

Right ventricular assist device with extracorporeal membrane oxygenation for bridging right ventricular heart failure to lung transplantation: A single-center case series and literature review

Jae Guk Lee

Asan Medical Center <https://orcid.org/0000-0002-4338-1443>

Dong Kyu Oh

Asan Medical Center

Ho Cheol Kim

Asan Medical Center

Pil-Je Kang

Asan Medical Center

Geun Dong Lee

Asan Medical Center

Se Hoon Choi

Asan Medical Center

Sung-Ho Jung

Asan Medical Center

Sang-Bum Hong (✉ hongsangbum@gmail.com)

Asan Medical Center <https://orcid.org/0000-0003-2737-7695>

Research

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Abstract

Background

Right ventricular heart failure (RVHF) is a critical complication in patients with respiratory failure particularly among those who transitioned to lung transplantation using veno-venous (V-V) extracorporeal membrane oxygenation (ECMO). In these patients, both cardiac and respiratory functions are supported using veno-arterial (V-A) or veno-arterial-venous (V-AV) ECMO. However, these modalities increase the risk of device-related complications, such as thromboembolism, bleeding, and limb ischemia, and they may disturb early rehabilitation. Due to these limitations, a right ventricular assist device with an oxygenator (Oxy-RVAD) using ECMO may be considered for patients with RVHF with V-V ECMO.

Methods

The study included patients who underwent Oxy-RVAD using ECMO due to RVHF while on V-V ECMO as a bridge to lung transplantation (BTT) due to severe respiratory failure. The patients were enrolled at a tertiary care, university hospital between 2018 and 2020.

Results

Eight patients underwent Oxy-RVAD using ECMO due to RVHF for BTT. Seven patients were bridged successfully to lung transplantation. One patient died prior to transplantation from complications of interstitial lung disease. There were no major ECMO-related complications during the Oxy-RVAD using ECMO period in any patient. For those patients who were successfully bridged, the average duration of V-V ECMO was 10 days and Oxy-RVAD using ECMO was 12 days. All patients with BTT were discharged with a 30-day survival rate of 100% (7/7 patients). The 180-day survival rate was 85% (6/7 patients).

Conclusions

This study suggests that Oxy-RVAD using ECMO may be a viable option for bridging patients with RVHF to lung transplantation.

Background

Lung transplantation has become a standard of care for patients with nonmalignant, end-stage lung disease(1). However, despite the high demand for lung transplantation, the waiting time for a transplant is getting longer worldwide due to a shortage of donors(2). Therefore, many patients awaiting a lung transplant require mechanical ventilation and extracorporeal membrane oxygenation (ECMO).

Veno-venous (V-V) ECMO, which supports respiratory function, can serve as a bridge to lung transplantation (BTT)(3). However, waiting time on ECMO is usually unpredictable and often prolonged(4). Long-term V-V ECMO support may lead to right ventricular heart failure (RVHF) and cause hemodynamic instability(5). Without proper treatment of hemodynamic instability caused by RVHF, patients waiting for lung transplantation may no longer be adequate candidates for transplantation and have poor survival. This potentially fatal complication requires both cardiac and respiratory support, and immediate interventions are necessary.

Several types of mechanical circulatory support have been developed for the management of RVHF. These include the addition of arterial cannulation and switching to peripheral or central veno-arterial (V-A) or veno-arterial-venous (V-A-V) ECMO(5). In previous studies, including our center, central V-A ECMO has been reported to be effective for lung transplantation candidates with RVHF(6, 7). However, these modalities require skillful technique and may increase the risk of device-related complications such as bleeding, thromboembolism, and limb ischemia and may interfere with rehabilitation(8).

Instead of V-A / V-AV ECMO with its limitations, right ventricular assist device with an oxygenator (Oxy-RVAD) using ECMO may be considered for patients with BTT(8). However, only a few studies have reported this technique. Herein, we report our experience that using Oxy-RVAD using ECMO as a BTT for lung transplantation candidates who developed RVHF during V-V ECMO.

Methods

This case series included patients with RVHF who underwent Oxy-RVAD using ECMO while undergoing V-V ECMO as a BTT due to severe respiratory failure. The study was conducted on patients hospitalized between 2018 and 2020 at a single tertiary care university hospital, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

Oxy-RVAD using ECMO was part of the study's stepwise ECMO BTT strategy. The full ECMO deployment strategy is described below. The university's institutional review board approved the study and waived the need for informed consent.

ECMO Deployment Strategy

When a patient on the lung transplantation list develops respiratory failure, mechanical ventilation is started following intubation. When the patient's vital signs cannot be maintained by mechanical ventilation alone, V-V ECMO is applied. Because bicaval dual lumen catheters are not available in this country, a femoral-right internal jugular vein or femoral–femoral vein approach is used. If hemodynamic instability subsequently occurs, a multidisciplinary review process, including a cardiology evaluation, is performed. A change from V-V ECMO to Oxy-RVAD using ECMO is considered under the following conditions: the patient is a good transplantation candidate, hemodynamic instability caused by RVHF has been identified and requires more than 0.2 mcg/kg/minute epinephrine, hemodynamic instability interferes with rehabilitation, and the patient experiences difficulty breathing due to RVHF. Depending on the patient's hemodynamic condition or rehabilitation, the ECMO mode was changed to Oxy-RVAD using ECMO after applying V-A/V-A-V ECMO, or directly to Oxy-RVAD using ECMO without changing to V-A/V-A-V ECMO (Figure 1). Oxy-RVAD using ECMO was performed in the operating room with the patient under general anesthesia. The reinfusion cannula was inserted into the main pulmonary artery by performing a left anterior thoracotomy in the second intercostal space with an end-to-side anastomosis. The previously used drainage cannula was inserted into the left femoral vein of the V-V or V-A or V-A-V ECMO system (Figure 2). Oxy-RVAD using ECMO was maintained until the patient received a lung transplant or died.

Results

Eight patients with severe respiratory failure underwent Oxy-RVAD using ECMO as BTT for RVHF during V-V ECMO. Baseline characteristics included age, sex, body mass index, underlying lung disease, comorbidities, simplified acute physiology score, and sequential organ failure assessment score. All patients had interstitial lung disease, with four having interstitial pulmonary fibrosis, two with connective tissue disease-associated interstitial lung disease, and two with combined pulmonary fibrosis and emphysema (Table 1).

Three patients (patients 1, 7, and 8) were immediately changed from V-V ECMO to Oxy-RVAD using ECMO for easier rehabilitation. In five patients (patients 2, 3, 4, 5, and 6), the ECMO mode was changed from V-V ECMO to V-A or V-A-V ECMO due to hemodynamic instability caused by RVHF. However, their hemodynamic instability did not resolve, and they were changed to Oxy-RVAD using ECMO.

The maximum length of time for Oxy-RVAD using ECMO was 32 days. The average total length of time on ECMO was 27 days of which the average duration for Oxy-RVAD using ECMO was 15 days. In patients who experienced successful BTT, the maximum period for Oxy-RVAD using ECMO was 32 days, with an average total length of time on ECMO of 20 days, with 12 days on Oxy-RVAD using ECMO. Before applying Oxy-RVAD using ECMO, the average duration of V-V ECMO was 10 days.

Of the eight patients, seven (patients 1, 2, 3, 4, 5, 7, and 8) were bridged successfully to lung transplantation. The one patient (patient 6) who did not receive lung transplantation died from complications of interstitial lung disease. All patients who underwent lung transplantation were discharged and survived at least 30 days following lung transplantation. Of the seven patients who received lung transplantation, six survived for at least 180 days. The one patient (patient 1) who did not survive at least 180 days died of septic shock 4 months following lung transplantation.

Of the eight patients, seven were able to rehabilitate after Oxy-RVAD using ECMO quite well. One patient (patient 3) was not able to rehabilitate, because lung transplantation was performed immediately following Oxy-RVAD using ECMO (Table 2).

One patient (patient 1) had an ECMO-related complication. They experienced minor bleeding around the cannula inserted into the main pulmonary artery which stopped following suturing around the cannula. No adverse events were reported among the other patients.

Discussion

All seven patients who received lung transplants using Oxy-RVAD using ECMO as BTT were discharged without serious side effects associated with ECMO. This outcome suggests the feasibility of Oxy-RVAD using ECMO as a BTT in patients who develop RVHF with V-V ECMO.

Many lung transplantation candidates require invasive mechanical ventilation and ECMO support while on the waiting list(9). In these patients, complications associated with ECMO and deterioration of their lung condition can result in RVHF leading to hemodynamic instability, multiple organ failure, and a poor prognosis. There are several current therapies for right heart decompensation including fluid optimization, inotropes, adjustment of ventilator settings, and inhaled nitric oxide. However, these may not be sufficient for patients with hemodynamic instability and, in such patients, mechanical support may be required.

Considering hemodynamic instability of lung transplantation candidates with RVHF during V-V ECMO, hemodynamic stability should be maintained longer, and with fewer complications, when associated with ECMO. Additionally, ECMO should not interfere with the patient's rehabilitation, as muscle strength is one of the major factors associated with successful lung transplantation outcomes(10). Oxy-RVAD using ECMO, has several advantages and can provide a successful BTT. Oxy-RVAD using ECMO is more physiologic, can prevent right ventricular distension, preserve transpulmonary blood flow, and prevent peripheral arterial cannula complications such as limb ischemia and Harlequin syndrome(11, 12). In addition, it has been reported that there are fewer thromboembolic complications with Oxy-RVAD than V-A ECMO(12). Furthermore, the main pulmonary artery tissue at the cannula insertion site is firm, allowing the cannula to be maintained for an extended period of time(11). The position of the ECMO cannula does not affect lung transplantation surgery, and the main pulmonary artery cannula has the advantage of being used as the drain cannula during lung transplantation surgery. Finally, rehabilitation with Oxy-RVAD using ECMO is easier when compared to peripheral V-A or V-A-V ECMO(13).

Only a few studies have reported using Oxy-RVAD using ECMO for BTT. Lee et al. reported on Oxy-RVAD using ECMO as a BTT. Their successful lung transplantation rate was 10/14 (71.4%), 9/10 (90%) of the patients who underwent transplantation were discharged, the total ECMO application period was 21.5 days, and the average Oxy-RVAD using ECMO application period was 8 days. Their 1-year survival rate was 8/10 (80%)(14) (Table 3). These results are similar to this study. Taken together, these two studies suggest that Oxy-RVAD using ECMO as a BTT in patients with RVHF is safe and feasible.

V-AV or V-A ECMO can immediately correct hemodynamic instability caused by RVHF. However, these techniques have several limitations. In the terminal stage of lung disease, it can be difficult or impossible to properly control the flow of V-AV ECMO, because the reinfusion cannulas are located in the artery and vein respectively. The disadvantages of peripheral V-A ECMO are distal limb ischemia, compartment syndrome, retroperitoneal hemorrhage, poor upper body oxygenation, and difficulty in performing rehabilitation for lung transplantation patients. Additionally, the duration of ECMO is short, and the ability to perform rehabilitation is difficult (Table 3).

Applying central V-A ECMO, Chicotka et al.(5), reported a successful lung transplantation rate of 64.5% (20/31) with a mortality rate during ECMO of 35.4% (11/31). The average duration of ECMO was 26.1 days. Our previous study also showed a transplant success rate of 66.6 % with a mortality rate during ECMO of 33.3%. The average duration of ECMO was 11 days(7). Taken together, it appears that Oxy-RVAD using ECMO is noninferior compared to V-A ECMO as BTT, in terms of the duration of ECMO, the success rate of lung transplantation, and the mortality rate during ECMO.

Rehabilitation during the waiting period for a lung transplant is an important factor in the success of the procedure, and it is important that ECMO does not interfere with rehabilitation in patients who have undergone ECMO as BTT. The proportion of patients who underwent rehabilitation with a peripheral ECMO reinfusion cannula inserted into the femoral artery was 28% (2/7) in a study by Hoetzenecker et al.(15) and 33% (2/6) in the study by Lus et al(16). For central ECMO, where the reinfusion cannula was inserted into either the axillary or innominate artery, 77% (24/31) of the patients underwent rehabilitation(6). In Lee et al.'s study applying Oxy-RVAD using ECMO as BTT, 14/14 (100%) of the patients received rehabilitation as did (7/8) 87% of the patients in this study(14). It appears that central ECMO or Oxy-RVAD using ECMO may be more advantageous than peripheral ECMO for allowing rehabilitation, an important factor for successful lung transplantation (Table3).

There are, however, complications and disadvantages to Oxy-RVAD using ECMO. In a previous study, Lee et al. found a 21.4% (3/14) incidence of pulmonary congestion and 7.1% (1/14) incidence of infection(14). This study noted minor bleeding around the cannula inserted into the main pulmonary artery, but no patient experienced pulmonary congestion. When Oxy-RAVD using ECMO is performed, blood from the right ventricle and ECMO flow into the lungs and as the amount of blood to the lungs increases, there is an increase in pulmonary arterial pressure(17). In patients with severe pulmonary hypertension, increased pulmonary arterial pressure can lead to pulmonary hemorrhage and edema(18). Therefore, it may be useful to minimize this flow to maintain hemodynamic stability and to reduce the complications of pulmonary hemorrhage and edema.

Limitations of this study include its small sample size, its retrospective nature, and being conducted in a single center. Future studies on the safety and effectiveness of Oxy-RVAD using ECMO as a BTT should be prospective and multicenter to include a large sample population. Lastly, because only a few studies on ECMO for BTT with RVHF have been reported, there are limitations in the comparisons of various types of ECMO.

Conclusion

Lung transplantation candidates on prolonged V-V ECMO as a BTT may develop RVHF, which can lead to hemodynamic instability. An effective ECMO strategy is necessary to continue preoperative rehabilitation for lung transplantation candidates. This case series suggests that Oxy-RVAD using ECMO support may provide a successful BTT that can easily allow rehabilitation in a patient with RVHF and hemodynamic instability during V-V ECMO.

Declarations

Ethics approval and consent to participate

This study was approved by the institutional review board of Asan Medical Center (2020-1119, Seoul, Republic of Korea) and conformed to the tenets of the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated during the current study are available from the corresponding author on reasonable request.

Competing interests

All authors declare that there is no conflict of interest to report.

Funding

Not applicable.

Authors' contributions

- (1) Concept and design of the study: LGK, HSB, JSH
- (2) Provision of study patients: LGK
- (3) Data analysis and interpretation: LGK, HSB
- (4) Manuscript writing: LGK
- (5) Writing - review and editing: HSB
- (6) Approval of final manuscript: all authors

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Tables

Table 1. Baseline characteristics.

Pt	Age/Sex	BMI	Lung Disease	Comorbidity	SAPS II	SOFA
1	65/M	20.93	IPF	HTN	29	4
2	48/F	22.85	CTD-ILD	DM r/o dermatomyositis	25	4
3	65/M	20.11	CTD-ILD	Sjogren syndrome	42	4
4	62/M	18.13	ILD (CPFE)		36	4
5	35/F	19.03	IPF	SLE	24	3
6	50/M	25.99	IPF	HCV	26	3
7	60/M	36.1	IPF	HTN	24	2
8	56/M	36.6	ILD (CPFE)		22	3

Abbreviations: BMI, body mass index; CPFE, combined pulmonary fibrosis and emphysema; CTD, connective tissue disease; DM, diabetes mellitus; F, female; ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis; HCV, Hepatitis C virus; HTN, hypertension; M, male; Pt, patient; SAPS, simplified acute physiology score; SLE, systemic lupus erythematosus; SOFA, sequential organ failure assessment

Table 2. Duration of ECMO, cannulation type, outcome, survival, and rehabilitation.

Pt	ECMO mode duration (days)			Oxy-RVAD cannulation	Outcome	Survival		Rehabilitation after Oxy-RVAD (days)
	V-V CMO	V-A/V-A-V ECMO	Oxy-RVAD			30-Day Survival	180-Day Survival	
1	18		10	MPA - Lt. FV	Transplanted	Alive	Death (d/t septic shock)	8
2	10	1	32	MPA-Rt. FV	Transplanted	Alive	Alive	23
3	7	2	2	MPA-Rt. FV	Transplanted	Alive	Alive	0
4	1	2	14	MPA-Rt. FV	Transplanted	Alive	Alive	7
5	1	4	14	MPA-Rt. FV	Transplanted	Alive	Alive	12
6	18	3	32	MPA-Lt. FV, Rt. FV	Death (d/t ILD aggravation)			8
7	15		7	MPA-Rt. FV	Transplanted	Alive	Alive	2
8	16		7	MPA-Rt. FV	Transplanted	Alive	Alive	4

Abbreviations: ECMO, extracorporeal membrane oxygenation; FV, femoral vein; Lt., left; MPA, main pulmonary artery; Oxy-RVAD, right ventricular assist device with an oxygenator; Pt, patient; Rt., Right; V-A, veno-arterial; V-A-V, veno-arterial-venous; V-V, veno-venous.

Table 3. ECMO for bridging to lung transplantation studies.

Author	Type of ECMO (Cannulation Site)	n	Survival n (%)	Successful lung transplantation n (%)	Death on ECMO n (%)	Duration on ECMO (days)	DC to Home n (%)	Long-Term Outcome n (%)	Rehabilitation on ECMO n (%)
Current study	Oxy-RVAD (Vf-MPA)	8	7 (87)	7 (87)	1 (13)	14.75* (IQR 7–27.5)	7 (87)	180-day survival: 6 (85)	7 (87)
Lee et al. (2020)	Oxy-RVAD (Vj-MPA)	14	10 (71.4)	10 (71.4)	4 (28.6)	8* (IQR 2.8–12.5)	9 (90)	1 year survival: 8 (80)	14 (100)
Nam et al. (2019)	Central (Vf-As)	3	2 (66.6)	2 (66.6)	1 (33.3)	11 ± 3.2	4 (66.6)	1 year survival: 2 (100)	
Chicotka et al. (2018)	Central (Vj-Aa or Ai)	31	20 (64.5)	20 (64.5)	11 (35.4)	26.1 ± 26.2	20 (64.5)		24 (77)
Hakim et al. (2018)	Peripheral (Vf-Af)	6	5 (83.3)	5 (83.3)	1 (16.6)	6.8 ± 6.7			
Hoetzenecker et al. (2018)	Peripheral (Vf-Af)	7	6 (85.7)	6 (85.7)	1 (14.2)				2 (28.4)
Ius et al. (2015)	Peripheral (Vf-Af-Vj)	6	3 (50)	3 (50)	3 (50)	10 ± 3.2	2 (33.3)		2 (33)
Lafarge et al. (2013)	Peripheral	9	6 (66.6)	6 (66.6)	3 (33.3)	4.6 ± 1.9	3 (33.3)		
Lang et al. (2012)	Peripheral (Vf-Af)	15	12 (80)	12 (80)	3 (20)		8 (53.3)		

NOTE, Plus-minus values are means ± standard deviation.

Abbreviations: Aa, axillary artery; Af, femoral artery; Ai, innominate artery; As, subclavian artery; BTT, bridge to lung transplantation; DC, discharge; ECMO, extracorporeal membrane oxygenation; IQR, Interquartile range; LTx, lung transplantation; MPA, main pulmonary artery; Oxy-RVAD, right ventricular assist device with an oxygenator; PT, personal training; V-A, veno-arterial; Vf, femoral vein; Vj, internal jugular vein.

* Duration of Oxy-RVAD ECMO

Figures

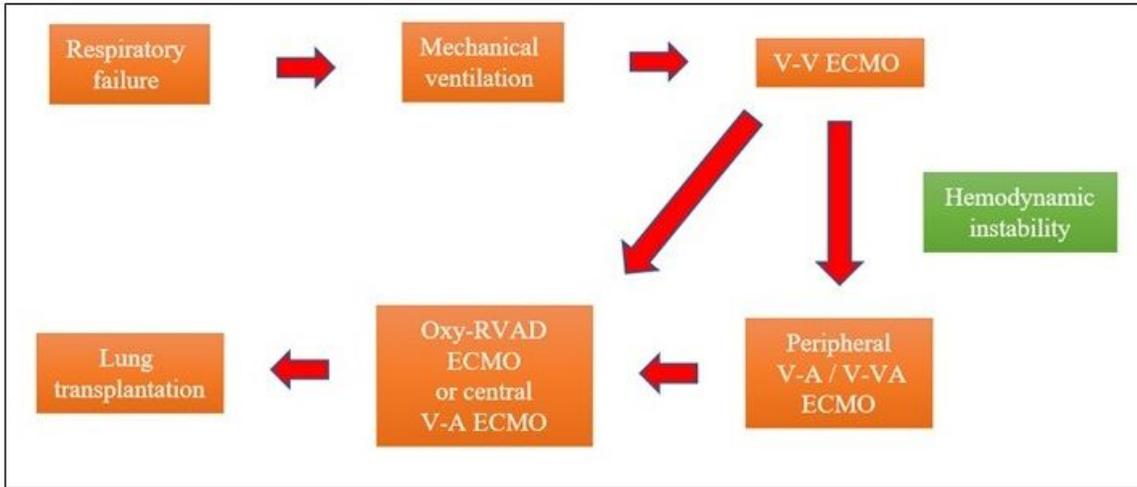


Figure 1

ECMO deployment strategy for bridging to lung transplantation. Abbreviations: ECMO, extracorporeal membrane oxygenation; Oxy-RVAD, right ventricular assist device with an oxygenator; V-A, veno-arterial; V-V, veno-venous; V-A-V, veno-arterial-venous

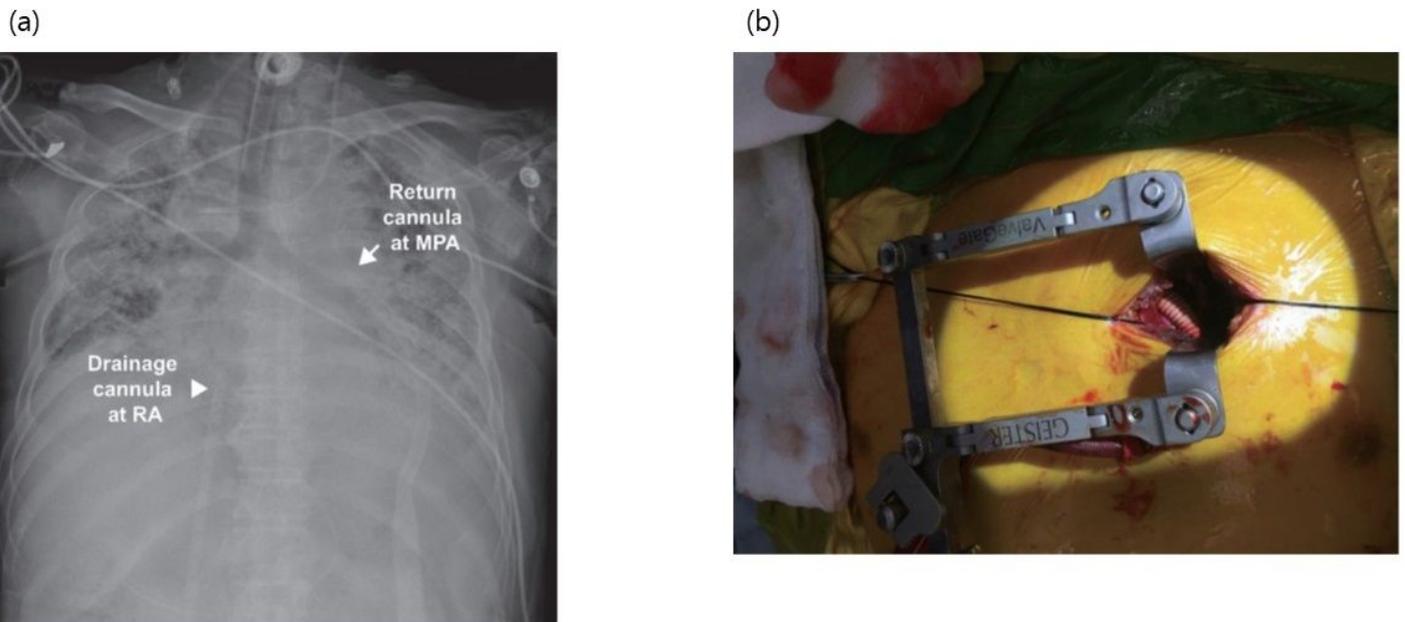


Figure 2

(a) A chest radiograph showing the drainage cannula at the right atrium and return cannula at the main pulmonary artery (MPA) in the right ventricular assist device with an oxygenator support. Adapted from Oh et al. ACC 2020 May;35(2):117-121 with the permission of Acute And Crit Care (b) A clinical photograph showing end-to-side anastomosis of return cannula to main pulmonary artery in right ventricular assist device with an oxygenator support. Adapted from Oh et al. ACC 2020 May;35(2):117-121 with the permission of Acute And Crit Care