ECLS thus is an important therapy to buy time for transplant patients especially when youth is on their side and when you are an ECMO and Transplant centre. There is scope and potential of ECMO support perioperatively in transplant recipients that all transplant and ECMO teams should be aware of especially when the waiting times for a donor organ are long and quality of organs are compromised. There is an urgent need to have an Indian registry for ECMO accounting for such cases in future to learn from.

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