EUROPEAN JOURNAL OF PHYSICAL AND REHABILITATION MEDICINE
EDIZIONI MINERVA MEDICA

Identifying clinical complexity in patients affected by severe acquired brain injury in neurorehabilitation: a cross sectional survey

Scarponi Federico, Zampolini Mauro, Zucchella Chiara, Bargellesi Stefano, Fassio Chiara, Pistoia Francesca, Bartolo Michelangelo on the behalf of C.I.R.C.LE (Comorbidità in Ingresso in Riabilitazione nei pazienti con grave CerebroLEsione acquisita) study group

EUROPEAN JOURNAL OF PHYSICAL AND REHABILITATION MEDICINE

DOI: 10.23736/S1973-9087.18.05342-X

Article type: Original Article

Article first published online:
Manuscript accepted: December 12, 2018
Manuscript revised: November 7, 2018
Manuscript received: May 9, 2018

Identifying clinical complexity in patients affected by severe acquired brain injury in neurorehabilitation: a cross sectional survey

Scarponi Federico*[1], Zampolini Mauro[1], Zucchella Chiara[2,] Bargellesi Stefano[3], Fassio Chiara[4], Pistoia Francesca[5], Bartolo Michelangelo[6] on the behalf of C.I.R.C.LE (Comorbidità in Ingresso in Riabilitazione nei pazienti con grave CerebroLEsione acquisita) study group.

[1]Department of Rehabilitation, San Giovanni Battista Hospital, Foligno (Perugia), Italy

[2] Neurology Unit, University Hospital of Verona, Verona, Italy

[3]Physical Medicine and Rehabilitation-Severe Brain Injuries Rehabilitation Unit, Ca' Foncello Hospital, Treviso, Italy

[4] Rehabilitation Unit, IRCSS Fondazione Maugeri, Pavia, Italy.

[5] Neurological Institute, Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy

[6] Department of Rehabilitation, Neurorehabilitation Unit, HABILITA, Zingonia di Ciserano (Bergamo), Italy

*Corresponding author : Scarponi Federico , Brain Injury Unit , Department of Rehabilitation, San Giovanni Battista Hospital. Via Arcamone 1 , 06034 Foligno (Perugia), Italy. Email : federico.scarponi@uslumbria2.it

Abstract

Background: Literature shows that occurrence of comorbidities in people with severe acquired brain injury (sABI) is a common problem in rehabilitation stay. Consequently, patients could require an increase of interventions for diagnosis and treatment of clinical conditions, with a reduction of the rehabilitative take in charge for both clinical and organizational aspects.

Aim: the first aim was to evaluate the rate of clinical conditions of sABI patients at admission in rehabilitation and the types of rehabilitative interventions performed in the first week; second objective was to explore the impact of clinical conditions on real rehabilitative take in charge.

Design: cross sectional study.

Methods: Collected data regarded anamnestic information, functional status assessed by means of Glasgow Outcome Scale, Levels of cognitive functioning, Early Rehabilitation Barthel Index, comorbidities at admission and type of rehabilitative interventions carried out in first week of rehabilitation stay. Spearman correlation coefficients were applied to detect possible correlations between the number of treatments in first week and clinical variables; through a multiple regression analysis the effect of patient's characteristics on rehabilitative take in charge was explored.

Results: 586 sABI patients from 41 inpatient rehabilitation centres were enrolled (mean age 55.1±17.1 years;) aetiology of sABI was vascular in 315 patients (53.8%), anoxic in 83 (14.2%), neoplastic in 17 (2.9%), infectious in 15 (2.6%), traumatic in 150 (25.6%); 6 subjects (1%) presented a mixed aetiology. Need of cardiorespiratory monitoring, pressure sores, infections or presence of multi drug resistant bacteria were the most frequent comorbidities. Passive mobilization, sitting positioning, arousal/awareness stimulation, evaluation and management of dysphagia were the interventions most frequently carried out in the first week. The regression analysis showed that severe neurological and clinical conditions, acute organ failure, cardio respiratory instability and paroxysmal sympathetic hyperactivity significantly limit access to rehabilitative sessions.

Conclusion: in sABI patients clinical comorbidities requiring elevated care assistance are frequent at admission in rehabilitation from acute wards and may interfere with rehabilitative take in charge.

Clinical Rehabilitation Impact: the knowledge of clinical complexity of sABI patients may improve their care pathways, promoting early and appropriate transition from acute care to rehabilitation settings.

Key words: severe brain injury; comorbidities; rehabilitation; patient admission

Introduction

Several studies showed that people affected by severe Acquired Brain Injury (sABI) may have a high rate of medical complications during their stay both in the intensive care unit (ICU) both in rehabilitation ward[1,2]. Accordingly, in this population the prognosis for functional recovery does not just depend on the cerebral injury but comorbidities or clinical conditions, individually or associated, may increase the mortality risk[1,3,4]. Therefore, if on the one hand an early discharge from the acute care to the rehabilitation ward was shown to be related to a better patients' outcome[5,6], on the other it is likely that the clinical complexity of the patients may play an unfavourable role on recovery[7], sometimes requiring a readmission to acute care unit[8].

In order to reconcile these two requirements and to provide the best care pathways for persons affected by sABI, in some countries transition criteria were defined[9-11], providing a guidance about which patients may be considered appropriate for rehabilitation setting.

Nevertheless, it is still possible in real clinical practice that even when criteria are not completely fulfilled, sABI patients are discharged from ICU if rehabilitation needs become more evident.

Consequently, clinicians working in rehabilitation need to acquire a significant experience in dealing with different clinical complications, to ensure their optimal management and/or to prevent them[12]. Such an expert medical management may determine a reduction in mortality or readmissions to acute care facilities, but on the other hand requires an increase of interventions for diagnosis and treatment of clinical conditions, with a reduction of the rehabilitative take in charge for both clinical and organizational aspects (e.g., isolation for patients with Multi Drug Resistance – MDR - germs, need for 24hours ventilator support, need for cardio-circulatory monitoring, etc).

The main aim of this study was to evaluate in the real world the clinical complexity of patients affected by sABI at admission in Neurorehabilitation. Moreover, in order to define in which cases, the clinical complexity of the patients still permits rehabilitation care, the kind of rehabilitative intervention performed by patients in the first week after admission were evaluated.

Materials and Methods

The study enrolled adult (≥ 18 years) inpatients with a diagnosis of sABI hospitalized for rehabilitation.

sABI was defined as Central Nervous System (CNS) damage due to acute traumatic or non-traumatic (vascular, anoxic, neoplastic or infectious) causes that led to a variably prolonged state of coma (Glasgow Coma Scale ≤ 8), producing a potential wide range of impairments affecting physical, cognitive and/or psychological functioning[13-17].

The immediate relatives or the legal guardians of the patients gave informed consent to take part into the study. The study was conducted in accordance with the revised version of the Helsinki Declaration and was approved by the local Ethic Committee of the coordinator centre.

Study design and Procedure

This study was designed as a cross-sectional multicentre survey. Data refer to the first week of hospitalization of all patients present in the rehabilitation units between the 1st and 7th day of March 2016 and were collected from clinical records as part of routine care.

No specific treatments were tested in this study, while hospital rehabilitation care was recorded. All the enrolled patients underwent a complete clinical, neurological and functional examination; relevant clinical and anamnestic data were also collected (see Table 1).

Moreover, in order to obtain a multidimensional assessment of the patients', clinical and functional status, the following measures were recorded: Glasgow Outcome Scale (GOS)[18], The Rancho Los Amigos Levels of Cognitive Functioning Scale (LCF)[19], Early Rehabilitation Barthel Index (ERBI)[20].

Rehabilitative treatments carried out in the first week from admission were recorded. We included passive mobilization, assisted or active exercises, sitting positioning, verticalization, walking with physical assistance or orthosis, arousal/awareness stimulation, caregiver training, exercises focused on increasing the autonomy in performing activity of daily living (ADL), speech therapy, respiratory rehabilitation or bronchial drainage, evaluation and management of dysphagia.

Data were collected by means of schedules and then transferred into an electronic database, after the revision of each patient's files in order to avoid missing data. Each centre sent data to the coordinator centre for the storage and the offline statistical analysis.

Statistical analysis

Descriptive summary statistics, including frequencies and percentages for categorical data, mean and standard deviation (SD) for normally distributed data, were derived.
Spearman correlation coefficients were applied to detect possible correlations between the number of treatments in first week and the variables included in the database.
The effect of clinical characteristics on rehabilitation intervention was explored through multiple regression analysis, using the number of kind of treatments as dependent variable and the demographic and clinical features as explanatory variables.
All statistical tests were 2 sided, and significance was determined at the .05 probability level.
Statistical analyses were performed with the SPSS package for Windows® version 18.0.

Results

The study enrolled 586 patients [362 (61.78%) males/224 (38.22%) females], the mean age (±SD) was 55.16±17.1 years (range 18-89 years).Demographic and clinical features of the study sample are reported in Table I.
The average number of days from the acute event to admission in rehabilitation was 54±47.1, and 159 (27.13%) patients were admitted to rehabilitation wards within 30 days from the acute event.
Patients with brain injury due to vascular or infectious origin had a more prolonged acute phase: (62.47±29.75 and 64.76±70.17 days respectively) than other conditions (53.58 ± 46 days), even if the difference was not statistically significant.
Patients' provenance is shown in Figure 1, while main clinical features and anamnestic data of the study sample at rehabilitation admission are reported in Table II.

--- Figure 1 insert here ---

Clinical conditions observed at admission in rehabilitation stay are reported in Figure 2.
53 patients (9.04%) interrupted hospitalization within the first week for complications or to perform unplanned surgeries.

-- Table I insert here ---

When considering the clinical scales at admission in rehabilitation, mean GOS score was 2.62 ± 0.55; mean ERBI score was -202.15 ± 87.39 and mean LCF was 3.21 ± 1.53. Table III shows patient's distribution according to GOS and LCF values.
Rehabilitation treatments performed during the first week of stay are reported in Figure 3. Each patient performed at least a combination of 3 or more kind of treatments, including caregiver training.
Correlation analysis revealed that the "number of treatments" had a significant relationship with monitoring and with the score at the clinical scales (GOS, p=0.000, ERBI p=0.02, LCF, p=0.000), as described in Figure 4 and Figure 5; an inverse significant relationship was found between the "number of treatments" and the following variables: cerebral anoxia (p=0.004) and paroxysmal sympathetic hyperactivity (PSH) (p=0.04), as well as between the number of complications and the score at the GOS (p=0.01) and at the LCF (p=0.01).
At the regression analysis several factors (monitoring, organ failure, anoxia, PSH, GOS, LCF) were statistically significant in predicting the number of treatments performed by patients ($F(28.476) = 5.214$, $p < .0005$).

--- Table II insert here ---

Discussion

The present study explored the clinical features of patients affected by sABI admitted to neurorehabilitation units, identifying the main medical issues that defined the complexity of these patients. Increasing literature reported that patients with sABI, benefit of an early rehabilitative care[5,6], but only few studies addressed the issue if such behaviour determines a push towards a more early discharge of patients to rehabilitation wards, even when these are still not fully clinically stable.

This study addressed the specific research question of whether the sABI patients admitted to rehabilitation wards express a clinical complexity that may limit the rehabilitation care.

The main data from the study showed that when considering the current literature criteria for patients' admission to rehabilitation wards, only 44.7% of cases fulfilled the criteria, while the remaining showed one or more clinical conditions that would hinder admission; 12.3% of patients although not suitable for rehabilitation care were admitted to rehabilitation wards. In fact, as recently highlighted by Intiso[8], despite recommendations, pressure for transition of patients from acute care to neurorehabilitation wards is increasing for several reasons (i.e., need for prompt availability of intensive care beds, cost reduction, decreasing length of stay in intensive care).

General epidemiological data, showed a greater prevalence of sABI in males than in females and a higher prevalence of cerebrovascular aetiology, particularly in older patients, consistently with previous literature data.[16-17]

--- Table III insert here ---

Among clinical issues, about one third of patients reported infectious diseases at admission or within the first week of rehabilitation stay, and about a quarter of the sample needed isolation because MDR bacteria.

Passive mobilization, the improvement of awareness, evaluation and management of dysphagia, sitting positioning and breathing exercises were reported as the most frequent activities performed during the rehabilitative sessions (Figure 3). Interestingly, neither mechanical ventilation or infectious diseases were linked to a reduction in rehabilitative treatments, while rehabilitative treatments were significantly lower in patients who need instrumental monitoring of vital signs. In fact, since there is no clear consensus about the definition of hemodynamic "instability", cardiocirculatory monitoring indicates a usual practice to identify vasopressor instability that according to clinical judgment is unsafe for starting exercises. On the other hand, respiratory instability/distress or ventilator asynchrony are commonly considered barriers for mobilization[38], but not the presence of mechanical ventilation. At the same time, fever in the first week could be a barrier for physical therapy, while rehabilitative sessions in presence of multidrug resistant bacteria without sign of infection could be performed using routinary protocols of isolation, such as hand washing, physical isolation, gloves and masks.

Demographic data seem to confirm recent observations from studies performed in rehabilitative settings[21-24], while the prevalence of cerebrovascular aetiology was recently reported in two survey[25-26] different from the past when traumatic aetiology was the most frequent[27]. An increased frequency of post anoxic brain injury, was also confirmed[17,21,26].

With regard to nutritional aspects literature reports contrasting data; data from this study showed higher percentages of patients with PEG or NGT, as previously reported in patients with traumatic disorders of consciousness[11], although a multicentre study showed lower percentages for PEG and NGT considered together (lower than 50%), and parenteral nutrition (3.2%)[5]. The higher rate of enteral nutrition observed in our sample could be likely due to the increasing complexity of patients admitted to rehabilitation units with respect to older studies and to an earlier attention to global care for sABI patients already in ICU.

With respect to actual trend[5,29,30], in this study the frequency of pressure sores (34.3%) was higher. The overall prevalence of pressure injury declined in the last years[32] among patients in acute care hospitals, from 38% in 2003[31] to an actual range from 3 to 17% [32-37]. However, higher rates are reported in high-risk groups. A study performed in ICU patients, reported that over 50 percent of patients developed a stage 1 or greater pressure injury when managed with a standard mattress bed[33]. These data could reflect the combined effect

of clinical complexity of patients and insufficient rehabilitative treatment in ICU, due to various barriers, as described by Dubb et al. These authors reviewed 40 studies and identified a total of 28 unique barriers for mobilization: 14 patient-related, 5 structural, 5 related to ICU culture, 4 process-related, underlying the need of developing rehabilitative protocols in ICU.[38]

As reported by previous papers, it is very difficult to define the incidence of Neurogenic Heterotopic Ossification (NHO). Data from this study are in line with recent papers that demonstrated that NHO occurs in 4% up to 23% of patients after TBI[26,39].

The occurrence of PSH in literature is not well defined and contrasting data are reported with an estimated incidence following traumatic brain injury between 7.7% and 33%[40-42]. At the same time there is also a lack of evidence about possibility of intervention by physical therapist in these patients, that usually have longer ICU stays, and worse outcomes[43]. Moreover, even when PSH does not appear to influence the outcome, they are more likely to undergo psychoactive medications and PSH is then perceived as a complication for rehabilitation care[44]. Our data seems to show a difficulty to indicate as mandatory discharging patients with PSH not controlled by drugs in rehabilitative units. This is due to lower possibility of carry out rehabilitative treatments due to need for monitoring patients.

--- Figure 2 insert here ---

As reported by previous studies performed in ICU, cardiocirculatory instability due to tachycardia, hypotension, arrhythmias or respiratory symptoms (e.g. dyspnoea), as well as acute organ failure, can interrupt or interfere with the rehabilitative sessions[38,45,46].

Functional scores (GOS, LCF) seem to be in line with data reported from recent studies[8,21,47], although GOS score was lower if compared with a national prospective study[27] due to higher percentage of patients with GOS value 2; ERBI scores were similar to the data reported at discharge from ICU[25].

Although LCF1 and 2 correspond to GOS 2, in our sample the sum of the data does not match (15 cases). In our view, it is possible that in real life, the clinical evaluation is wider showing limitation in the use of standardized clinical scales, and justifying not significant discrepancies in the data.

A significant relationship between GOS, ERBI and LCF scores, and the number of rehabilitative interventions, was observed. Orthostatic training, exercises for the gait, or active/assisted exercise are more frequent in higher GOS and LCF scores, while training for informal caregiver are related to worse GOS and LCF scores. Conversely, an inverse relationship between the score at GOS and LCF and the number of complications was found. Overall, these data seem to indicate a greater need of intensive rehabilitation in "higher functional" patients, and also a lower indication of carry out rehabilitative session in most severe patients, except for basic procedures.

It's well known that the absence of N20 in post-anoxic survivors represents an early predictor of poor outcome[48-50] with implications in terms of rehabilitative management that imply an intervention based only on basic procedures (i.e. passive mobilization, or training for caregivers). Accordingly, data from this study showed that post-anoxic survivors with bilateral absence of N20 performed a lower number of rehabilitative treatments in the first week.

--- Figure 3 insert here ---

This survey presented some limitations: first, the occurrence and impact of different clinical conditions (e.g. anemia, fractures), as well as the tracheostomy tube and seizures could be underestimated. The tracheostomy tube and seizures were not considered because it is widely accepted[11,17,21,26] that they don't represent a limitation for transition to rehabilitative units. Second, in this study were considered the kind of treatments continuously performed during the first week, instead of the time of treatments. This in order to avoid missing data, because in a multicentre study, it would have been very difficult to calculate the minutes of treatment carried out for each patient, due to different organizational models.

--- Figure 4 and 5 insert here ---

Notwithstanding the above limitations, this study represents a relevant contribution to get a picture of the actual situation about the clinical conditions of sABI patients at admission in neurorehabilitation. Moreover, these data could help to improve the care pathways for sABI patients, promoting early and appropriate transition from acute care to rehabilitation settings.

Conclusion

This study provides a picture of the actual situation about clinical conditions of sABI patients at admission in neurorehabilitation. People with sABI frequently show relevant complications or clinical conditions that need elevated care assistance.

However, overall, data from this study confirmed that rehabilitation treatments are widely possible even in patients with relevant comorbidities (need for isolation, infection by multi drug resistant bacteria, etc.), and that only few conditions seem to be related to a reduction of rehabilitative session. These data could help to improve the care pathways for sABI patients, promoting early and appropriate transition from acute care to rehabilitation settings.

References

1. Pistoia F, Sacco S, Franceschini M, Sarà M, Pistarini C, Cazzulani B , Simonelli I, Pasqualetti P, Carolei A. Comorbidities: a key issue in patients with disorders of consciousness. J Neurotrauma. 2015;32(10):682-8.
2. Ganesh S, Guernon A, Chalcraft L, Harton B, Smith B, Louise-Bender Pape T. Medical comorbidities in disorders of consciousness patients and their association with functional outcomes. Arch Phys Med Rehabil. 2013;94(10):1899-907.
3. Godbolt AK, Stenberg M, Jakobsson J, Sorjonen K, Krakau K, Stålnacke BM, Nygren DeBoussard C. Subacute complications during recovery from severe traumatic brain injury: frequency and associations with outcome. BMJ Open. 2015;5(4):e007208.
4. Fu TS, Jing R, McFaull SR, Cusimano MD. Recent trends in hospitalization and in-hospital mortality associated with traumatic brain injury in Canada: A nationwide, population-based study. J Trauma Acute Care Surg. 2015;79(3):449-54.
5. Zampolini M, Zaccaria B, Tolli V, Frustaci A, Franceschini M, GISCAR Group. Rehabilitation of traumatic brain injury in Italy: a multi-centred study. Brain Inj. 2012;26(1):27-35.
6. Johns RH, Dawson D, Ball J. Considerations and proposals for the management of patients after prolonged intensive care unit admission. Postgrad Med J. 2010;86(1019):541-51.
7. Seel RT, Douglas J, Dennison AC, Heaner S, Farris K, Rogers C. Specialized early treatment for persons with disorders of consciousness: program components and outcomes. Arch Phys Med Rehabil. 2013;94(10):1908-23.
8. Intiso D, Fontana A, Maruzzi G, Tolfa M, Copetti M, DI Rienzo F. Readmission to the acute care unit and functional outcomes in patients with severe brain injury during rehabilitation. Eur J Phys Rehabil Med. 2017;53(2):268-276.
9. Evans RL, Haselkorn JK, Bishop DS, Hendricks RD. Factors influencing the decision to rehabilitate: an initial comparison of rehabilitation candidates. Soc Sci Med 1991; 33(7): 801-806.
10. Maulden SA, Gassaway J, Horn SD et al. Timing of initiation of rehabilitation after stroke. Arch Phys Med Rehabiil 2005; 86 (Suppl.2): S34-S40.
11. Taricco M, De Tanti A, Boldrini P, Gatta G. National Consensus Conference. The rehabilitation management of traumatic brain injury patients during the acute phase: criteria for referral and transfer from intensive care units to rehabilitative facilities (Modena June 20-21, 2000). Eura Medicophys. 2006;42(1):73-84.
12. Whyte J, Nordenbo AM, Kalmar K, Merges B, Bagiella E, Chang H, ablon S, Cho S, Hammond F, Khademi A, Giacino J.Medical complications during inpatient rehabilitation among patients with traumatic disorders of consciousness. Arch Phys Med Rehabil. 2013;94(10):1877-83.

13. Teasell R, Bayona N, Marshall S, Cullen N, Bayley M, Chundamala J, Villamere J,Mackie D, Rees L, Hartridge C, Lippert C, Hilditch M, Welch-West P, Weiser M, Ferri C, McCabe P, McCormick A, Aubut JA, Comper P, Salter K, Van Reekum R, Collins D, Foley N, Nowak J, Jutai J, Speechley M, Hellings C, Tu L. A systematic review of the rehabilitation of moderate to severe acquired brain injuries. Brain Inj. 2007;21(2):107-12.
14. Cullen NK, Park YG, Bayley MT. Functional recovery following traumatic vs non-traumatic brain injury: a case-controlled study. Brain Inj. 2008;22(13-14):1013-20.
15. Andriessen TM, Horn J, Franschman G, van der Naalt J, Haitsma I, Jacobs B *et al.* Epidemiology, severity classification, and outcome of moderate and severe traumatic brain injury: a prospective multicenter study. J Neurotrauma. 2011;28(10):2019-31.
16. Colantonio A, Gerber G, Bayley M, Deber R, Yin J, Kim H. Differential profiles for patients with traumatic and non-traumatic brain injury. J Rehabil Med. 2011;43(4):311-5.
17. Avesani R, Roncari L, Khansefid M, Formisano R, Boldrini P, Zampolini M, Ferro S, De Tanti A, Dambruoso F. The Italian National Registry of severe acquired brain injury: epidemiological, clinical and functional data of 1469 patients. Eur J Phys Rehabil Med. 2013;49(5):611-8.
18. Jennett B, Bond M. Assessment of outcome after severe brain damage. Lancet.1975;1(7905):480-4.
19. Hagen, C., Malkmus, D., Durham, P. (1979). Levels of cognitive functioning, Rehabilitation of the Head Injured Adult; Comprehensive Physical Management, Downey, CA: Professional Staff Association of Rancho Los Amigos National Rehabilitation Center.
20. Rollnik JD. The Early Rehabilitation Barthel Index (ERBI). Rehabilitation (Stuttg). 2011;50(6):408-11.
21. Formisano R, Azicnuda E, Sefid MK, Zampolini M, Scarponi F, Avesani R. Early rehabilitation: benefits in patients with severe acquired brain injury. Neurol Sci. 2017;38(1):181-184.
22. Paci M, Infante-Rivard C, Marcoux J. Traumatic Brain Injury in the Workplace. Can J Neurol Sci. 2017;44(5):518-524.
23. Niemeier JP, Perrin PB, Holcomb MG, Rolston CD, Artman LK, Lu J *et al.* Gender differences in awareness and outcomes during acute traumatic brain injury recovery. J Womens Health (Larchmt). 2014;23(7):573-80.
24. Chraa M, Louhab N, Kissani N. Stroke in young adults: about 128 cases. Pan Afr Med J. 2014;17:37.
25. Bartolo M, Bargellesi S, Castioni CA, Bonaiuti D; Intensive Care and Neurorehabilitation Italian Study Group. Early rehabilitation for severe acquired brain injury in intensive care unit: multicenter observational study. Eur J Phys Rehabil Med. 2016;52(1):90-100.
26. Bargellesi S, Cavasin L, Scarponi F, De Tanti A, Bonaiuti D, Bartolo M, Boldrini P, Estraneo A, Heterotopic Ossification Cross Sectional Survey group (HOCSS). Occurrence and predictive factors of heterotopic ossification in severe acquired brain injured patients during rehabilitation stay: cross-sectional survey. Clin Rehabil. 2017 Aug 1:269215517723161.
27. Zampolini, M, Corea F, Avesani R, Boldrini P, De Tanti A, Di Stefano MG, Formisano R, Lamberti G, Lombardi F, Mazzucchi A, Pistarini C, Taricco M, Citterio A. Rehabilitation of acquired brain injuries: a multicentric prospective survey. Eur J Phys Rehabil Med. 2013 Jun;49(3):365-72
28. Dhandapani M, Dhandapani S, Agarwal M, Mahapatra AK. Pressure ulcer in patients with severe traumatic brain injury: significant factors and association with neurological outcome. J Clin Nurs. 2014;23(7-8):1114-9.
29. Montalcini T, Moraca M, Ferro Y, Romeo S, Serra S, Raso MG *et al.*Nutritional parameters predicting pressure ulcers and short-term mortality in patients with minimal conscious state as a result of traumatic and non-traumatic acquired brain injury. J Transl Med. 2015;13:305.
30. VanGilder C, Lachenbruch C, Algrim-Boyle C, Meyer S. The International Pressure Ulcer Prevalence™ Survey: 2006-2015: A 10-Year Pressure Injury Prevalence and Demographic Trend Analysis by Care Setting. J Wound Ostomy Continence Nurs. 2017;44(1):20-28.
31. Lyder CH. Pressure ulcer prevention and management. JAMA 2003;289:223-6.
32. Bergstrom N, Braden B, Kemp M, Champagne M, Ruby E. Multi-site study of incidence of pressure ulcers and the relationship between risk level, demographic characteristics, diagnoses, and prescription of preventive interventions. J Am Geriatr Soc. 1996;44(1):22-30.
33. Petzold T, Eberlein-Gonska M, Schmitt J. Which factors predict incident pressure ulcers in hospitalized patients? A prospective cohort study. Br J Dermatol. 2014;170(6):1285-90.
34. Lyder CH, Wang Y, Metersky M, Curry M, Kliman R, Verzier NR, Hunt DR. Hospital-acquired pressure ulcers: results from the national Medicare Patient Safety Monitoring System study. J Am Geriatr Soc. 2012;60(9):1603-8.
35. Li Y, Yin J, Cai X, Temkin-Greener J, Mukamel DB. Association of race and sites of care with pressure ulcers in high-risk nursing home residents. JAMA. 2011;306(2):179-86.
36. Baumgarten M, Margolis DJ, Localio AR, Kagan SH, Lowe RA, Kinosian B *et al.* Pressure ulcers among elderly patients early in the hospital stay. J Gerontol A Biol Sci Med Sci. 2006;61(7):749-54.

37. Inman KJ, Sibbald WJ, Rutledge FS, Clark BJ. Clinical utility and cost-effectiveness of an air suspension bed in the prevention of pressure ulcers. JAMA. 1993;269(9):1139-43.
38. Dubb R, Nydahl P, Hermes C, Schwabbauer N, Toonstra A, Parker AM *et al.* Barriers and Strategies for Early Mobilization of Patients in Intensive Care Units. Ann Am Thorac Soc. 2016;13(5):724-30.
39. Almangour W, Schnitzler A, Salga M, Debaud C, Denormandie P, Genêt F. Recurrence of heterotopic ossification after removal in patients with traumatic brain injury: A systematic review. Ann Phys Rehabil Med. 2016;59(4):263-9.
40. Verma R, Giri P, Rizvi I. Paroxysmal sympathetic hyperactivity in neurological critical care. Indian J Crit Care Med. 2015;19(1):34-7.
41. Meyer KS. Understanding paroxysmal sympathetic hyperactivity after traumatic brain injury. Surg Neurol Int. 2014;5(Suppl 13):S490-2.
42. Mathew MJ, Deepika A, Shukla D, Devi BI, Ramesh VJ. Paroxysmal sympathetic hyperactivity in severe traumatic brain injury. Acta Neurochir (Wien). 2016;158(11):2047-2052.
43. Lv LQ, Hou LJ, Yu MK, Qi XQ, Chen HR, Chen JX, Hu GH, Luo C, Lu YC. Prognostic influence and magnetic resonance imaging findings in paroxysmal sympathetic hyperactivity after severe traumatic brain injury. J Neurotrauma. 2010;27(11):1945-50.
44. Laxe S, Terré R, León D, Bernabeu M. How does dysautonomia influence the outcome of traumatic brain injured patients admitted in a neurorehabilitation unit? Brain Inj. 2013;27(12):1383-7.
45. Riberholt CG, Thorlund JB, Mehlsen J, Nordenbo AM. Patients with severe acquired brain injury show increased arousal in tilt-table training. Dan Med J.2013;60(12):A4739.
46. Luther MS, Krewer C, Müller F, Koenig E. Comparison of orthostatic reactions of patients still unconscious within the first three months of brain injury on a tilt table with and without integrated stepping. A prospective, randomized crossover pilot trial. Clin Rehabil. 2008;22(12):1034-41.
47. Intiso D, DI Rienzo F, Fontana A, Tolfa M, Bartolo M, Copetti M. Functional outcome of critical illness polyneuropathy in patients affected by severe brain injury. Eur J Phys Rehabil Med. 2017 Apr 14.
48. Sandroni C, Cavallaro F, Callaway CW, D'Arrigo S, Sanna T, Kuiper MA, Biancone M, Della Marca G, Farcomeni A, Nolan JP. Predictors of poor neurological outcome in adult comatose survivors of cardiac arrest: a systematic review and meta-analysis. Part 2: Patients treated with therapeutic hypothermia. Resuscitation. 2013;84(10):1324-38.
49. Pfeifer R, Weitzel S, Günther A, Berrouschot J, Fischer M, Isenmann S, Figulla HR. Investigation of the inter-observer variability effect on the prognostic value of somatosensory evoked potentials of the median nerve (SSEP) in cardiac arrest survivors using an SSEP classification. Resuscitation. 2013;84(10):1375-81.
50. Zhang Y, Su YY, Haupt WF, Zhao JW, Xiao SY, Li HL, Pang Y, Yang QL.Application of electrophysiologic techniques in poor outcome prediction among patients with severe focal and diffuse ischemic brain injury. J Clin Neurophysiol. 2011;28(5):497-503.

Appendix

The C.I.R.C.L.E (Comorbidità in Ingresso In riabilitazione nei pazienti con Grave CerebroLesione acquisita) study group:

- Antenucci Roberto, Gruppi Maria Paola, Raggi Rossella Bozzini Emilia, Cassio Anna (Unità Operativa di Neuroriabilitazione Ospedale "S. Sebastiano" di Correggio,Reggio Emilia)
- Beatrici Maurizio, Macchetta Claudia, Cocchini Lorella (S.C. Neuroriabilitazione GCA- AOU Città della Salute e della Scienza di Torino, Presidio CTO, Torino)
- Benedetti Adonella (Struttura Complessa Riabilitazione Intensiva Neuromotoria , Trevi (PG))
- Bianconi Fortunato, indipendent researcher, via Mario Guerrieri , 06132 Perugia
- Bramanti Placido, Marino Silvia, Corallo Francesco (IRCCS Centro Neurolesi "Bonino-Pulejo", Messina)
- Brambilla Massimo (Struttura Complessa Neuroriabilitazione - Unità Spinale, Presidio Ospedaliero Sondalo, ASST Valtellina e Alto Lario)

- Carboncini Maria Chiara, Spina Vincenzo (Dipartimento di Ricerca Traslazionale sulle nuove tecnologie in Medicina e Chirurgia , Scuola di Medicina FIsica e Riabilitativa Università of Pisa, Italy)
- Cervigni Giuliana (Medicina fisica e riabilitazione, Ospedale Riabilitativo Villa Rosa, Pergine Valsugana (TN))
- Cimenti Fabio, Previato Chiara, Semerjian Monica (Struttura Complessa di Medicina Riabilitativa - Unità Gravi Cerebrolesioni e Mielolesioni, Azienda Ulss 9 - Ospedale "Ca' Foncello", Treviso)
- Colombari Mauro (Unità di Riabilitazione ad alta specialità, Sol et Salus Ospedale Privato Accreditato, Torre Pedrera di Rimini)
- De Cicco Domenico (U.O. Neuroriabilitazione Intensiva, Fondazione S. Maugeri, P.O. "Giovanni Paolo II", Sciacca (AG))
- De Tanti Antonio, Iardella Laura (Centro Cardinal Ferrari, Fontanellato (PR))
- Diverio Manuela, Camilla Grifoni, Valentina Carli, Eugenia Pasqualone (Polo Riabilitativo del Levante Ligure, Fondazione Don Carlo Gnocchi, La Spezia)
- Estraneo Anna (Unità Operativa di Riabilitazione Intensiva Neuromotoria , ICS Fondazione S. Maugeri, Telese Terme (BN))
- Formisano Rita, Ciurli Maria Paola (Unità Post-Coma Ospedale di Riabilitazione Fondazione Santa Lucia, Roma)
- Galardi Massimo, Santangelo Antonino (Unità Operativa Complessa di Riabilitazione Fondazione Istituto "San Raffaele Giglio", Cefalù)
- Giorgini Tullio, Biasutti Emanuele (Unità Gravi Cerebrolesioni e Riabilitazione generale, Istituto di Medicina Fisica e Riabilitazione, Udine)
- Iaia Vincenzo (UOC Cerebrolesioni Fondazione Ospedale San Camillo - I.R.C.C.S., Venezia)
- Intiso Domenico (UOC di Medicina Fisica e Riabilitativa- Neuroriabilitazione IRCCS " Casa Sollievo della Sofferenza", San Giovanni Rotondo (FG))
- Lamberti Gianfranco, Antoniono Elena (SC Neuroriabilitazione, U.O Stati vegetativi ASL CN1 Ospedale "SS. Trinità" - Fossano (CN))
- Lanfranchi Maurizio (Unità Gravi Cerebrolesioni, Ospedale Valduce Divisione Riabilitativa Villa Beretta , Costamasnaga (CO)
- Lavezzi Susanna, Chiavaroli Roberta (Unità Operativa di Neuroriabilitazione, Ospedale "S. Sebastiano" di Correggio, AUSL di Reggio Emilia)
- Lucca Lucia Francesca (Unità Risveglio, Istituto S.Anna ,Crotone)
- Maggioni Giorgio (U.O. Neuroriabilitazione – ICS Fondazione S .Maugeri – Veruno (NO))
- Mancuso Mauro, Canova Stefania (Centro di Riabilitazione Terranuova Bracciolini)
- Mandalà Giorgio (U.O.C. Medicina Riabilitativa, Ospedale "Buccheri La Ferla Fatebenefratelli", Palermo)
- Melizza Gianni (Riabilitazione Specialistica Azienda Ospedaliera Papa Giovanni XXIII, Mozzo (BG))
- Montis Andrea , Pilia Felicita (SSD Neuroriabilitazione, Ospedale San Michele, Azienda Ospedaliera "G.Brotzu" ,Cagliari)
- Mulè Chiara (UO Riabilitazione Specialistica, Fondazione Poliambulanza Istituto Poliospedaliero, Brescia)
- Navarro Jorge, Lanzillotti Crocifissa (Fondazione San Raffaele, Ceglie Messapica (Br))
- Perin Cecilia (Dipartimento Medicina e Chirurgia, Istituti Clinici Zucchi- Carate Brianza)
- Petrozzino Salvatore, Schierano Gabriella (Dipartimento di Riabilitazione, Azienda Ospedaliera Nazionale SS. Antonio e Biagio e Cesare Arrigo – Alessandria)
- Piperno Roberto, Battistini Alberto (UOC di Medicina Riabilitativa e Neuroriabilitazione, Ospedale Bellaria Bologna)
- Premoselli Silvia (SC Riabilitazione Neuromotoria Specialistica PO Seregno - ASST – Vimercate)
- Salvi Piero , Simonini Marcello (U.F. Riabilitazione Neuromotoria e Cognitiva Istituto Clinico Quarenghi, San Pellegrino Terme (BG))
- Sarà Marco, Pardo Moira (UO Neuroriabilitazione ad Alta Specialità, Istituto San Raffaele, Cassino)
- Serafini Paolo, Fortuna Rossella (Istituto di Riabilitazione Santo Stefano, Unità di riabilitazione subintensiva per gravi cerebrolesioni acquisite, Porto Potenza Picena (MC))
- Sergio Maria Antonietta (Unità di Riabilitazione, Ospedale S Giovanni Battista Acismom, Roma)
- Volanti Paolo (U.O. Neuroriabilitazione Intensiva, Centro SLA, Fondazione S. Maugeri, Mistretta (ME))

Titles of tables and figures

Table I. Overall description of sample

Table II. Relevant clinical features and anamnestic data

Table III. Patients' distribution according to GOS and LCF values at rehabilitation admission

Figure 1. Patients' provenance from acute care

Figure 2. Clinical conditions reported in the first week of rehabilitation stay.

Figure 3. Rehabilitative treatments performed during the first week.

Figure 4. Average number of rehabilitative interventions according to GOS value

Figure 5. Average number of rehabilitative interventions according to LCF value

Table I. Overall description of the sample at admission.

		N (%)	Mean ± SD	Range
Gender	M	362 (61.8)		
	F	224 (38.2)		
Age (*years*)			55.16 ± 17.1	18 – 89
Aetiologies	Anoxic	83 (14.2)		
	Neoplastic	17 (2.9)		
	Infectious	15 (2.6)		
	Vascular	315 (53.8)		
	Traumatic	150 (25.6)		
	Mixed	6 (1)		
GOS			2,63 ± 0.56	2 - 5
ERBI			(-202,5) ± 87.07	(-325) - 100
LCF			3,22 ± 1.53	1 - 8

Table II. Relevant clinical features and anamnestic data at rehabilitation admission.

	Yes n (%)	No n (%)	Missing data n (%)
Nasogastric tube	250 (42.7)	331 (56.4)	5 (0.9)
Percutaneous Endoscopic Gastrostomy	214 (36.5)	354 (60.4)	18 (3.1)
Pressure sores	201 (34.3)	378 (64.5)	7 (1.2)
Cardiocirculatory instability *with multiparametric monitoring necessary or recommended*	352 (60.1)	224 (38.2)	10 (1.7)
Need for Isolation due to multi drug resistant bacteria	154 (26.3)	431 (73.5)	1 (0.2)
Nutrition (per os)	133 (22.7)	445 (75.9)	8 (1.4)
Infectious disease at admission	100 (17.1)	486 (82.9)	-
Infectious disease within the first week	91 (15.5)	493 (84.1)	2 (0.4)
Assisted breathing	77 (13.1)	495 (84.5)	14 (2.4)
Paroxysmal sympathetic hyperactivity	77 (13.1)	507 (86.6)	2 (0.3)
Acute organ failure	67 (11.4)	517 (88.2)	2 (0.3)
Fungine infection	62 (10.6)	523 (89.2)	1 (0.2)
Parenteral nutrition over 7 days	51 (8.7)	535 (91.3)	-
Evidence of Brain tumor after craniolacunia	38 (6.5)	542 (92.5)	6 (1.1)
Neurogenic heterotopic ossification	30 (5.2)	523 (89.2)	33 (5.6)
Pre-existing disability	21 (3.6)	562 (95.9)	3 (0.5)
Worsening postoperative subdural hygroma	18 (3.1)	558 (95.2)	10 (1.7)
Cerebral anoxia with bilateral absence of N20 wave at SEPP	14 (2.4)	476 (81.2)	96 (16.4)
Pre-existing cancer	12 (2.0)	569 (97.2)	5 (0.8)
Anamnestic heart failure with ejection fraction <25%	8 (1.4)	575 (98.1)	3 (0.5)
Surgery within the 1st week	5 (0.9)	581 (99.1)	-

Table III. Patients' distribution according to GOS and LCF at rehabilitation admission.

	n (%)		n (%)
GOS 1	0 (0)	LCF 1	37 (6)
GOS 2	238 (41)	LCF 2	216 (37)
GOS 3	331 (56)	LCF 3	126 (22)
GOS 4	14 (2)	LCF 4	79 (13)
GOS 5	3 (1)	LCF 5	66 (11)
		LCF 6	46 (8)
		LCF 7	13 (2)
		LCF 8	3 (1)

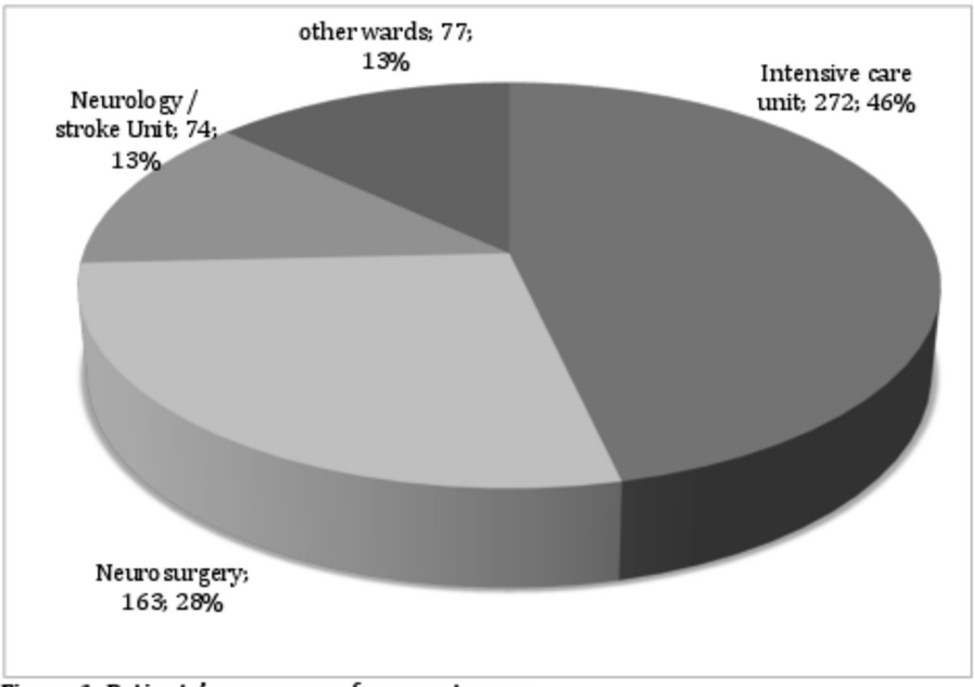

Figure 1. Patients' provenance from acute care

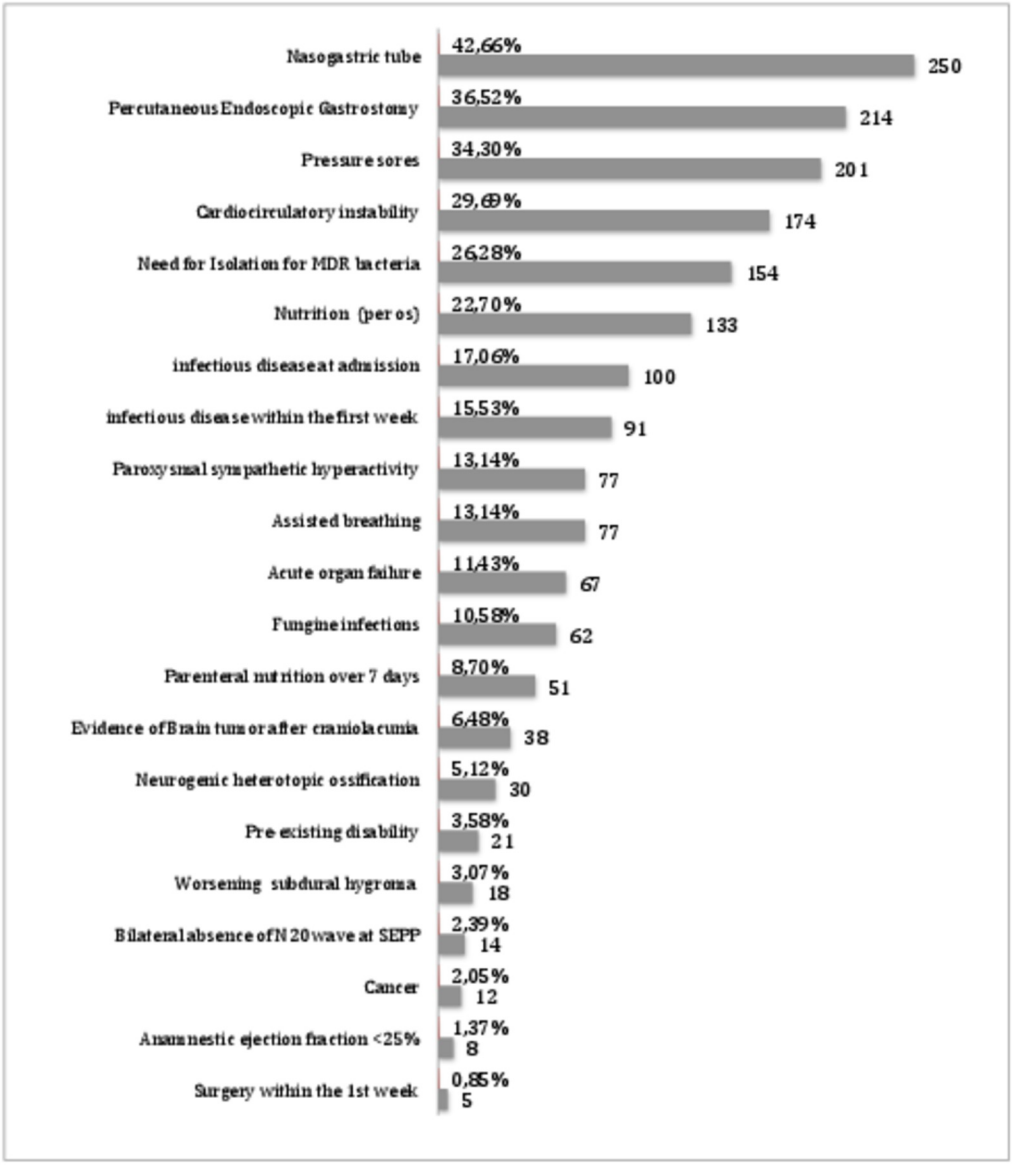

Figure 2. Clinical conditions reported in the first week of rehabilitation stay.

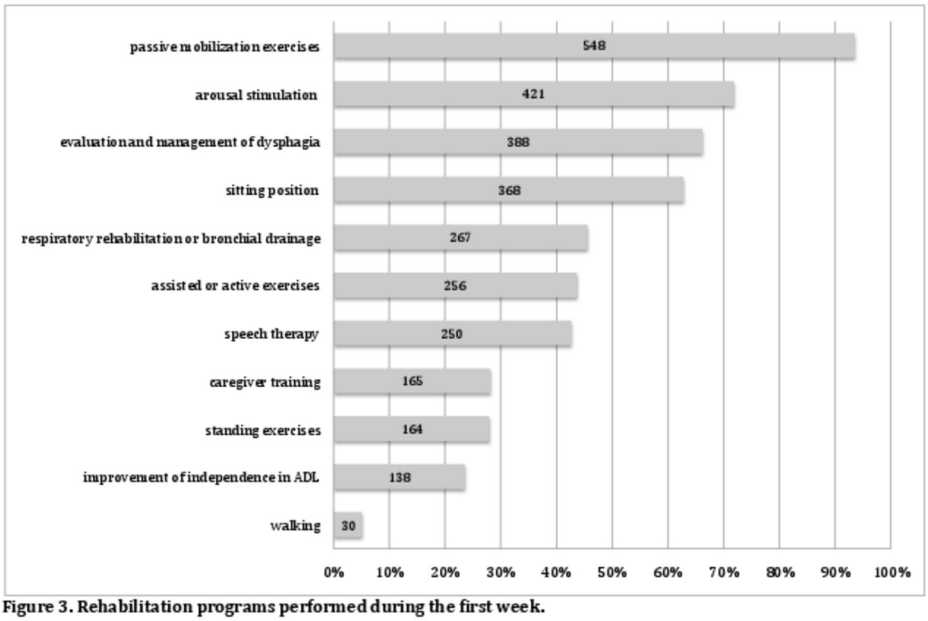

Figure 3. Rehabilitation programs performed during the first week.