

A prospective, randomized trial of continuous lateral rotation (“kinetic therapy”) in patients with cardiogenic shock

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Abstract

Background Continuous lateral rotation [“Kinetic therapy” (KT)] has been shown to reduce complications and to shorten hospital stay in trauma patients. Data in non-surgical patients is inconclusive. Retrospective data suggest a beneficial effect of KT in patients with cardiogenic shock (CS) requiring ventilator therapy. KT, however, has not been tested prospectively in those patients.

Methods A prospective, randomized, open-label trial was performed to compare KT using oscillating beds (TryaDyne Proventa, KCI) with standard care (SC). Patients with cardiogenic shock requiring ventilator therapy for more than 24 h were included. Primary endpoint was the occurrence of hospital-acquired pneumonia. Secondary endpoints were the occurrence of pressure ulcers during the hospital stay and 1-year all-cause mortality.

Results Forty-five patients were randomized to KT, and 44 to SC. All patients required at least one inotropic agent and one vasopressor for circulatory assistance. The groups were comparable in the etiology of heart disease, in the use of revascularization procedures, the use of balloon counterpulsation, and APACHE-II score (33 ± 5 vs. 33 ± 4) and SOFA score (11 ± 1 vs. 11 ± 1) at inclusion;

however, more patients in SC were subject to resuscitation before inclusion. Hospital-acquired pneumonia occurred in 10 patients in KT and 28 patients in SC ($p < 0.001$); pressure ulcers were seen in 10 versus 2 patients ($p < 0.001$). Hospital mortality tended to be lower in KT, and 1-year all-cause mortality was 41 % in KT and 66 % in SC ($p = 0.028$).

Conclusion The use of KT reduces rates of pneumonia and pressure ulcers as compared to SC. Moreover, in this study, patients with KT had a better outcome. The study suggests that KT should be used in patients with cardiogenic shock requiring ventilator therapy for a prolonged time.

Keywords Cardiogenic shock · Continuous lateral rotation · Kinetic therapy · Critical care · Ventilator-associated pneumonia

Introduction

Kinetic therapy (KT), also referred to as continuous lateral rotation, is defined as continuous turning of a patient slowly along the longitudinal axis to $>40^\circ$ onto each side. Initially invented to prevent pressure ulcers, it rapidly became obvious that KT improves pulmonary conditions in critically ill patients. In patients with trauma, a variety of studies showed that KT reduces pulmonary complications [1]. For non-trauma patients, evidence supporting KT is limited. Various studies did demonstrate a shortening of ICU stay in patients treated with KT, but no reduction in the incidence of pneumonia [2]. In contrast, four other studies could not demonstrate a reduction in ventilator dependency or hospital days in patients with non-traumatic critical illness despite a reduction in the rate of pneumonia

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[3–6]. In a very recent work, Staudinger showed reductions in the duration of ventilation and in the length of hospital stay together with reduced rates of pneumonia in critically ill medical patients [7], which has been shown to influence outcomes [8, 9]. The conflicting results of those studies are most likely due to a high variability of the patients included.

The effect of kinetic therapy in patients with cardiogenic shock is subject to debate. These patients differ from other non-trauma patients with lung failure by their hemodynamics, with a high rate of pulmonary congestion and pulmonary edema due to left ventricular failure, a condition secondary to the lung. Patients with unstable hemodynamics may, in the view of some experts, even deteriorate with continuous turning and are thus nursed in supine position. In addition, an increasing number of patients receive hemodynamic support by aortic counterpulsation and are subjected to early revascularization procedures following the favorable results of the SHOCK trial [10]. This makes conventional turning of patients even more difficult. Recently, a retrospective analysis performed by our group demonstrated a reduction of pneumonia and pressure ulcers in patients with cardiogenic shock requiring prolonged ventilatory support when treated with KT [11]. To our knowledge, no other data exist on KT in cardiogenic shock. These results were, however, challenged by many discussants due to their retrospective nature. To overcome this criticism, we decided to perform a prospective, randomized trial to evaluate the effects of KT in patients with cardiogenic shock. The trial presented here is the first randomized, prospective study of patients with CS subjected to KT.

Patients and methods

Setting

The study was performed at the cardiac-care Intensive Care Unit (ICU) of a single University Hospital. Kinetic therapy on this unit was started in August 2002. Since then, roughly 400 patients were treated using oscillating beds. The care of the patients has been standardized using written standard operating procedures in 2004. A retrospective analysis of kinetic therapy performed in patients treated on this ward has been reported previously [11].

Patients

All consecutive patients with cardiogenic shock (defined by a systolic blood pressure of <90 mmHg, or a cardiac index of <2.2 l/m² and a pulmonary wedge pressure >15 mmHg, or the need for inotropic or vasopressor support, according to previously specified criteria [10])

treated on this ICU were screened between September 2007 and July 2009. Patients needing prolonged ventilatory support, defined as modified oxygenation index ($\text{PaO}_2/\text{FiO}_2$) <300 torr (40 kPa) after 24–30 h of ventilator therapy were eligible for randomization. The only exclusion criteria were rhythmogenic instability requiring repeated resuscitation procedures, active bleeding precluding rotation of the patients, or a body weight above the upper weight limit for the KT device (i.e., more than 140 kg). Informed consent was obtained from the next of kin before inclusion. In addition, after recovery, the possibility to exclude their data from the analysis was offered to all patients. The study conformed to the Declaration of Helsinki and was approved by the Ethics Committee of the Medical Faculty of Dresden University of Technology.

Sample size calculation

At time of ethical approval of this study, a sample size was calculated. The database was an interim analysis of our previous retrospective work [11]. We used the parameter of pneumonia (primary endpoint of the previous study) for the estimation of the event rate. The estimation was performed with standard values (type I error probability for a two sided test of 0.05 and a power of 0.8). The following points in the study design were included in the calculation: prospective design, independent case control, uncorrected χ^2 test for the dichotomous variable of pneumonia, 1:1 ratio of control to case patients, event rate among standard care 0.47, event rate among kinetic therapy 0.268. The applied software was: PS: Power and Sample Size Calculation (Version: 2.1.31) from the Department of Biostatistics, Vanderbilt University (Nashville, TN, USA). Assuming the above-mentioned parameter, the sample size was calculated with 88 patients [12].

To cross-check this result, the calculation was repeated with the standard software package SAS, Version 3.1 (Cary, NC, USA) with the help of the Institute of Biometrics and Medical Information, University of Magdeburg. With the above-mentioned data a total sample size with 89 was computed based on the on-calculated power of 0.8027. For a more conservative approach with the Fisher's exact test for dichotomous data, a sample size of 98 for both groups together with a calculated power of 0.80104 was computed. In summary, the standard statistic program SAS supplies comparable results for the sample size estimation with 88 versus 89 cases. Together, it was decided to include 89 patients in this study.

Intervention

Immediately after inclusion, patients were randomized to KT or SC without further stratification for risk factors. If

the patients were randomized to KT, they were repositioned to the therapy device within 2 h. KT was routinely performed using oscillating air-flotation beds (TryaDyne Proventa[®], KCI, San Antonio, USA). In those beds, patients were continuously turned through an arc of about 80° every 7 min by alternating inflation of air cells within the bed's support surface. Additionally, percussion was administered by the automated percussion mode of the beds at nine beats/s for 10 min every 2 h. Suction was performed after percussion using closed systems. During KT, sedation was performed with sulfentanil and propofol. All patients were orally intubated and ventilated using pressure-controlled protocols with a target tidal volume of 6 ml/kg/min and titrated positive end-expiratory pressures (best-PEEP). The cuff pressures were checked every 8 h and maintained >20 cm H₂O. Enteral nutrition using gastric tubes was instituted at the third day of ventilation with slowly increasing volumes. Proton-pump inhibitors were used in all patients.

Kinetic therapy was performed until oxygenation indexes stabilized at >350 mmHg (46.7 kPa) for more than 24 h, with a FiO₂ ≤0.3 and a positive end-expiratory pressure ≤8 cm H₂O. Then, sedation was stopped, and patients were transferred into normal beds. Extubation was then rapidly performed after the patients had regained alertness and cooperativeness and were able to cough.

In the SC group, manual repositioning was performed every 2 h according to the standardized care on this ward. When in supine position, patients were cared in semi-recumbent position (45°) whenever hemodynamically tolerated. Criteria for extubation were the same than in the KT patients.

End points

The primary end point was:

1. the occurrence of nosocomial pneumonia (defined as combined occurrence of fever, a new radiological infiltrate occurring more than 48 h after admission, and growth of typical microorganism in tracheal aspirates). Therefore, all patients had daily bedside chest radiographs. Tracheal aspirates were performed when a new infiltrate was diagnosed. The analysis of the chest radiographs was done by a radiologist blinded to the therapy and had to confirm a pattern of infiltrate more persistent with pneumonia than with atelectasis. Sample size estimation was done with this variable.

The secondary end points were:

2. the occurrence of pressure ulcer (defined as de novo-occurrence or progression on a 4-point Shea-scale).

3. and all-cause mortality during the first year after hospital admission. Mortality data after hospital discharge were obtained by telephone interviews with the patients or their relatives, which were routinely performed after 6 and 12 months. If not possible, the survival status was checked by contacting the patient's health insurance. Using this method, a complete follow-up of the patient's mortality 1 year after inclusion could be achieved.

Moreover, the duration of ventilator therapy, the length of ICU stay, and the time to discharge or to referral to another hospital were analyzed. Further parameters analyzed were complications directly related to the use of the oscillating beds, i.e., dislocations of respiratory tubings or venous or arterial lines during the rotation or during the transfer into the oscillating beds. This safety data were analyzed using bedside protocols. The nurses directly in care of the patient had to report dislocations of lines and tubings in relation to the rotation of the patients or in relation to other maneuvers, i.e., change of beds, patient transport, or chest X-ray. They were, in addition, requested to report any unforeseen issues in relation to the oscillating beds or to manual repositioning in text form into the study documents.

Statistics

Results are presented as mean values ± SD for continuous normally distributed variables and as median (25–75 % percentile range) for continuous non-normally distributed data. Analysis of normality was performed with the Kolmogorov–Smirnov test. For the comparisons between normally distributed variables, the *t* test (modified by Welch for non-equal variance) was used. Non-normally distributed data were analyzed using box plots and the variable differences between groups were compared with the Mann–Whitney *U* test. Additionally, the χ^2 test was applied for dichotomous variables. The Kaplan–Meier method was used to graphically display the event rates and the groups were compared using the log-rank test. Adjusting in the multivariate analysis was performed using Cox- and logistic regression. A *p* value <0.05 was considered statistically significant.

Results

Patients

Between September 2006 and July 2008, 99 patients with cardiogenic shock and a PaO₂/FiO₂ <300 mmHg (40 kPa) on day 2 of respirator therapy were screened for the inclusion into this trial. Ten patients were not included: six patients had rhythmogenic instability necessitating repeated resuscitation measures, and four patients had bleeding

problems resulting from a combined anticoagulation and antiplatelet therapy after myocardial infarction so that rotation therapy was felt to be contraindicated in those patients. Together, 89 patients were randomized, 45 to KT, and 44 to SC. The baseline characteristics of both groups are given in Table 1. The patients in the KT group were less often subject to cardiopulmonary resuscitation before inclusion into the study. There were no differences in respect to age, the etiology of heart disease, the treatment modalities, and comorbidities.

Ventilator dependency, ICU and hospital stay

The length of ventilator dependency, of ICU stay and of hospital stay is given in Fig. 1. The length of ventilator dependency was 300 h (95 % confidence interval, 232; 639) in SC and 248 h (95 % confidence interval, 194; 391) in KT. The ICU stay was 18.1 (95 % confidence interval, 15.0; 21.2) versus 15.8 (95 % confidence interval, 13.2; 18.4) days. The hospital stay amounted for 20.3 (95 % confidence interval, 16.6; 24.1) versus 18.1 (95 %

confidence interval, 15.2; 21.0) days. There were no significant differences between the groups.

Pneumonia and pressure ulcer

As shown in Fig. 2, rates of pneumonia were significantly reduced by 60 % in the KT group. The microorganism detected are given in Table 2 and were roughly comparable in both groups. Comparably, the rate of pressure ulcers was halved by KT.

Patients with pneumonia were treated according to the resistograms obtained after testing. There was no correlation between the occurrence of pneumonia and 30-day-mortality ($r = 0.052$).

Procedure-related complications

Basically, dislocation of an endotracheal tube or of central venous lines are complications directly related to automated rotation. These complications were observed when introducing KT into the clinical routine of this ward.

Table 1 Baseline characteristics and treatment

	Kinetic therapy ($n = 45$)	Standard care ($n = 44$)	p value
Population characteristics			
Age (years, mean \pm SD)	64.9 \pm 13.2	68.7 \pm 11.0	0.15
Male gender [n (%)]	37 (82 %)	32 (73 %)	0.28
Body mass index (kg/m ² , mean \pm SD)	29.0 \pm 5.2	28.6 \pm 5.3	0.79
Underlying disease			
Ischemic heart disease [n (%)]	35 (77 %)	33 (75 %)	0.76
Acute myocardial infarction [n (%)]	31 (69 %)	27 (61 %)	0.46
Non-ischemic heart failure [n (%)]	6 (13 %)	8 (18 %)	0.53
Valvular heart disease [n (%)]	4 (8 %)	3 (6 %)	0.72
CPR due to malignant arrhythmia [n (%)]	24 (53 %)	33 (75 %)	0.03
Previously known lung disease [n (%)]	8 (18 %)	8 (18 %)	0.96
Previously known diabetes [n (%)]	22 (49 %)	24 (54 %)	0.59
Creatinine at admission (mmol/l, mean \pm SD)	153 \pm 65	145 \pm 52	0.53
Treatment			
Urgent coronary revascularization [n (%)]	33 (72 %)	31 (70 %)	0.76
Hypothermia [n (%)]	14 (33 %)	21 (47 %)	0.11
Aortic counterpulsation [n (%)]	23 (51 %)	20 (45 %)	0.59
Inotropes [n (%)]	45 (100 %)	44 (100 %)	–
Vasopressors [n (%)]	45 (100 %)	44 (100 %)	–
Hemofiltration/dialysis [n (%)]	12 (27 %)	11 (25 %)	0.86
Blood transfusions [n (%)]	23 (51 %)	20 (46 %)	0.59
Disease severity at inclusion			
APACHE-II score (points, mean \pm SD)	32.8 \pm 5.0	33.2 \pm 4.4	0.70
SOFA score (points, mean \pm SD)	11.2 \pm 1.4	10.9 \pm 1.3	0.28
LV ejection fraction (Echo; mean \pm SD)	34 \pm 13	31 \pm 11	0.38

SD standard deviation, LV left ventricular, CPR cardiopulmonary resuscitation

Value in italics indicates statistical significance ($p < 0.05$)

Fig. 1 Ventilator dependency, ICU stay, and hospital stay in patients subjected to standard care or kinetic therapy

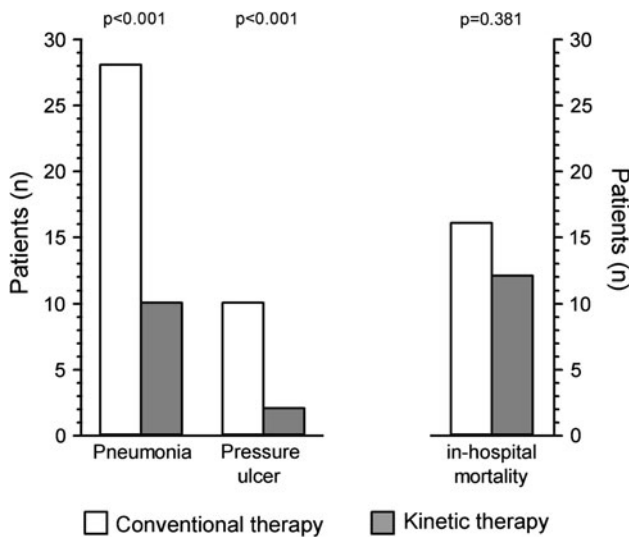
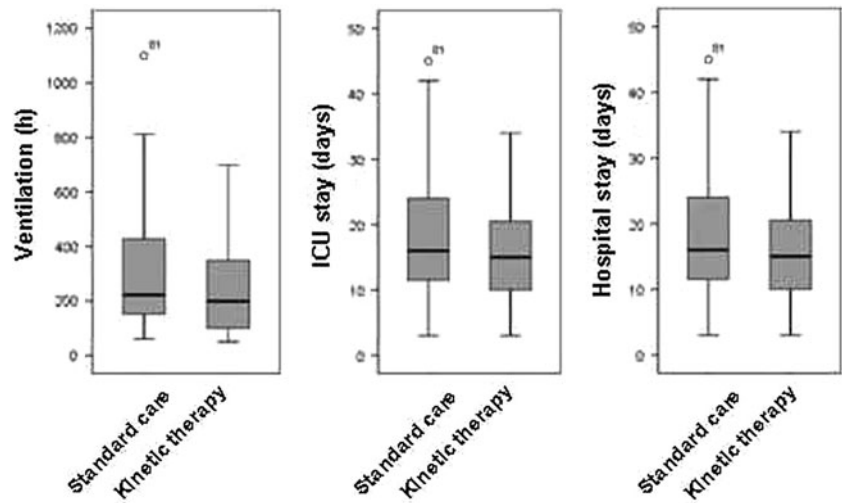


Fig. 2 KT reduces the incidence of pneumonia and of pressure ulcer. The in-hospital mortality was not different. (*n* denotes the numbers of the respective patients)

Table 2 Microorganism detected in tracheal aspirates in patients with pneumonia

	Kinetic therapy (<i>n</i> = 10)	Standard care (<i>n</i> = 28)
<i>Strep. pneumoniae</i>	2	3
<i>Staph. aureus</i>	4	12
<i>E. coli</i>	2	2
<i>Serratia</i> spp.	1	2
<i>Enterococcus</i> spp.	0	3
<i>Pseudomonas</i> spp.	1	3
<i>Haemophilus</i> spp.	0	3

Noteworthy, no procedure-related complications were observed during the course of this randomized study.

Mortality

In-hospital mortality of the patients showed a trend to a lower mortality in patients treated with KT: In the KT group, 12 of 45 patients died, and in the SC group, 16 of 44 patients died during the hospital stay (*p* = 0.381, Fig. 2). In both groups, the majority of the patients died by worsening heart failure or progressive multi-organ dysfunction. To discover long-term effects of KT on mortality, patients were followed up for 1 year. Surprisingly, the survival in KT patients was better than in SC patients (59 vs. 34 % of patients surviving, *p* = 0.028, Fig. 3).

Multivariate adjustment

To exclude that the difference in 1-year mortality between the groups was due to the baseline difference of patients subjected to CPR, a multivariate adjustment was performed, adjusting the mortality data with the baseline difference for CPR. The level of significance changed from *p* = 0.033 (hazard ratio 1.932, 95 % confidence interval, 1.056; 3.536) to *p* = 0.032 (hazard ratio 1.985, 95 % confidence interval, 1.060; 3.716) in the cox regression.

To validate this result, a second, independent calculation method was used, i.e., logistical regression. After adjusting the mortality with the CPR data, a very comparable result was obtained (*p* = 0.032, hazard ratio 1.985, CI 1.060; 3.716).

Discussion

The salient findings of this study are that in patients with cardiogenic shock, use of kinetic therapy can reduce the

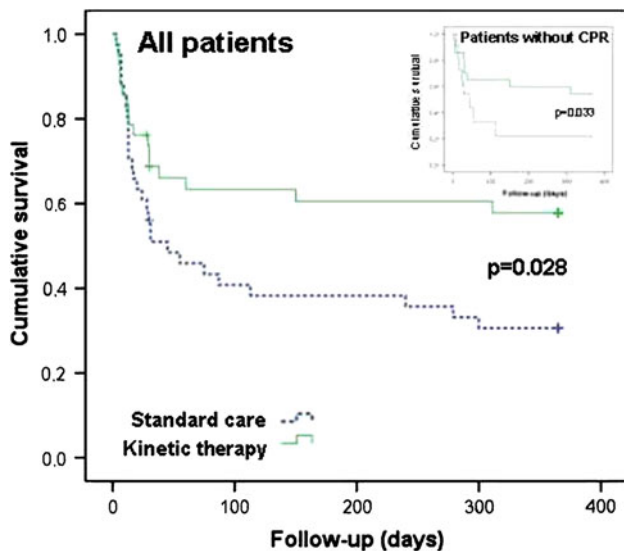


Fig. 3 1-year survival after cardiogenic shock. The Kaplan–Meier analysis was performed with the data obtained from telephone interviews. Follow-up of the patients was complete (100 %). The patients treated with KT had a better survival after 1 year. This difference persisted after the exclusion of all patients which were resuscitated prior to admission (see text)

rate of pneumonia and pressure ulcer. Moreover, in this cohort with some baseline differences, the long-term mortality of patients randomized to KT was lower as of those randomized to SC despite multivariate adjustment. The prospective randomized study included nearly 90 % of all patients with cardiogenic shock requiring prolonged ventilation that were admitted during the observational period, showing the high feasibility of the devices.

Whereas in trauma patients, the effects of kinetic therapy have been shown by various authors [1, 13–16], data in medical patients are variable to date. Broad evidence exists that KT reduces the rate of pneumonia also in medical patients [3–7, 11]. A reduction of ICU stay could be shown by some authors [7, 11] whereas four other studies saw no effect of KT on this parameter [3–6]. This study could show a reduction in mortality by KT. These differences may be explained by the relatively small number of patients included in every single study, and by the different underlying medical conditions [4–6]. Of note, the APACHE-II score of the patients in this study was higher than in previous work by other groups [17, 18]. This may explain why the rate of ventilator-associated pneumonia is higher in this work compared to other work. Usually, a rate between 15 and 40 % of patients has been reported [7, 17–19]. The APACHE-II scores in most of these studies were between 20 and 25, as compared to 33 in this study. The rate of pressure ulcer in this study (20 % in the control group) was comparable to other work [20].

To our knowledge, the data presented here is the first prospective study of KT in patients with cardiogenic shock.

Of note, the patients were treated according to contemporary standards, namely with urgent revascularization in patients with evidence of myocardial ischemia and with therapeutic hypothermia in patients after CPR [21–24]. This analysis shows that this subgroup of patients, with respiratory failure primary due to congestion, benefits from KT. Furthermore, it demonstrates that KT is feasible in those patients or and that continuous rotation does not lead to hemodynamic or rhythmogenic instability due to fluid shifts or other mechanisms. The number of procedure-related complications was low. Somewhat surprisingly, the short- and long-term mortality in the KT group was reduced, a finding which was not seen in any other study examining KT in medical patients. Since the number of patients in this study was relatively small for a mortality study, this finding may clearly be due to chance and has to be confirmed by further studies. It, however, points in the direction of better outcome parameters in patients treated with KT, which has been also seen in other studies [7, 11]. The hypothesis of the authors is that the reduced rate of pneumonia leads to a better functional status of the patients at discharge, which translates into better long-term survival despite a comparable in-hospital mortality. Therefore, besides mortality, further studies should also address the functional status of the patients at discharge, which has not been done in this study. Moreover, other adjunctive therapies, which were recently suggested to be beneficial, such as frequency control, should be included [25, 26].

It should be emphasized that this study on KT is, to our knowledge, the first randomized work dealing with respiratory failure in cardiogenic shock patients. Until now, the ESC and AHA guidelines give no clear recommendation on this topic [27, 28]. The recently published German-Austrian S3 guideline on the treatment of cardiogenic shock complicating myocardial infarction [29] recommends a lung-protective ventilatory protocol comparable to that protocol used in this study in all patients. Supportive measures such as KT are not discussed for the lack of data. The recommendations given in this guideline on respiratory support are fully based on expert opinion (Level of evidence, 3/4), and the guidelines emphasize the need for clinical trials. The data presented here is the first evidence-based dataset on this topic and should, in our eyes, be evaluated to be part of the next revision of the guidelines.

Kinetic therapy has to be compared with other repositioning maneuvers. Among them, prone positioning is one of the most promising. Prone positioning has been reported to improve oxygenation in patients with acute respiratory failure when compared to SC [30, 31], with unchanged overall outcome. One study found comparable outcome of KT compared to prone positioning in patients with the acute respiratory distress syndrome [32]. Prone positioning has the advantage of no additional cost for devices. It was,

however, only recommended for acute respiratory failure in other than cardiac conditions. For the subgroup of patients with cardiogenic shock, prone positioning seems in many cases inadvisable since patients subjected to aortic counterepulsation are at a high risk for complications when prone. Therefore, proning of patients was not performed in the patients analyzed.

As every study, this work has shortcomings. Due to the nature of the devices, the study had an open design. The number of patients was relatively small. The sample size, however, was prospectively calculated from the previous, retrospective analysis [11] using the reduction in pneumonia as a reference parameter, so that an expansion of the study seemed not feasible. The primary end points pneumonia and pressure ulcer are not fully standardized and thus subject to bias. We tried to overcome this by a blinded evaluation of chest radiographs by a radiologist and by including microbial data into the definition of pneumonia. The criteria for extubation were not fully characterized and to some extent left to the treating physicians (see “Intervention” of “Patients and methods”), and discharge from ICU and from the hospital was completely at the discretion of the treating physician. This regimen, however, was unchanged during the study period. Hemodynamic data were obtained only in a minority of patients. Since we, however, included all suitable consecutive patients during the study period, we believe that the cohort of patients examined represents the “real world” of a cardiac-care ICU.

In summary, this analysis gives preliminary evidence that early use of kinetic therapy can reduce complications in ventilator-dependent patients with cardiogenic shock. Thus, early use of KT should be considered in patients with cardiogenic shock requiring prolonged ventilatory support.

Conflict of interest There are no relationships or financial interests influencing this work.

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