Carbapenemase-producing Enterobacteriaceae in an inpatient post-acute care facility: impact on time to functional recovery.

N. H. Loukili, J. F. Jusot, Etienne Allart, G. Celani, A. Perrin, O. Gaillot, A. Blanchard, V. Pardessus, André Thevenon, Vincent Tiffreau

Carbapenemase-producing *Enterobacteriaceae* in a post-acute care facility: Impact on time to functional recovery

Noureddine Henoun Loukili, MD[1]; Jean-François Jusot, MD, PhD[2]; Etienne Allart, MD, PhD[3]; Gael Celani, MD[4]; Agnes Perrin, MD[1]; Olivier Gaillot, PhD[5]; Anne Blanchard, MD[6]; Vinciane Pardessus, MD[4]; André Thevenon, MD[6,7]; Vincent Tiffreau, MD, PhD[6,7]

[1]Infection Control Unit, University Hospital of Lille, F-59000, Lille, France

[2]Department of Medical Informatics, University Hospital of Lille, F-59000, Lille, France

[3]CHU Lille, Neurorehabilitation Unit, University Hospital of Lille, F-59000 Lille, France; University of Lille, INSERM UMR-S-1172 - Lille Neuroscience and Cognition, F-59000 Lille, France

[4]General Rehabilitation Unit, University Hospital of Lille, F-59000, Lille France

[5]Microbiology, University Hospital of Lille, F-59000, Lille, France

[6]Physical and Rehabilitation Medicine, University Hospital of Lille, F-59000, Lille France

[7]ULR 7369 - URePSSS - Unité de Recherche Pluridisciplinaire Sport Santé Société, University of Lille, F-59000, Lille

Corresponding Author

Vincent Tiffreau

Service de MPR, Hôpital Swynghedauw, rue André Verhaeghe, 59000 Lille, France

vincent.tiffreau@chu-lille.fr; Tel = +33 3 20 44 58 31

Carbapenemase-producing *Enterobacteriaceae* in an inpatient post-acute care facility: impact on time to functional recovery

Abstract

Background. The carriage of carbapenemase-producing *Enterobacteriaceae* (CPE) might lengthen the time to functional recovery (TTFR) for inpatients in post-acute care (PAC) units.

Objective. We aimed to assess the impact of CPE carriage on TTFR in a PAC facility.

Methods. This 2-year retrospective cohort study included 20 CPE-positive patients and 54 CPE-negative patients admitted to 3 PAC units (general, orthopaedic and neurologic rehabilitation units) in a teaching hospital from January 2017 to December 2019. Potential risk factors and demographic data were collected from patients' medical records, the French national hospital discharge database, and the hospital's CPE surveillance database. Functional recovery was defined as the median difference in functional independence measure (FIM) between admission and discharge from each unit. Survival analysis and multiple Cox regression models were used to predict the TTFR and identify factors associated with functional recovery.

Results. The overall median [interquartile range] TTFR was 50 days [36–66]. Longer median TTFR was associated with CPE carriage (63 vs 47 days in the CPE-negative group; adjusted hazard ratio (aHR) 0.35, 95% CI 0.13–0.97) and presence of a peripheral venous catheter (aHR 3.51, 1.45–8.46); shorter TTFR was associated with admission to an orthopaedic versus general rehabilitation unit (aHR 3.11, 1.24–7.82).

Conclusions. CPE carriage in inpatient PAC facilities was associated with long TTFR. Further studies are needed to explore the mechanisms involved in these adverse events and to identify possible preventive measures.

Keywords. post-acute care, carbapenemase-producing *Enterobacteriaceae*, nosocomial, functional independence measure

Abbreviations

CPE: carbapenemase-producing *Enterobacteriaceae*

FIM: Functional Independence Measure

LOS: length of stay

PAC: post-acute care

PVC: peripheral venous catheter

RU: rehabilitation unit

TTFR: time to functional recovery

Introduction

Carbapenemase-producing *Enterobacteriaceae* (CPE) are considered a major threat to public health worldwide [1]. CPE infections are difficult to treat and are associated with a high mortality rate [2]. Furthermore, CPE are able to easily spread their resistance-associated mobile genetic elements [3]. Hence, CPE are considered priority pathogens by the World Health Organization [4].

CPE were first identified in the early 2000s. They quickly spread around the world and have become a serious threat in the last decade. Many clusters or outbreaks of CPE have been reported in various hospital wards, and most outbreaks have been healthcare-related [5,6]. As for other human *Enterobacteriaceae*, CPE colonize the gut, and asymptomatic carriage may last for months or years [7]. The first guidelines on containing the dissemination of CPE were published in the United States and in France in 2012 and 2015, respectively [8,9]. To limit the spread of CPE in hospital wards, a patient is isolated in a single-bed room, contact precautions are taken, and anal swab samples are cultured weekly. CPE-positive (CPE+) patients are usually discharged to post-acute care (PAC) facilities such as rehabilitation units (RUs) and long-term care units to facilitate their recovery from injury, illness or disease. This type of care facility contributes to the spread of CPE in hospitals [10, 11]. Nevertheless, compliance with infection control measures for CPE+ patients may limit their access to certain types of physiotherapy sessions implemented outside their room, such as those requiring technical facilities or performed in groups. Hence, a patient's CPE+ status might lengthen the time to functional recovery (TTFR) and thus their hospital stay. This situation should be a concern for both patients and healthcare workers.

The objective of the present retrospective cohort study was to determine whether CPE carriage affects the time to recovery among patients in PAC units.

Patients and methods

Hospital and setting

This retrospective cohort study was performed in 3 adult PAC units (a 21-bed general unit, an 18-bed neurological unit, and a 20-bed orthopaedic unit) at Swynghedauw Hospital, a 127-bed PAC hospital that is part of Lille University Medical Centre (Lille, France).

The reasons for patient admission and the rehabilitation processes vary among PAC units. In the neurological and orthopaedic RUs, patients perform at least 1 hr of active rehabilitation a day. The neurological RU usually admits patients with a chronic neurological disease (Parkinson's disease, multiple sclerosis, etc.) or an acute neurological disease (spinal cord injury, Guillain-Barré syndrome, acute neuropathy, etc.). Patients who had spine surgery and (in rare cases) other patients are also sometimes hospitalised in this RU. Patients with stroke or brain injury are hospitalised in a dedicated ward and were not included in the present study. The orthopaedic RU admits patients with orthopaedic impairments (fractures, skeletal disorders, and spine surgery) and, less frequently, patients with other diseases or disorders. Most people admitted to the general RU are orthopaedic patients requiring non-intensive rehabilitation (e.g., when limb load-bearing is contraindicated) or patients who had vascular or digestive tract surgery. The unit occasionally admits patients with neurological impairments for whom intensive rehabilitation is delayed or contraindicated.

A total of 811 patients were hospitalized for rehabilitation during the study period. The CPE infection control measures usually included single-room isolation with strict contact precautions, hand hygiene with hydro-alcoholic rubs, meticulous environmental disinfection, and weekly surveillance rectal swab cultures for both CPE+ patients and CPE-negative (CPE-) patients hospitalized in the same unit. CPE+ patients were placed in isolation throughout their hospital stay. To check for the absence of cross-contamination, CPE- patients were screened systematically at 1 week after a CPE+ patient had been discharged.

Participants and variables

The study period was from January 1, 2017, to December 31, 2018. All patients admitted to one of the 3 above-mentioned PAC units were eligible for the study. For patients admitted more than once, only the first hospital stay was analysed. All patients who were CPE+ on admission were included. Patients lacking data on CPE status or the functional independence

measure (FIM) or who stayed in hospital for < 7 days were excluded. For each CPE+ patient, 3 CPE- patients were selected blindly and at random from the cohort, with no replacement. All participants were followed from admission to discharge, and the end date for follow-up was April 1, 2019. The patient was discharged when the rehabilitation programme's functional goal had been achieved or when the functional independence remained stable despite rehabilitation efforts. CPE+ patients were defined as those with a positive CPE culture from at least 2 separate rectal swabs in the 3 months before their admission. Briefly, rectal swabs were plated on commercially available CPE-selective chromogenic agar plates; broth enrichment was not performed. Presumptive colonies were identified by using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (microflex Bruker, Wissembourg, France), and *Enterobacteriaceae* colonies were then assessed for the production of the OXA-48-like, NDM, KPC and VIM carbapenemases by a multiplex lateral flow assay (OKNV K-SeT, Coris BioConcept, Gembloux, Belgium).

The FIM is used to determine the degree of disability that patients experience and signs of progress during rehabilitation. The FIM comprises 18 items grouped into a 13-item motor subscale and a 5-item cognition subscale. Each item is scored on a 1-to-7 ordinal scale, so the total score for the FIM ranges from 18 to 126 points; the higher the score, the more independent the patient. The motor FIM subscale ranges from 13 to 91 and the cognition subscale from 5 to 35 [12].

Functional recovery was defined on the basis of the difference between the individual FIMs measured on admission and discharge. The median ΔFIM for each rehabilitation unit was selected as a cut-off to define functional recovery. When the patient's ΔFIM exceeded the median ΔFIM of the unit, the patient was considered to have recovered (event=1); otherwise, the patient was considered not to have recovered (event=0). The study's primary outcome was the TTFR, defined as the time between admission in the unit and the event (= time at achievement of the ΔFIM of the unit).

Data for the following variables were extracted from patients' medical records, the French national administrative hospital discharge database (Programme de Médicalisation des Systèmes d'Information) and our hospital's local CPE monitoring database. The information collected included demographic data, the underlying disease or condition, body mass index, the number of physiotherapy sessions, urinary and/or faecal incontinence, the use of indwelling catheters (a urinary catheter, central venous catheter, or peripheral venous catheter

[PVC]), wound dressings, the Charlson comorbidity index, and motor and cognitive FIMs at the time of admission and discharge.

A total of 25 CPE+ patients and 786 CPE- patients were admitted to the 3 units during the study period; 75 CPE- patients were randomly selected. We excluded 20 patients (17 CPE- and 3 CPE+) who lacked data on the FIM at discharge and 6 who had been discharged at < 7 days (Fig. 1).

Statistical methods

Continuous variables are expressed as mean (standard deviations) when the distribution was normal or median (range or interquartile range [IQR]) otherwise. Categorical variables are described as frequency (percentage). The characteristics of the CPE+ and CPE- groups were compared by chi-square test or Fisher's exact test for categorical data. For continuous variables, Student *t* test or the Kruskal-Wallis test was used, depending on the distribution of the variable. We considered that the patient had recovered if the ΔFIM was above the median value for the RU. Data were analysed by using the Kaplan–Meier procedure, log-rank test, and a Cox regression model to predict the TTFR and identify predictors of functional recovery. Variables with $p<0.25$ on bivariate analyses were introduced into a multivariable Cox regression model. CPE status (+/-) was always included in the model, regardless of the level of significance in the bivariate analysis. Adjusted hazard ratios (aHRs) and their 95% confidence intervals (CIs) were computed, and the threshold for statistical significance was set at $p<0.05$. An HR < 1 indicated longer TTFR. The proportional-hazards assumption was checked by using graphical diagnostics and statistical tests based on the scaled Schoenfeld residuals. All statistical analyses were performed with R.3.6 (R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org/). We used the Strengthening the Reporting of Observational studies in Epidemiology criteria for reporting the results [13].

Results

Characteristics of patients

The CPE+/CPE- patient groups were similar with regard to almost all variables, including mean Charlson comorbidity index before admission to the RU (Table 1). However, in the CPE+ group, the median motor FIM on admission and discharge was low (0.77- and 0.70-fold vs. the CPE- group, $p = 0.025$ and 0.011, respectively), median length of stay (LOS) was longer (2.3-fold, $p = 0.017$) and PVC use was more frequent (2.8-fold, $p= 0.027$).

Outcomes

The overall median (range) ΔFIM was 8.5 (-11 to 70) and patients in each RU had different median ΔFIM values: 3 (range 0 to 70) in the neurological unit, 8.5 (-11 to 64) in the general unit, and 12.0 (0 to 47) in the orthopaedic units (Table 2). The median [IQR] recovery rate was 40% [20 to 63] in the CPE+ group and 52% [39 to 65] in the CPE- group (p = 0.053).

Univariate and bivariate analyses of TTFR

The median [IQR] overall TTFR was 50 days [36–66]. CPE status was significantly associated with TTFR: 47 versus 63 days for the CPE- and CPE+ groups, respectively (Fig. 2). The use of a PVC, wound dressing, and type of RU were all associated with TTFR ($p < 0.25$) (Table 2). Patients with a PVC had shorter median TTFR (31 vs. 57 days without a PVC), and most were hospitalised in the general RU unit (n=10) and the neurological RU (n=6). Patients requiring wound dressings had shorter median TTFR (49 days) than those not requiring wound dressings. Median TTFR was longer for patients in the general RU than the orthopaedic and neurological RUs (63, 33 and 31 days, respectively).

Multivariate analysis of factors associated with TTFR

Multiple covariate analysis revealed TTFR significantly associated with CPE+ status, use of a PVC and hospitalization in the orthopaedic RU (Table 3). Longer median TTFR was associated with CPE+ versus CPE- status (aHR 0.35, 95% CI 0.13–0.97) and with than without use of a PVC (aHR 3.51, 1.45–8.46). Likewise, shorter median TTFR was associated with admission to the orthopaedic versus general RU (aHR 3.11, 1.24–7.82). Lastly, wound dressing was not associated with TTFR (p= 0.117). All variables fulfilled the proportional hazards assumption (p=0.39).

Discussion

In the present research, the CPE+ and CPE- patient groups differed significantly in terms of 4 of the 21 study variables: motor FIM on admission and discharge, LOS, and PVC use. However, the two FIMs and LOS were used to define the outcome (functional recovery and TTFR). Hence, the 2 groups of patients differed significantly in use of a PVC only (45% in the CPE+ group vs 16% in the CPE- group; p= 0.027). CPE+ patients may be more likely to have severe medical conditions requiring infusion placement than CPE- patients. To control for this potential source of bias, we adjusted the final model for the PVC factor. Therefore, the 2 groups could be considered balanced in most of the study variables.

Our results showed CPE+ status associated with longer TTFR in an inpatient PAC facility. For CPE+ patients, the median TTFR was 63 days (vs 47 days in CPE- patients) and thus seemed a harmful factor for recovery and discharge. Our data agree with Colorado et al. [14], who found that patients in contact isolation in an acute inpatient PAC facility showed reduced FIM efficiency (defined as the change in FIM score divided by the length of stay: 1.2 vs. 2.0 for other patients; $p< 0.01$) and longer LOS (by 39%; $p=0.017$). However, given the differences in study design and study outcomes, the comparison remains limited.

The ΔFIMs recorded in the RUs appeared to be low relative to the literature data. Furthermore, the ΔFIM data were not normally distributed (median and mean ΔFIM: 8.5 and 14.5, respectively). Hence, we decided to analyse the median ΔFIM. Indeed, use of the median ΔFIM enabled us to limit the potential effect of outliers on the measurements. especially given the small number of patients in the CPE+ group. Therefore, the ΔFIM values from various studies should be compared with caution.

Isolation is one component of stringent containment strategies that also include strict hand hygiene, contact precautions, cleaning and disinfecting equipment and facilities, screening for CPE carriage, active management of contacts, and antimicrobial stewardship (to avoid the over-use of broad-spectrum antibiotics) [8,9,15]. None of these measures is compatible with rehabilitation programmes, which usually include group-based activities and the use of shared facilities (e.g., gyms, hydrotherapy pools and other treatment areas). Thus, CPE+ patients are often unable to access this range of care activities, which may lead to poorer functional outcomes and thus extend their TTFR. Other researchers have also reported a negative impact of contact isolation on a patient's mental well-being, satisfaction, safety, or the time spent by healthcare workers on direct patient care, which might also lengthen the time to recovery or lead to care failure [16, 17].

In our bivariate analysis, the median TTFR was shorter in patients with than without a PVC (31 vs 57 days). PVCs are commonly used in medical and surgical care to administer infusions; this increases the workload of the healthcare workers and testifies to the continuation of acute treatment [18]. Hence, patients with a PVC are more likely to develop medical complications and to be discharged to acute care units. Consequently, the LOS in the RU and the TTFR would both be shorter. Nevertheless, none of these patients was discharged to an acute unit. Also, PVCs require close monitoring of infusions and possibly lead to adverse events including nosocomial infections. Hence, patients (particularly CPE+ carriers)

with a PVC presumably received more direct care than other patients, which might have reduced the potential impact of isolation and shortened the TTFR.

Admission to the orthopaedic RU was associated with shorter median TTFR (33 vs 63 days overall). On admission to the orthopaedic RU, patients had a high median [IQR] motor FIM: 71 [62–80] overall and 52 [30–68] for the CPE+ group, which indicates the presence of mild-to-moderate motor impairment in this group. Hence, the orthopaedic patient's health status at the time of admission may have helped limit the impact of CPE+ carriage on the TTFR. Sahota et al. (2019) reported greater motor FIM values on admission associated with shorter LOS. This latter finding agrees with other literature reports in which motor FIM predicted rehabilitation LOS after total hip arthroplasty [19, 20, 21]. Given that orthopaedic patients and therapists identify specific motor goals on admission to a rehabilitation unit, patients who are closer to achieving these goals would frequently require shorter LOS and thus have shorter TTFR.

Survival analysis to model the TTFR used in this study overcomes the problem of the normal distribution of time to dependent variables. To this end, we used the median ΔFIM between admission and discharge in each rehabilitation unit as a cutoff to define patient recovery. Indeed, the median ΔFIM varied among units. It was 12 (range 0–47) in the orthopaedic unit and 3 (range 0–70) in the neurological unit, which suggests that the nature of a patient's disability influences the FIM gain. Hence, applying the median ΔFIM for the whole cohort as a cutoff would have biased the recovery of patients in the neurological or the general RU. Furthermore, the median ΔFIM would allow a clinician to pragmatically evaluate a patient's recovery by comparing the patient's FIM gain to the unit's median ΔFIM.

The present study has several limitations. First, the relatively small sample size might have masked the effect of other factors on the TTFR. Indeed, the low incidence rate of CPE (3%) in our patient cohort limited the number of CPE+ patients. Furthermore, 5 of 25 eligible patients were excluded because FIM data were missing. Second, the study's single-centre observational design limits the generalizability of the results. Hence, further prospective, multicentre studies of the impact of intestinal CPE carriage on the TTRF in PAC patients are needed to consolidate our results. However, to the best of our knowledge, this is the first study to investigate TTFR in patients with CPE carriage, which remains a serious issue for patients and healthcare workers in hospitals. Thus, further investigations on this topic would increase

knowledge of the association between CPE isolation measures and TTFR, particularly by studying the role or the mechanism of other factors that might independently affect the TTFR.

In conclusion, our results show that CPE carriage prolonged the TTFR in patients undergoing rehabilitation, probably owing to the restrictions typically associated with infection control measures. Further research should focus on the mechanism leading to these poor outcomes, including infection control strategies in PAC units.

Legends

Figure 1. Study flow chart. CPE, carbapenemase-producing *Enterobacteriaceae*; FIM, functional independence measure.

Figure 2. Kaplan-Meier survival curve for recovery as a function of CPE status (CPE+).

References

1. Latania K. Logan, Robert A. Weinstein. The Epidemiology of Carbapenem-Resistant Enterobacteriaceae: The Impact and Evolution of a Global Menace. J Infect Dis. 2017; 15; 215(Suppl 1): S28–S36.

2. Mirjam J. D. Dautzenberg, Ann N. Wekesa, The Association Between Colonization With Carbapenemase-Producing Enterobacteriaceae and Overall ICU Mortality: An Observational Cohort Study. Crit Care Med. 2015; 43(6): 1170–1177.

3. Nordmann P, Dortet L, Poirel L. Carbapenem resistance in enterobacteriaceae: here is the storm! Trends Mol Med. 2012; 18: 263–272.

4. WHO, Global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics, 2017, https://www.who.int/medicines/publications/WHO-PPL-Short_Summary_25Feb-ET_NM_WHO.pdf

5. Logan LK, Weinstein RA. The epidemiology of Carbapenem-resistant enterobacteriaceae: the impact and evolution of a global menace. J Infect Dis. 2017; 215:28–36

6. Decraene V, Phan HTT, George R, Wyllie DH, Akinremi O, Aiken Z, et al. A Large, Refractory Nosocomia Outbreak of Klebsiella pneumoniae Carbapenemase-Producing Escherichia coli Demonstrates Carbapenemase Gene Outbreaks Involving Sink Sites Require Novel Approaches to Infection Control. Antimicrob Agents Chemother. 2018; 62:e01689–e01718.

7. Bar-Yoseph H, Hussein K, Braun E, Paul M. Natural history and decolonization strategies for ESBL/carbapenem-resistant Enterobacteriaceae carriage: systematic review and meta-analysis. J Antimicrob Chemother. 2016; 71:2729–39.

8. Lepelletier D, Berthelot P, Lucet JC, Fournier S, Jarlier V, Grandbastien B; National Working Group. French recommendations for the prevention of 'emerging extensively drug-resistant bacteria' (eXDR) cross-transmission. J Hosp Infect. 2015; 90(3):186-95.

9. Centers for Disease Control and Prevention. 2012 CRE toolkit: Facility guidance for control of carbapenem-resistanceEnterobacteriacea (CRE). https://www.cdc.gov/hai/pdfs/cre/cre-guidance-508.pdf. [accessed nov 2015]

10. Rossini A, Di Santo S G, Libori M F, Tiracchia V, Balice M P, Salvia A Risk factors for carbapenemase-producing Enterobacteriaceae colonization of asymptomatic carriers on admission to an Italian rehabilitation hospital. J Hosp Infec. 2016; 92(1):78-81.

11. Michael Y Lin , Karen Lolans et al. Prevention of colonization and infection by Klebsiella pneumoniae carbapenemase-producing enterobacteriaceae in long-term acute-care hospitals. Clin Infect Dis. 2015; 15; 60(8):1153-61.

12. Linacre JM, Heinemann AW, Wright BD, Granger CV, Hamilton BB. The structure and stability of the Functional Independence Measure. Arch Phys Med Rehabil. 1994; 75(2):127-32.

13. Von Elm E, Altman DG, Egger M, Pocock SJ, Vandenbroucke JP, STROBE Initiative. The Strengthening the Reporting of Observational Studies In Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Int J Surg 2014; 12:1495-9.

14. Colorado B, Del Toro D, Tarima S.Impact of contact isolation on FIM score change, FIM efficiency score, and length of stay in patients in acute inpatient rehabilitation facility. PM R. 2014; 6(11): 988-91.

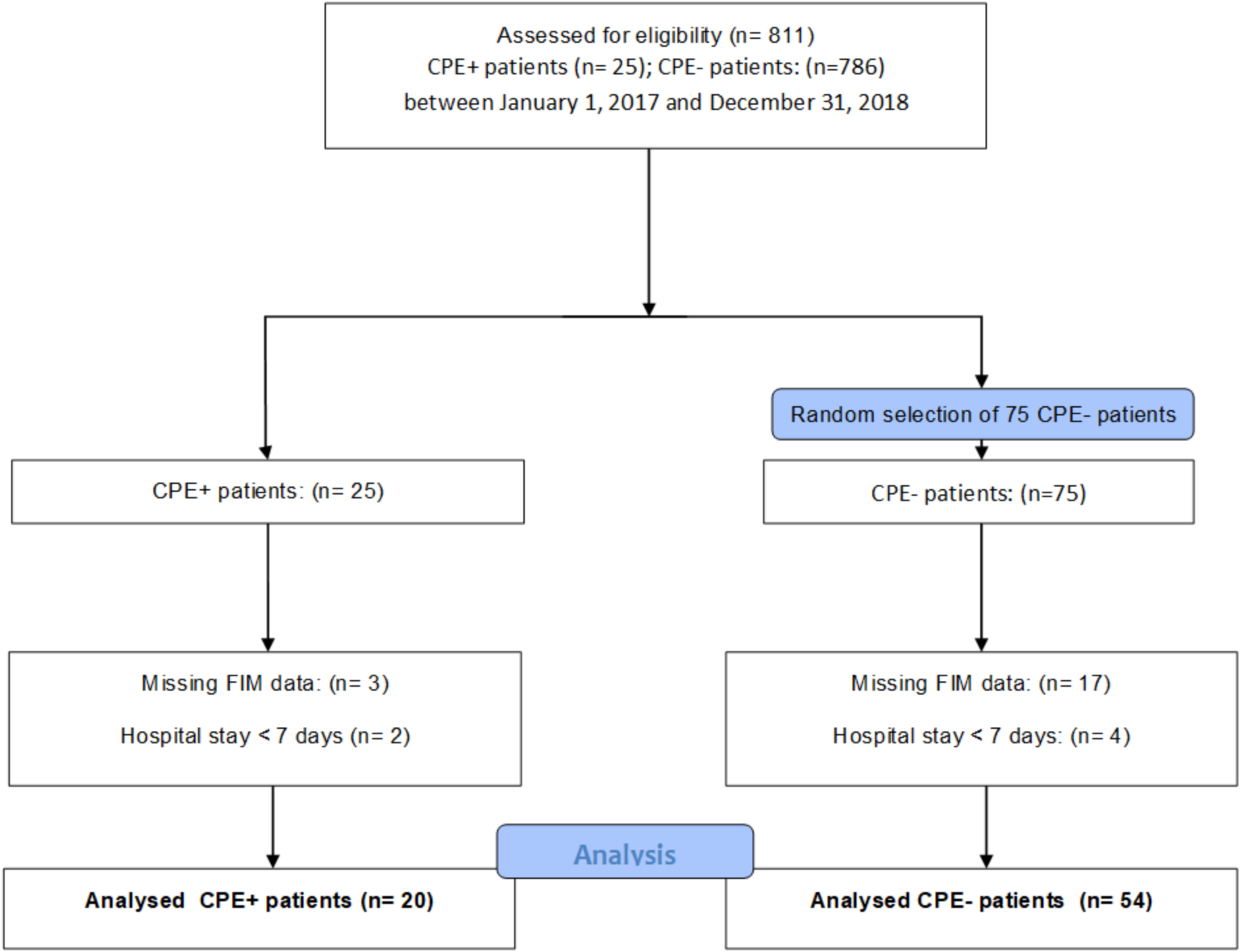
15. British Society of Rehabilitation Medicine. Framework for Action to contain carbapenemase-producing Enterobacteriacae (CPE) - application in rehabilitation. https://www.bsrm.org.uk/downloads/framework-for-action-to-contain-cpe-rehabilitation-settings-november-2020-combined-finalwithack-20-1-21.pdf. [Accessed April 5, 2021]

16. Abad C, Fearday A, Safdar N. Adverse effects of isolation in hospitalised patients: a systematic review. J Hosp Infect. 2010; 76(2):97-102.

17. Tarzi S, Kennedy P, Stone S, Evans M. Methicillin-resistant Staphylococcus aureus: psychological impact of hospitalization and isolation in an older adult population. J Hosp Infect 2001; 49:250-54.

18. Rickard CM, Marsh NM, Larsen LM and al. Effect of infusion set replacement intervals on catheter-related bloodstream infections (RSVP): a randomised, controlled, equivalence (central venous access device)-non-inferiority (peripheral arterial catheter) trial. Lancet. 2021; 17; 397(10283):1447-58.

19. Sahota B, Alavinia SM, Kumbhare D, Sangha H, Flannery J, Furlan A. A Retrospective Study of the Association between Pain Intensity and Opioid Use with Length of Stay during Musculoskeletal Inpatient Rehabilitation after Primary Knee and Hip Arthroplasty. PM R. 2020; 12(5):462-69.
20. Yeung SM, Davis AM, Soric R. Factors influencing inpatient rehabilitation length of stay following revision hip replacements: a retrospective study. BMC Musculoskelet Disord. 2010; 28;1:252.
21. Tal-Akabi A, Schmid S, Taeymans J. Determinants of inpatient rehabilitation length of stay and discharge modality after hip and knee replacement surgery in Switzerland - a retrospective observational study. Swiss Med Wkly. 2013; 143:w13832.


Assessed for eligibility (n= 811)
CPE+ patients (n= 25); CPE- patients: (n=786)
between January 1, 2017 and December 31, 2018
Random selection of 75 CPE- patients
CPE+ patients: (n= 25)
CPE- patients: (n=75)
Missing FIM data: (n= 3)
Hospital stay < 7 days (n= 2)
Missing FIM data: (n= 17)
Hospital stay < 7 days: (n= 4)
Analysis
Analysed CPE+ patients (n= 20)
Analysed CPE- patients (n= 54)

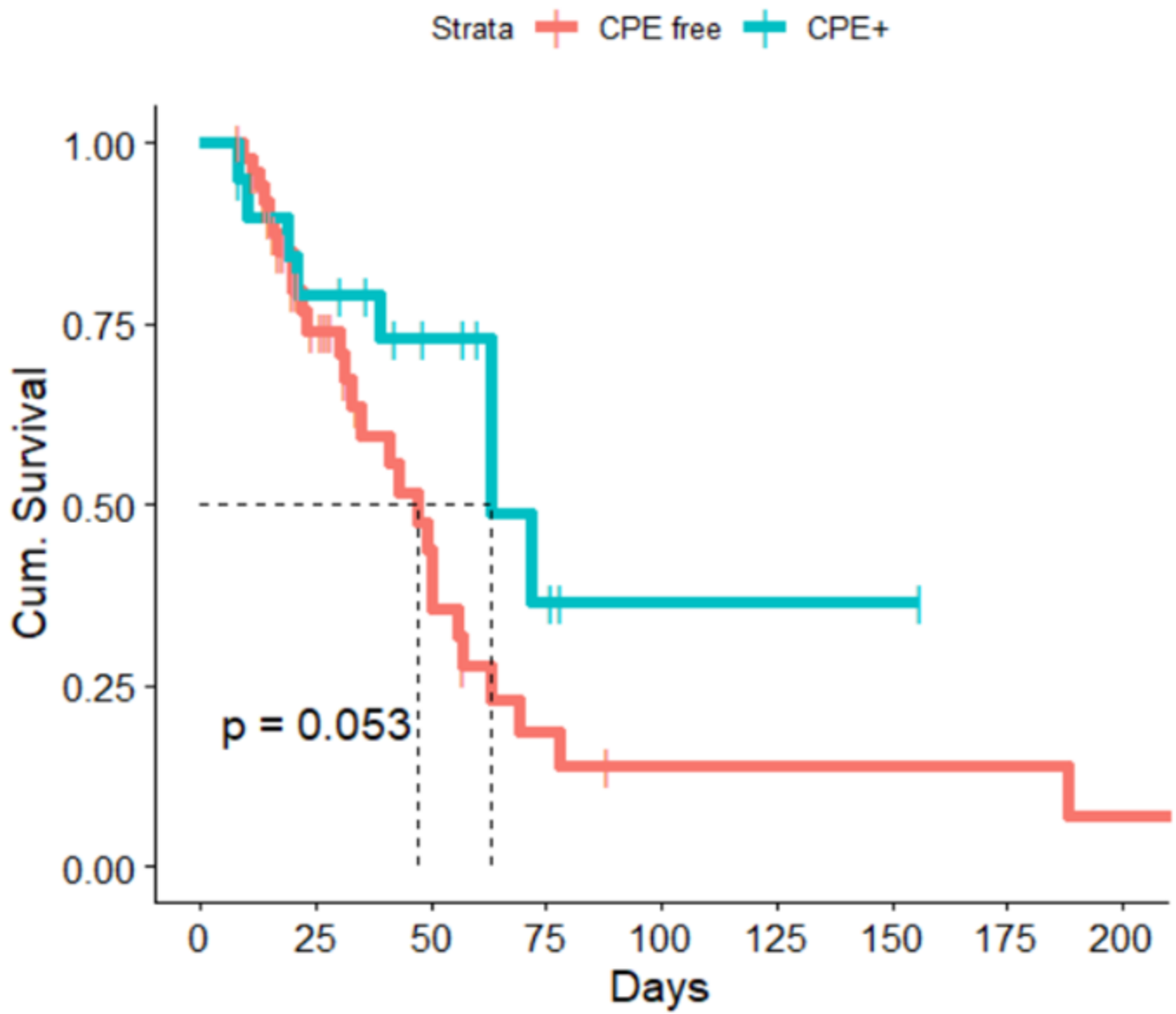

Strata
CPE free
CPE+
1.00
0.75
0.50
0.25
0.00
Cum. Survival
p = 0.053
0
25
50
75
100
125
150
175
200
Days

Table 1. Characteristics of study participants with and without carbapenemase-producing *Enterobacteriaceae* (CPE).

	Total (n=74)	**CPE- (n=54)**	**CPE+ (n=20)**	***P* value**
Age, mean (SD)	64.9(16)	65.8 (15.5)	62.6 (17.5)	0.563
Sex (M/F)	1.2	1.1	1.5	0.825
BMI, mean (SD)	25.2 (3.8)	25.6(4)	24.1 (3.3)	0.114
Charlson comorbidity index, mean (SD)	3.9 (2.4)	3.9 (2.3)	3.8 (2.6)	0.740
Source of admission, n (%)				0.747
Medical ward	13 (18%)	8 (14%)	5 (20%)	
Surgical ward	42 (57%)	31 (57%))	11 (55%)	
Home	14 (19%)	11 (20%)	3 (15%)	
ICU	5 (8%)	4 (7%)	1 (5%)	
FIM.a-motor, median (range)	62.0 [13–91]	67.0 [13–91]	52.0 [13–85]	0.025
FIM.a-cognitive, median (range)	35.0 [5–35]	35 [5–35]	35.0 [7–35]	0.799
FIM.a, median (range)	94.0 [18–126]	97.5 [18–126]	88.5 [20–120]	0.08
General unit	88.5 [46–126]	94.0 [46–126]	83.0 [50–120]	
Orthopaedic unit	103.0 [70–123]	105.0 [70–123]	102.0 [90–114]	
Neurological unit	88.0 [18–125]	97.0 [18–125]	55.5 [20–98]	
Number of physiotherapy sessions, mean (SD)	36.7 (44.7)	34.6 (48.1)	42.4 (34.3)	0.130
Faecal incontinence, n (%)	24 (32%)	16 (30%)	8 (40.0%)	0.571
Urinary incontinence, n (%)	24 (32%)	17 (31%)	7 (35%)	0.994
Urinary catheter, n (%)	21 (28%)	13 (24%)	8 (40%)	0.289
Wound dressing, n (%)	39 (52%)	28 (51.9%)	11 (55%)	0.999
Peripheral venous catheter, n (%)	18 (24%)	9 (16%)	9 (45%)	0.027
Central venous catheter, n (%)	4 (5%)	3 (5%)	1 (5%)	1.000
Hospital stay (days), median (range)	29 [8–226]	22 [8–226]	52 [8–156]	0.017
FIM.d-motor, median (range)	79.0 [13–106]	81.0 [21–106]	57.0 [13–91]	0.011
FIM.d-cognitive, median (range)	35.0 [7.0–35]	35 [12–35]	35.0 |7–35]	0.960
FIM.d at discharge, median (range)	113.5 [20–126]	114 [44–126]	111.5 [20–126]	0.216
General unit (n=36)	111.5 [58–126]	113 [75–126]	99.0 [58–126]	

Orthopaedic unit (n=15)	117.0 [85–124]	117 [85–124]	119.5 [90–124]	
Neurological unit (n=23)	113.0 [20–126]	103.6 [44–126]	100.0 [20–126]	
ΔFIM, median (range)	8.5 [0–70]	8.5 [2–64]	7.5 [0–70]	0.821
General unit (n=36)	8.5 [0–64]	11.5[0–64]	5.0 [0–48]	
Orthopaedic unit (n=15)	12.0 [0–47]	12.0 [0–47]	12.0 [0–21]	
Neurological unit (n=23)	3.0 [0–70]	3.0 [0–51]	23.5 [20–126]	

BMI, body mass index; FIM.a, FIM on admission; FIM.d, FIM on discharge; ΔFIM, (FIM.d–FIM.a); ICU, intensive care unit

Table 2. Bivariate (Log-rank) analysis of functional recovery.

	Recovery (Yes) n=36	Recovery (No) n=38	p-value
Age, mean (SD)	63.8 (17.4)	65.9 (14.6)	0.586
Sex, n (%)			0.52
male	21 (58%)	20 (53%)	
female	15 (42%)	18 (47%)	
BMI, mean (SD)	25.1	25.2	0.870
Charlson comorbidity index, mean (SD)	3.8 (2.4)	3.9 (2.3)	0.853
Number of physiotherapy sessions per week, mean (SD)	6.5(3.1)	6.5 (3.8)	0.987
CPE status			
CPE+	8	12	0.053
CPE-	28	26	
Faecal incontinence, n (%)			
Yes	25 (69%)	25 (66%)	0.431
No	11 (31%)	13 (34%	
Urinary incontinence, n (%)			
Yes	25 (69%)	25 (66%)	0.280
No	11 (31%)	13 (34%	
Urinary tract catheter, n (%)			
Yes	9 (25%)	12 (32%)	0.290
No	27 (75%)	26 (68%)	
Wound dressing, n (%)			
Yes	29 (81%)	10 (26%)	0.079
No	7 (19%)	28 (74%)	
Peripheral venous catheter, n (%)			
Yes	9 (25%)	9 (24%)	0.053
No	27 (75%)	29 (76%)	
Central venous catheter, n (%)			
Yes	3 (8%)	1 (3 %)	0.680
No	33 (92%)	37 (97%)	
Hospital stay (days)	34 [8; 226]	25 [8; 156)	0.209
Rehabilitation unit			
General (reference)	17 (47%)	19 (50%)	0.11
Orthopaedic	8 (22%)	7 (18%)	
Neurological	11 (31%)	12 (32%)	

BMI, body mass index; CPE, carbapenemase-producing *Enterobacteriaceae*

Table 3. Multivariate analysis of time to functional recovery in CPE+ and CPE- patients

	Adjusted HR [95% CI]	*P* value
CPE+ patients (ref. CPE- patients)	0.35 [0.13–0.97]	0.016
Peripheral venous catheter (ref. No)	3.51 [1.45–8.46]	0.005
Wound dressing (ref. No)	1.97 [0.84–4.64]	0.117
Rehabilitation unit		
General unit (ref.)	1	
Orthopaedic unit	3.11 [1.24–7.82]	0.015
Neurological unit	1.78 [0.80–3.93]	0.151

CPE, carbapenemase-producing *Enterobacteriaceae*; HR, hazard ratio; 95% CI, 95% confidence interval