Resuscitation xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Four-year experience of providing mobile extracorporeal life support to out-of-center patients within a suprainstitutional network—Outcome of 160 consecutively treated patients☆,☆☆

Hug Aubin[a,1], George Petrov[a,1], Hannan Dalyanoglu[a], Maximillian Richter[a], Diyar Saeed[a], Payam Akhyari[a], Detlef Kindgen-Milles[b], Alexander Albert[a,*], Artur Lichtenberg[a]

[a] Department of Cardiovascular Surgery, Heinrich-Heine University Düsseldorf, Moorenstr. 5, 40225 Düsseldorf, Germany
[b] Department of Anesthesiology, Heinrich-Heine University Düsseldorf, Moorenstr. 5, 40225 Düsseldorf, Germany

ARTICLE INFO

Article history:
Received 26 March 2017
Received in revised form 23 August 2017
Accepted 25 August 2017

Keywords:
Extracorporeal life support
Extracorporeal membrane oxygenation
Acute circulatory failure
Cardiogenic shock
Extracorporeal cardiopulmonary resuscitation

ABSTRACT

Aim: Mobile extracorporeal life support (ECLS) may soon be on the verge to become a fundamental part of emergency medicine. Here, we report on our four-year experience of providing advanced mechanical circulatory support for out-of-center patients within the Düsseldorf ECLS Network (DELSN).
Methods: This retrospective cohort study analyses the outcome of 160 patients with refractory circulatory failure consecutively treated with mobile veno-arterial extracorporeal membrane oxygenation (vaECMO) between July 2011 and October 2015 within the DELSN.
Results: Out of the 160 patients (56 ± 16 years, vaECMO initiation under CPR 68%), 59 patients (36%) survived to primary discharge, with 50 patients (31%) still alive after a median follow-up of 1.74 years. Time-discrete mortality was highest during the first 24 h. There was no difference between survivors and non-survivors regarding age, etiology of circulatory failure, presence of CPR during implantation or distance to implantation site. Incidence of kidney injury requiring dialysis (61% vs. 24%, $p < 0.0001$), shock liver (27% vs. 12%, $p = 0.031$) and visceral ischemia (19% vs. 3%, $p = 0.013$) were the only complications increased in non-survivors. Subgroup analysis showed no significant outcome difference for ECPR vs. non-ECPR patients. Outcome was significantly impaired with initial neuron-specific enolase ≥45.4 μg/L (AUC 0.75, $p < 0.0001$) and lactate ≥5.5 mmol/L (AUC 0.70, $p < 0.0001$). Program-year-dependent in-center mortality showed an increasing trend, while program-year-dependent follow-up mortality decreased over time.
Conclusions: This study illustrates that regional mobile ECLS rescue therapy can be provided with encouraging outcomes, although patient selection criteria and early outcome parameters reflecting on therapy success or futility still need to be refined.

Introduction

Technological advances of extracorporeal membrane oxygenation (ECMO) systems have enabled us with the possibility to provide remote advanced mechanical circulatory support in out-of-center settings, leading to mobile ECMO therapy entering the stage of emergency medicine [1]. Today, on-site initiation of veno-arterial ECMO (vaECMO) – also referred to as extracorporeal life support (ECLS) – allows us to temporarily restore and secure vital hemodynamics of patients presenting with refractory circulatory failure outside of specialized tertiary care centers, thereby increasing their chance of survival [2–8]. When applied during cardiac arrest this is referred to as extracorporeal CPR (ECPR), which is increasingly being used despite limited observational data available.

Due to recent approaches trying to provide systematic mobile ECLS support and comprehensive follow-up therapy on a regional scale [8], mobile ECLS networks are now increasingly in the spotlight [9] and may soon be on the verge to become a fundamental part not only of emergency medicine but also of resuscitative therapy. However, there is still a lack of adequate patient selection criteria as well as early outcome parameters correlating to survival.

After previously introducing the Düsseldorf ECLS Network (DELSN) [8], a supra-institutional ECLS network providing remote advanced mechanical circulatory support on a regional scale, we

☆ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at http://dx.doi.org/10.1016/j.resuscitation.2017.08.237.
☆☆ Meeting presentation: Abstract has been selected for oral presentation at the 30th Annual EACTS Meeting, 1st to 5th October 2016 in Barcelona, Spain.
* Corresponding author.
E-mail address: alexander.albert@med.uni-duesseldorf.de (A. Albert).
[1] The first 2 authors contributed equally.

http://dx.doi.org/10.1016/j.resuscitation.2017.08.237
0300-9572/

now report on our four-year experience of mobile vaECMO rescue therapy for out-of-center patients with refractory circulatory failure, analyzing patient outcome and program characteristics. We hypothesized that although an encouraging survival rate for a patient population otherwise doomed with a fatal prognosis can be achieved and maintained over time by an established program for mobile vaECMO therapy, early mortality will remain conditioned by the initial clinical status and primary pathology related complications. Hence, this study aims to identify early outcome parameters reflecting on mobile vaECMO therapy success or futility. Therefore, we compared the outcome of ECPR vs. non-ECPR-patients, – since in many centers there still seems to be reluctance for vaECMO therapy initiation under cardiac arrest – and evaluated the value of the initial neuron-specific enolase (NSE) and lactate values upon arrival on the ICU as prognostic markers for survival, – as they are immediately available after therapy initiation and have already been discussed as outcome predictors after cardiac arrest and/or ECMO therapy in the past [10–12].

Methods

Setting

The DELSN was launched 2011, as a supra-institutional network for rapid-response remote ECLS based at the Düsseldorf Heart Center (Düsseldorf, Germany), in order to provide advanced mobile vaECMO support to all participating institutions within the immediate metropolitan area and adjacent urban and suburban regions. Detailed characteristics have been reported previously [8]. Briefly, the Department of Cardiovascular Surgery of the Düsseldorf Heart Center serves as a central hub, organizing 24/7 rapid-response mobile ECLS support upon emergency request on a regional level and coordinating comprehensive and interdisciplinary customized follow-up therapy for supported patients. Mobile ECLS support can be requested in cases of refractory circulatory failure non-manageable on-site or cardiac arrest without return of spontaneous circulation, independent of etiology. Upon emergency request, a specially trained mobile ECMO team, consisting of a cardiovascular surgeon and a perfusionist, are immediately dispatched to the patient, starting advanced mechanical circulatory support via peripheral vaECMO (Sorin Lifebox, Sorin Group, Munich, Germany) [13] as fast as possible. Decision-to-treat is made by the cardiovascular surgeon on duty, and is only denied when life-limiting medical conditions or strong evidence for hypoxic brain damage are present. After hemodynamic stabilization, the ECMO team escorts the patient to the Düsseldorf Heart Center, where a standardized diagnostic and therapeutic algorithm is immediately started [8].

Study design

This retrospective cohort study includes 160 patients consecutively treated with mobile vaECMO rescue therapy for refractory circulatory failure within the *DELSN* between July 2011 and October 2015. None of those patients were primary related to cardiac surgery. vaECMO rescue therapy was defined as mobile, when an advanced logistic effort was required to reach the patient, only including patients in whom vaECMO was implanted in facilities spatially separated from the Department of Cardiovascular Surgery. Refractory circulatory failure was defined as failure to maintain sufficient mean arterial pressure (60 mmHg) with evidence of end-organ hypo-perfusion despite maximal medical therapy under exhaustion of all on-site available supportive measures and/or ongoing CPR, independent from underlying etiology. All patients in whom vaECMO implantation was denied on-site or patients primarily treated with veno-venous ECMO were excluded from the study.

Follow-up was conducted either by direct patient contact or through relatives or the referring physician to gather survival status after primary discharge. Survival after primary discharge was primary clinical endpoint, follow-up survival secondary endpoint. Additionally, a subgroup analysis for patients in whom ECLS was initiated under CPR (ECPR-group) was performed. Complications under vaECMO therapy (kidney injury requiring, shock liver, visceral ischemia, bleeding, leg ischemia, acute respiratory distress syndrome (ARDS), ischemic, sepsis) [8], neuron-specific enolase (NSE) as marker of brain damage and lactate as marker of hypoperfusion related organ damage were not treated as an endpoint, but also included into the analysis protocol to estimate their potential impact on survival.

The *DELSN* registry, in which all patients are prospectively registered after vaECMO rescue therapy initiation, served as primary data source. Registry data was complemented by an extensive retrospective review of the patients' medical records until primary discharge, including specific laboratory parameters, documentation on diagnostic exams and complication management. All data were recorded following institutional quality assurance standards and recommendations of the "Association for Clinical Data Management" [14].

Ethics committee approval

This study was approved by the ethics committee of the medical faculty of the Heinrich-Heine-University, complying with the principles outlined in the Declaration of Helsinki.

Statistical methodology

This manuscript was prepared according to recommendations of the STROBE initiative [15]. The statistical analysis was performed using IBM SPSS Statistics, version 22, and R, version 2.15.2. Unless otherwise indicated continuous variables are presented as mean ± SD or median (25th, 75th percentile) according to normality of their distribution and compared using unpaired Student *t*-test or Mann-Whitney test as appropriate. Discrete variables are reported as percentages and tested by Pearson's Chi^2 test or, when validity conditions were not satisfied, by Fisher's exact test. The univariate analysis was supplemented by binary logistic regression. Because highly skewed distributions were explored in a subset of linear baseline and laboratory parameters, a natural log transformation was necessary prior to model inclusion. Survival was estimated using the Kaplan-Meier method. Comparisons of survival curves were based on the Log-Rank test. All tests were two-tailed and p-values <0.05 considered statistically significant. In case of multiple comparisons Bonferroni correction was applied. C-statistics were used to assess the prognostic value of initial NSE [μg/l] and lactate [mmol/l] regarding early in-hospital mortality, which were obtained immediately after hemodynamic stabilization upon arrival on our ICU. Multivariate cox regression was performed for NSE and lactate cut-offs as well as ECPR status in order to analyze predictive effect on in-center survival.

Results

Study population

During the study period approximately 185 emergency requests for mobile vaECMO support reached our institution. Out of those 160 emergency requests were fulfilled, leading to vaECMO implantation on-site and subsequent treatment of those patients at our institution. Median follow-up was 1.74 years (CI95%, 1.33–2.15). Baseline characteristics of the study population and selected laboratory parameters upon ICU-arrival after mobile vaECMO-implantation are outlined in Table 1. Briefly, mean patient

Please cite this article in press as: Aubin H, et al. Four-year experience of providing mobile extracorporeal life support to out-of-center patients within a suprainstitutional network—Outcome of 160 consecutively treated patients. Resuscitation (2017), http://dx.doi.org/10.1016/j.resuscitation.2017.08.237