Early goal directed Physiotherapy in Patients undergoing Extracorporeal cardiac life support

Gottschalk, Antje, MD, PhD[1]; Bräunig, Jochen, BA[2,]; Bause, Daniela, RN[1]; Volkert, Thomas, MD[1]; Lanckohr, Christian MD[1]; and Ellger, Björn MD, PhD[1]

[1] Department of Anesthesiology, intensive care medicine and pain therapy, University hospital Muenster, Germany
[2] Department of Physiotherapy, University hospital Muenster, Germany

Abstract

Objectives: We evaluated active early goal directed physiotherapy (EGDP) by implementing a physiotherapy algorithm in patients undergoing ECLS for post-cardiotomy shock with special respect to safety.

Design: Observational study

Setting: Intensive care unit, University hospital

Subjects: Patients who required veno-arterial ECLS-therapy due to post-cardiotomy shock

Interventions: Physiotherapy algorithm (early goal directed physiotherapy (EGDP)) was conducted daily starting upon admission to ICU performed with passive and active elements while patients were on ECLS.

Measurements and main results: We recorded no sever adverse event such as dislocation of cannulas or catheters, bleeding, hemodynamic or respiratory deterioration or neurologic symptoms neither during EGDP nor in the control group. Patients under EGDP revealed similar mortality as compared to controls; as well, time on ECLS and on ICU did not differ significantly. Patients under EGDP appear to be better mobilized at ICU discharge and to suffer from less neurological impairment (GCS upon discharge form ICU) as controls; numbers, however, did not reach significance levels.

Conclusions: Our trial indicates that early active goal directed physiotherapy in patients under ECLS for post-cardiotomy shock is safe, feasonable and might lead to a favorable prognosis of the patients.

Key words: Early goal directed Physiotherapy, ECLS

Introduction

Success of intensive care medicine is mostly measured in mortality and crude morbidity. The improvement in care and more sophisticated technologies broaden indications and make interventions possible or even routine care that were seldom applied just a couple of years ago. Extracorporeal cardiac life support (ECLS) is one of those techniques [1]. When severe critical illness is survived, patients are frequently discharged home with profound handicaps and impairment of neurocognitive and physical function even when originally disturbed organ function has fully recovered [2]. Unfortunately, little is known about the permanent impact of therapeutic interventions on daily life after discharge; the reasons for this lack of evidence are multifaceted [3].

Especially patients suffering from post-cardiotomy cardiogenic shock requiring ECLS to prevent sudden death present with profound hospital-mortality and a remarkable morbidity [4]. ECLS for post-cardiotomy shock is required in roughly 1% of the patients undergoing open heart surgery, less than one fourth of the patients are discharged from ICU and are still alive after 5 years, some with persistent symptoms of heart insufficiency [4]. Even in patients requiring ECLS for ARDS, a population with relatively optimistic survival as compared to post-cardiogenic shock ECLS, only a minority returns to their daily life as before the affliction [5]. Data about their functionality in daily life is scarce, but existing evidence draws a drab picture [6]. Among some potential strategies to improve functional outcome among critically ill in general, early active physiotherapy appears as a promising approach [6-9]. However, little is known about details of the therapy or which patient group may profit; apparently beginning as early as possible with active exercise appears to do a good job. Whether positive effects of early active physiotherapy in ICU-patients can be extrapolated to patients under ECLS for post-cardiotomy shock remains a matter of debate. Only very small case-series describe feasibility of active rehabilitation during ECLS [10]. Although not supported by evidence, especially safety concerns are frequently reducing activity of patients under invasive ventilation or ECLS to daily wake up calls and protective ventilation [4, 11] thus withhold a likely beneficial therapy.

We therefore evaluated active early goal directed physiotherapy (EGDP) by implementing a physiotherapy algorithm in patients undergoing ECLS for post-cardiotomy shock with special respect to safety.

Material and Methods

Patients

According to local ethical committee policy no formal approval by the committee was needed for this retrospective cohort study.

All patients who required veno-arterial ECLS-therapy due to post-cardiotomy shock in our university hospital received early goal directed physiotherapy (EGDP) according to a novel written algorithm starting from December 2012. Until end of June 2013 all patients undergoing ECLS for this indication where treated according to the algorithm (Fig. 1). Physiotherapy was conducted daily starting upon admission to ICU, active interventions took between 30 and 45 minutes time. Interventions where stopped or we went one step back in our protocol when hemodynamic instability occurred or the patient refused to collaborate. The same number of patients treated prior to the implementation of the algorithm served as a control group. Daily physiotherapy in this group was as well performed with passive and active elements. Interventions were left to the decision of the attending physiotherapist and no specific protocol or algorithm was followed.

No other changes in any therapeutic algorithms were done during this period.

Sedation, analgesia and mechanical ventilation were done, equal to patients without ECLS, by established institutional protocols that are based on current evidence and national guidelines [12, 13]. Briefly, consequent reduction of sedation was started the day after implantation of the ECLS and was terminated early or titrated to a Ramsy-score 2 whenever possible. Analgesia was adjusted to patient`s needs (VAS-score <3) by piritramide or oxycodone. Weaning from mechanical ventilation was consequently done targeting early extubation. Percutanous tracheostomy was done when appropriate. Neither an artificial airway nor the use of vasoactive agents nor inotropes where contraindications against EGDP.

ECLS protocol

Briefly, ECLS was established primarily via a central approach with the venous cannula in the femoral vein and the arterial cannula in the axillary artery via a conduit. Initial flow was 8-10 ml/kg bodyweight, adjusted to normalize hemodynamic and organ function parameters. After a stabilization phase, weaning from ECLS was either done by stepwise reduction of ECLS-flow with termination of therapy when flow was reduced below 2 l/min or when a permanent left ventricular assist device (LVAD) was placed due to non-recovery of ventricular function. When myocardial function showed no signs of recovery after at least 2 weeks on ECLS and LVAD-implantation was impossible, ECLS-therapy was stopped. Profound and permanent neurological impairment (major stroke, severe bleeding), uncontrollable

infectious complications, persistent dysfunction of vital organs (e.g. unresolving hepatopathy, mesenteric ischemia) were as well criteria to stop ECLS.

Endpoints

Primary endpoint of this retrospective study was safety of the EGDP. We thus recorded any adverse event during EGDP such as dislocation of cannulas or catheters, bleeding, hemodynamic, or respiratory deterioration or neurologic symptoms. Secondary endpoints were mortality and mobilization status at discharge from ICU (mobilization to standing upright or into the armchair and ability to walk).

Statistics

Data where retrospectively collected as this trial is a retrospective cohort study with historical control. Data was analyzed using Chi-square test or Man-Whitney test as appropriate. A $p<0.05$ was considered significant.

Results

Groups were comparable according to age, gender-distribution, and severity of illness (Table 1) as recorded by SAPS and SOFA scores. In the investigation period of 7 Month we included 37 patients into our trial, 37 consecutive patients prior to implementation of EGDP in a 9 month period served as controls.

We recorded no sever adverse event such as dislocation of cannulas or catheters, bleeding, hemodynamic or respiratory deterioration or neurologic symptoms neither during EGDP nor in the control group. Patients under EGDP revealed similar mortality as compared to controls; as well, time on ECLS and on ICU did not differ significantly. Patients under EGDP appear to be better mobilized at ICU discharge (Figure 2) and to suffer from less neurological impairment (GCS upon discharge form ICU) as controls; numbers, however, did not reach significance levels.

Discussion

In this retrospective evaluation of a novel physiotherapeutic approach in patients undergoing ECLS for post-cardiotomy cardiogenic shock we showed safety and feasibility of EGDT. Mortality was not affected but patients appear to be less handicapped upon discharge from ICU as compared to conventionally treated patients.

In critically ill patients, early protocol based weaning from sedation and mechanical ventilation is supported by evidence and is thus commonly accepted [13, 14]. However, implementation and adherence to the evidence

based protocols is challenging and adherence rates in real life are somehow discouraging [15]. The same appears true for active physiotherapy: Active physiotherapy emerged as a cornerstone in weaning concepts in recent years [3, 7-9], however, a recent German survey showed that this notion is far from being established in everyday life [11] . The group showed that less than a fourth of ventilated patient is mobilized to a level of sitting at the edge of the bed or higher. The main reasons for not mobilizing are hemodynamic instability and deep sedation. Obviously, in more instable patients the therapists consider it safer to do exercises in bed. The study does contradict this assumption: in the cohort of 783 patients no catheter was removed accidentally during active physiotherapy, cardiac arrests and removal of the endotracheal tube were only detected in the non-mobilized patients. The overall rate of complications did not differ between mobilized and non-mobilized patients. This does not surprise since safety and feasibility of active physiotherapy even in severely impaired patients was shown earlier in a prospective trial [7]. Also in patients requiring profound vasopressor doses, physiotherapy appears safe. Conclusively, being scared of mobilization because of dislocation of devices or threatening cardiorespiratory deteriorations when physiotherapy is conducted appropriately is contradicted by available evidence.

Alike, when patients are hemodynamically impaired to an extend that necessitates ECLS, the idea to sedate and withhold active training is imprinted in the heads of health care providers. To date, only very small case series suggest active physiotherapy as a safe therapeutic option [10]. Mainly ECLS for ARDS is addressed in the approaches suggesting physiotherapy as an option to improve outcome (see [1] for review). Since ECLS becomes easier to use the indication is widened and somehow overshoots the available evidence supporting medical practice [1]. Especially, in ECLS for post-cardiotomy shock mortality and morbidity remain high by far exceeding mortality for other indications [4, 5]. Notably, with 59% the mortality rate in our cohort is by far lower as compared to rates for ECLS-patients in cardiogenic shock reported in previous trials. So improved technologies and care-bundles appear to improve survival and prognosis cannot be considered futile in this severely ill population.

We showed in our trial that despite the high-risk group of patients, EGDP was safely performed and lead to physical ability upon ICU discharge. Since our cohort is rather small changes in the various parameters did not reach statistical evidence. Alike, in other critically ill not requiring ECLS, active mobilization does not subject patients to excessive risks like decannulation or major

bleeding [11]. Good reasons for this finding might be the experience in the team and the additional comfort of being back-upped by a consented algorithm as well as improved technologies of cannulas, connected devices and cannulation techniques. Algorithms on ICU are commonly accepted as tools to guide therapy. They allow formal consenting based on available evidence and make therapy, at least to some extent, independent from individuals.

Mortality was not affected by our EGDP-algorithm in our cohort that is far too small to draw sound conclusions on this outcome parameter anyway. It appears rather optimistic on first sight to expect an influence on short-term mortality and on weaning success from ECLS since this success is rather depending on recovery of myocardial function and on recovery of organ dysfunction associated with cardiogenic shock [1]. Indeed, most patients in our cohort died within the first 3 days after removal of ECLS, the reason is non-resolving organ function and a futile prognosis with regard to transplant or implantation of a permanent assist device. Recent research has shown some positive effects of active exercise not only on reduced muscle wasting, but also on cellular energy metabolism and life-saving cascades like autophagy [16-18], a clearance-mechanism for cell-detritus. Impaired autophagy is associated with organ dysfunction in critical illness [19]; affecting and regulating this autophagy network appears as a therapeutic target also in myocardial affliction [20, 21]. Hence it is tempting to speculate that active physiotherapy might influence the recovery and function of different organ systems, e.g. myocardial function. Future clinical research will determine whether EGDP can thus be appropriate to improve long-term prognosis of the patients under ECLS with special respect to physical and neurocognitive performance on long term. Since mobilization under ECLS appears safe, there is little reason to believe that positive and well published evidence of benefits of physiotherapy in ventilated ICU-patients should not be extrapolated to patients under ECLS [3].

As limitations, our data is retrospective and conclusions must be drawn with cautions. Due to the relatively small number of cases we cannot preclude the rare occurrence of complications neither can we conclude on the influence of EGDP on prognosis since this would require a prospective, randomized trial. However, evidence for active physiotherapy as a cornerstone of any weaning procedure appears compelling so that one might doubt whether such a trial is ethically appropriate.

In conclusion, our trial indicates that early active goal directed physiotherapy in patients under ECLS for post-cardiotomy shock is safe,

feasonable and might lead to a favorable prognosis of the patients.

Legends:

Figure 1: Algorithm for early active goal directed physiotherapy (EGDP).

Table 1: Demographic and survival data.

Figure 2: Mobilization status upon discharge from ICU. Filled bars control, dashed bars EGDP.

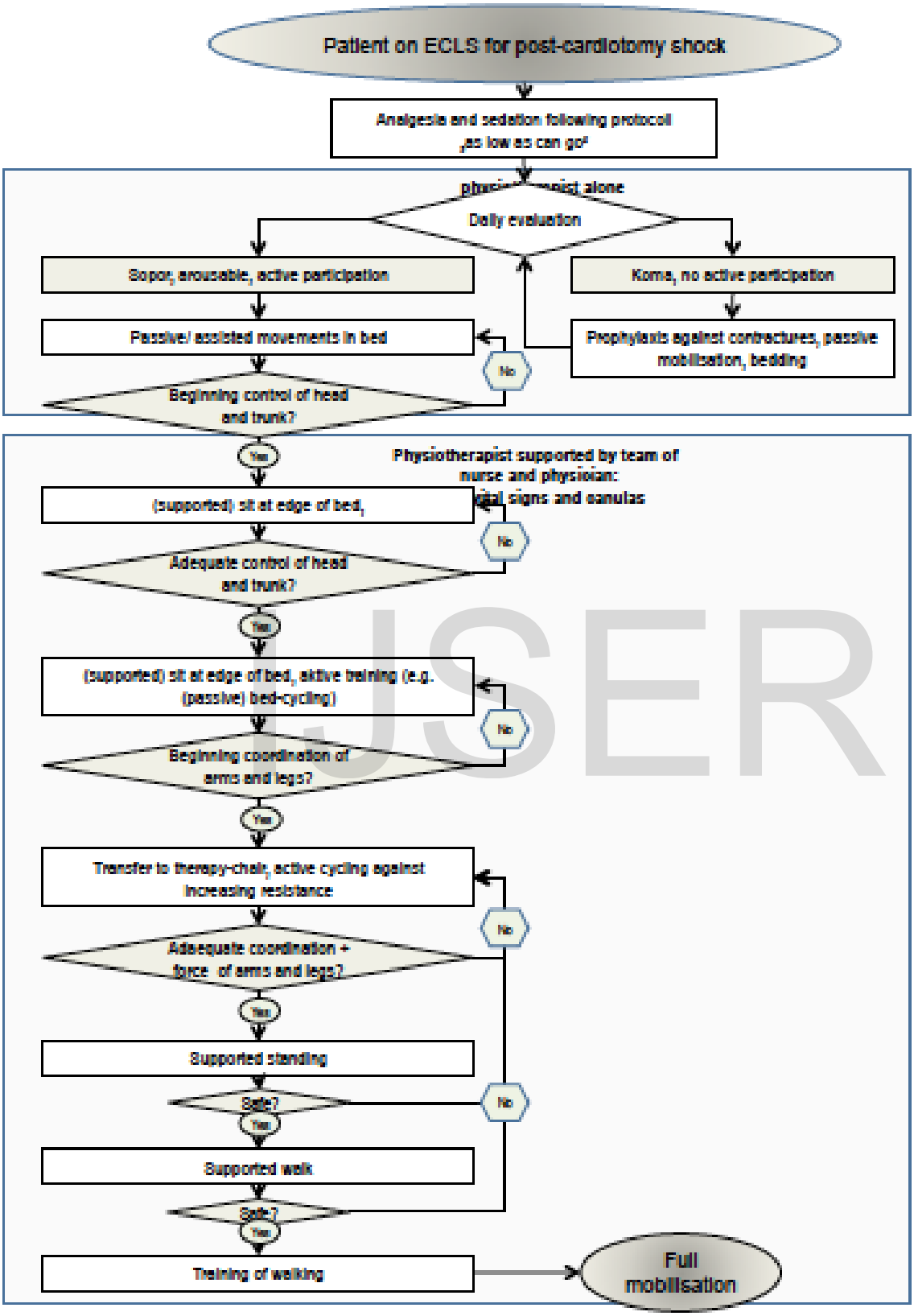
Patient on ECLS for post-cardiotomy shock
Analgesia and sedation following protocoll
„as low as can go"
Daily evaluation
Sopor, arousable, active participation
Koma, no active participation
Passive/ assisted movements in bed
Prophylaxis against contractures, passive mobilisation, bedding
No
Beginning control of head and trunk?
Yes
Physiotherapist supported by team of nurse and physician:
(supported) sit at edge of bed,
No
Adequate control of head and trunk?
Yes
(supported) sit at edge of bed, aktive training (e.g. (passive) bed-cycling)
No
Beginning coordination of arms and legs?
Yes
Transfer to therapy-chair, active cycling against increasing resistance
No
Adequate coordination + force of arms and legs?
Yes
Supported standing
Safe?
No
Yes
Supported walk
Safe?
Yes
Training of walking
Full mobilisation

Figure 1:

Figure 2:

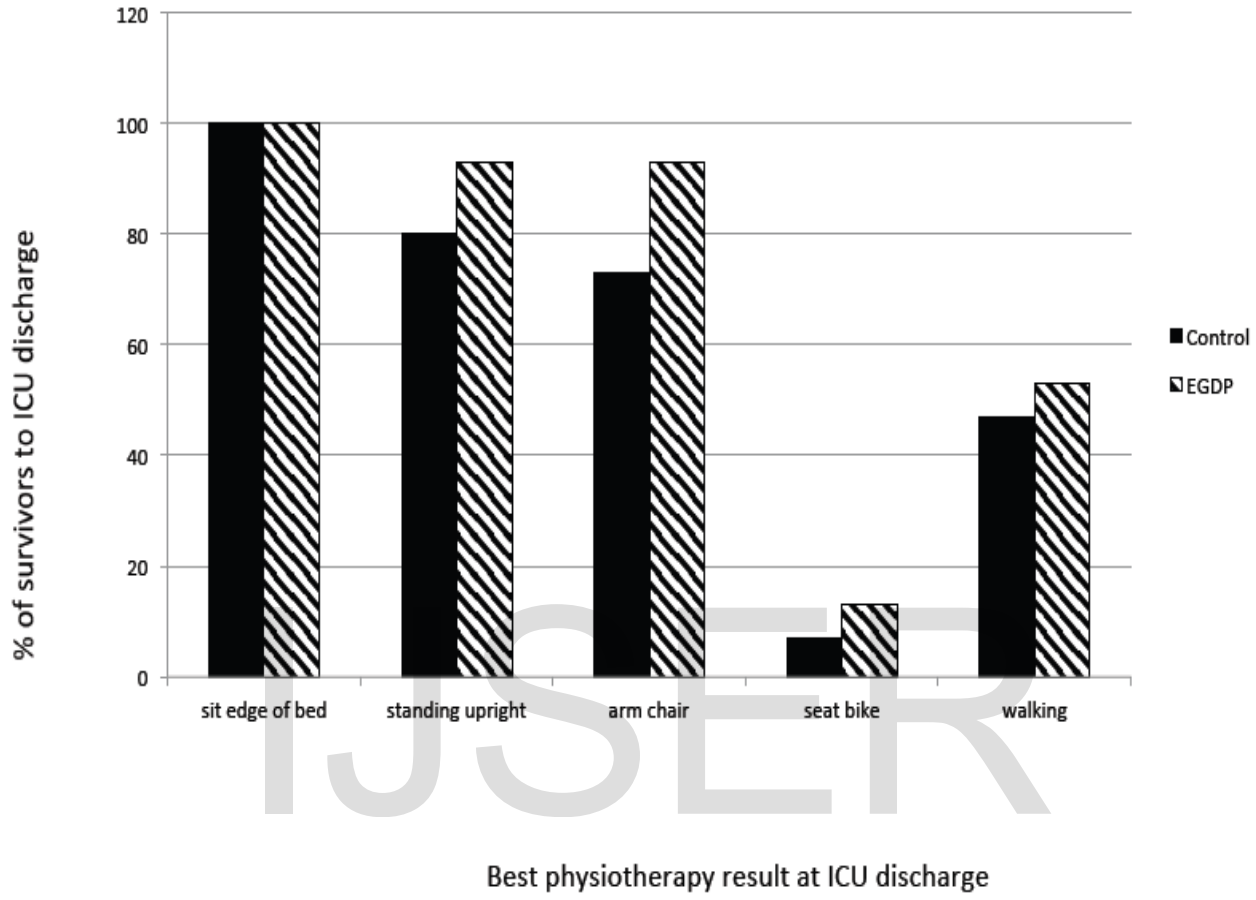

Table 1:

		EGDP	Control	p
N		37 (♂= 25 ; ♀=12)	37 (♂=28 ; ♀=9)	
Age [Mean] Age [Median] Age [Median]	 Survivors Non-survivors	65.3 62 68.5	66 61 71	0.503
Patients with LVAD after ECLS	 Survivors Non-survivors	9 5 4	3 2 1	
Mean GCS at ICU-discharge	Survivors Non-survivors	14.4 3.6	13.3 3.2	0.605
Days on ICU [Mean]	Survivors Non-survivors	39.6 16.3	36.8 11	0.444
Days on ECLS [Mean]	Survivors Non-survivors	12.7 6.7	15.2 7.4	0.436
Survived until ICU discharge	N [%]	15 [41%]	15 [41%]	1.0
Died after ECLS weaning on ICU	0-3 days 4-10 days 11-25 days >25 days	17 1 2 2	17 2 3 0	
Median SAPS2-score upon admission [± SEM]	All [Mean by Median] Survivors Non-survivors	72.5 72 73	70 64 76	0.691
Median SAPS2-scores during ICU stay [± SEM]	All [Mean by Median] Survivors Non-survivors	59 39 79	60 41 79	0.583
Median SOFA-score upon admission [SEM]	Survivors Non-survivors	14 14	14 15	0.969
Median SOFA-score during ICU stay [SEM]	Survivors Non-survivors	10.5 15.3	11 16	0.714

Literature

1. Abrams, D., A. Combes, and D. Brodie, *Extracorporeal membrane oxygenation in cardiopulmonary disease in adults.* J Am Coll Cardiol, 2014. **63**(25 Pt A): p. 2769-78.
2. Herridge, M.S., et al., *Functional disability 5 years after acute respiratory distress syndrome.* N Engl J Med, 2011. **364**(14): p. 1293-304.
3. Hough, C.L., *Improving physical function during and after critical care.* Curr Opin Crit Care, 2013. **19**(5): p. 488-95.
4. Papadopoulos, N., et al., *Risk factors associated with adverse outcome following extracorporeal life support: analysis from 360 consecutive patients.* Perfusion, 2014.
5. Hodgson, C.L., et al., *Long-term quality of life in patients with acute respiratory distress syndrome requiring extracorporeal membrane oxygenation for refractory hypoxaemia.* Crit Care, 2012. **16**(5): p. R202.
6. Iwashyna, T.J. and G. Netzer, *The burdens of survivorship: an approach to thinking about long-term outcomes after critical illness.* Semin Respir Crit Care Med, 2012. **33**(4): p. 327-38.
7. Pohlman, M.C., et al., *Feasibility of physical and occupational therapy beginning from initiation of mechanical ventilation.* Crit Care Med, 2010. **38**(11): p. 2089-94.
8. Schweickert, W.D., et al., *Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial.* Lancet, 2009. **373**(9678): p. 1874-82.
9. Needham, D.M., *Mobilizing patients in the intensive care unit: improving neuromuscular weakness and physical function.* JAMA, 2008. **300**(14): p. 1685-90.
10. Rahimi, R.A., et al., *Physical rehabilitation of patients in the intensive care unit requiring extracorporeal membrane oxygenation: a small case series.* Phys Ther, 2013. **93**(2): p. 248-55.
11. Nydahl, P., et al., *Early mobilization of mechanically ventilated patients: a 1-day point-prevalence study in Germany.* Crit Care Med, 2014. **42**(5): p. 1178-86.
12. Schonhofer, B., et al., *[Prolonged weaning: S2k-guideline published by the German Respiratory Society].* Pneumologie, 2014. **68**(1): p. 19-75.
13. McConville, J.F. and J.P. Kress, *Weaning patients from the ventilator.* N Engl J Med, 2012. **367**(23): p. 2233-9.
14. McGrane, S. and P.P. Pandharipande, *Sedation in the intensive care unit.* Minerva Anestesiol, 2012. **78**(3): p. 369-80.
15. Robertson, T.E., et al., *Multicenter implementation of a consensus-developed, evidence-based, spontaneous breathing trial protocol.* Crit Care Med, 2008. **36**(10): p. 2753-62.
16. Garber, K., *Neuroscience. All eyes on RNA.* Science, 2012. **338**(6112): p. 1282-3.
17. Renaud, G., et al., *Sparing of muscle mass and function by passive loading in an experimental intensive care unit model.* J Physiol, 2013. **591**(Pt 5): p. 1385-402.
18. Luo, L., et al., *Chronic resistance training activates autophagy and reduces apoptosis of muscle cells by modulating IGF-1 and its receptors, Akt/mTOR and Akt/FOXO3a signaling in aged rats.* Exp Gerontol, 2013. **48**(4): p. 427-36.
19. Gunst, J., et al., *Insufficient autophagy contributes to mitochondrial dysfunction, organ failure, and adverse outcome in an animal model of critical illness.* Crit Care Med, 2013. **41**(1): p. 182-94.
20. Kolwicz, S.C., Jr., S. Purohit, and R. Tian, *Cardiac metabolism and its interactions with contraction, growth, and survival of cardiomyocytes.* Circ Res, 2013. **113**(5): p. 603-16.
21. Yang, J., et al., *The regulation of the autophagic network and its implications for human disease.* Int J Biol Sci, 2013. **9**(10): p. 1121-33.

Corresponding author:
Antje Gottschalk, MD, PhD
Department of Anesthesiology, intensive care medicine and pain therapy,
University hospital Muenster, Germany
Albert-Schweitzer-Campus 1, building A1
D-48129 Muenster, Germany
Tel.: +49 251 8347269
Fax.: +49 251 88704
Mail: Antje.Gottschalk@ukmuenster.de