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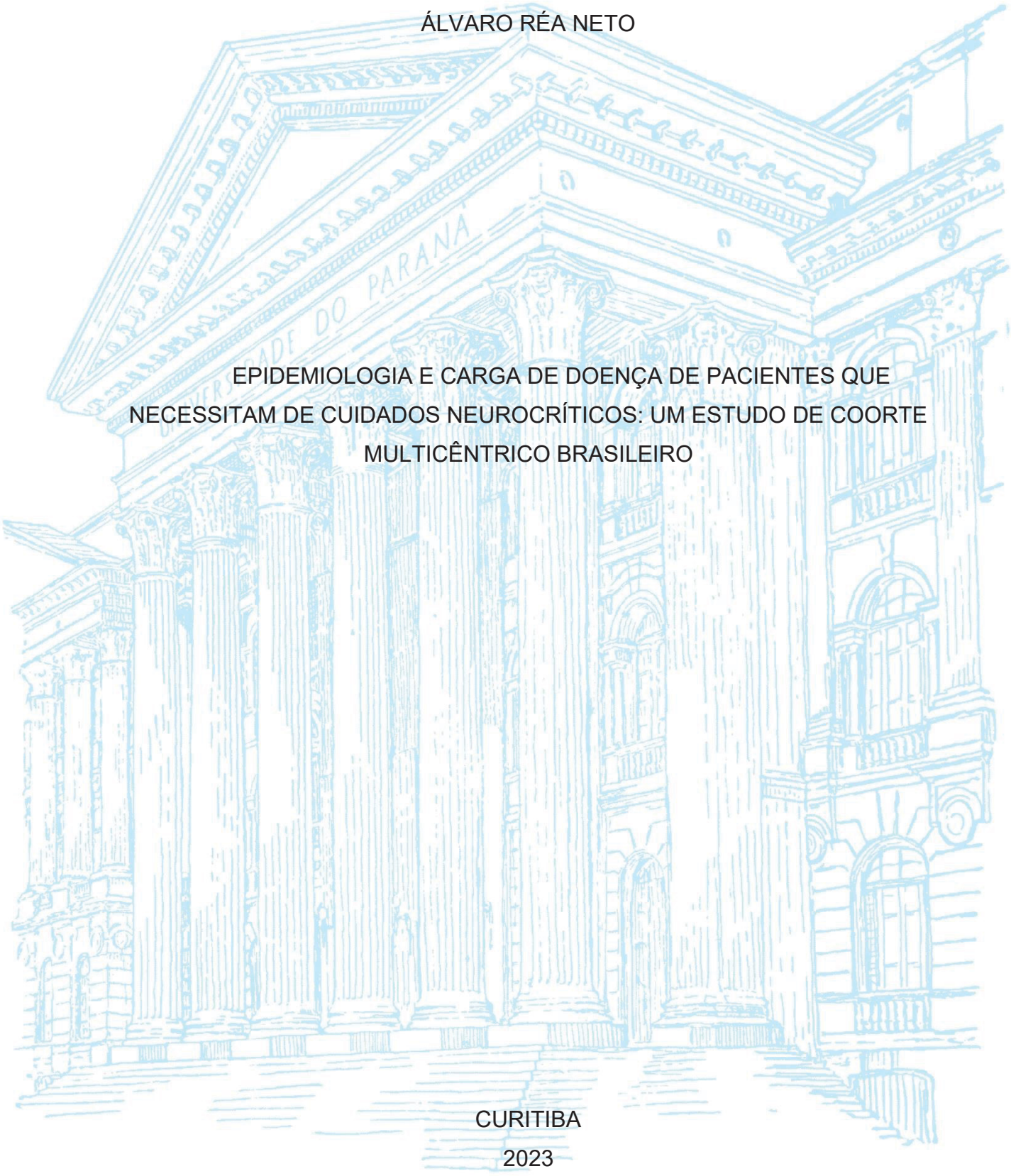

EPIDEMIOLOGIA E CARGA DE DOENÇA DE PACIENTES QUE NECESSITAM DE CUIDADOS NEUROCRÍTICOS: UM ESTUDO DE COORTE MULTICÊNTRICO BRASILEIRO

CURITIBA

2023

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Tese apresentada ao curso de Pós-Graduação em Medicina Interna e Ciências da Saúde, do Setor de Ciências da Saúde, da Universidade Federal do Paraná, como requisito à obtenção do título de Doutor.

Orientador: Prof. Dr. Hélio Afonso Ghizone Teive

CURITIBA

2023

R282 Réa Neto, Álvaro
Epidemiologia e carga de doença de pacientes que necessitam de cuidados neurocríticos: um estudo de coorte multicêntrico brasileiro [recurso eletrônico] / Álvaro Réa Neto. – Curitiba, 2023.

Tese (doutorado) – Programa de Pós-Graduação em Medicina Interna e Ciências da Saúde. Setor de Ciências da Saúde. Universidade Federal do Paraná.
Orientador: Prof. Dr. Hélio Afonso Ghizone Teive

1. Unidades de terapia intensiva. 2. Doenças do sistema nervoso. 3. Cuidados críticos. 4. Efeitos Psicossociais da Doença. I. Teive, Hélio Afonso Ghizone. II. Programa de Pós-Graduação em Medicina Interna e Ciências da Saúde. Setor de Ciências da Saúde. Universidade Federal do Paraná. III. Título.

FICHA CATALOGRÁFICA ELABORADA PELO SISTEMA DE BIBLIOTECAS/UFPR
BIBLIOTECA DE CIÊNCIAS DA SAÚDE, BIBLIOTECÁRIA: RAQUEL PINHEIRO COSTA JORDÃO CRB 9/991

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PROGRAMA DE PÓS-GRADUAÇÃO MEDICINA INTERNA E CIÊNCIAS DA SAÚDE - 40001016012P1

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Os membros da Banca Examinadora designada pelo Colegiado do Programa de Pós-Graduação MEDICINA INTERNA E CIÊNCIAS DA SAÚDE da Universidade Federal do Paraná foram convocados para realizar a arguição da tese de Doutorado de **ÁLVARO RÉA NETO** intitulada: **"EPIDEMIOLOGIA E CARGA DE DOENÇA DE PACIENTES QUE NECESSITAM DE CUIDADOS NEUROCRÍTICOS: UM ESTUDO DE COORTE MULTICÊNTRICO BRASILEIRO"**, sob orientação do Prof. Dr. HÉLIO AFONSO GHIZONI TEIVE, que após terem inquirido o aluno e realizada a avaliação do trabalho, são de parecer pela sua APROVAÇÃO no rito de defesa.

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Curitiba, 17 de Novembro de 2023.

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AGRADECIMENTOS

Agradecer é uma forma de reconhecer que a vida é feita de convívios e daquilo que você faz deles. Essa tese é um pouco do resultado desses convívios, sem os quais eu não teria conseguido fazê-la.

Tive a sorte de nascer numa família que me proporcionou princípios e condições para eu me desenvolver. Sinto falta de meu pai e de minha mãe e me penitencio de não poder mais lhes retribuir tudo que fizeram por mim.

Os meus professores me proporcionaram caminhos, mas também me ensinaram, meio na marra, o que eu não deveria fazer. O Dr. Acir Rachid, em especial, confiou em mim quando eu nem imaginava o que eu poderia fazer.

Minha vida em casa é gostosa e cheia de bons momentos. A Rosângela me acolhe e tem uma paciência infinita com minhas teimosias. O Ricardo e a Sílvia me dão um propósito e me recompensam com muito mais do que mereço ou sou capaz de retribuir.

Meu trabalho tem sido facilitado pela equipe do CEPETI. E a turma da Pesquisa Clínica demonstrou estar preparada para projetos cada vez mais complexos. A Rafaella, a Amanda, o Marcelo e a Verônica foram forças-motrizes fundamentais para este trabalho. Mas, mais que isso, aprendemos muitas coisas juntos, compartilhamos problemas e soluções e estamos irmanados como nunca.

Enfim, agradeço profundamente a todos aqueles com os quais convivi e me ajudaram neste projeto, mas, principalmente, me deram razões para ser feliz.

“…there are known knowns; there are things we know we know. We also know there are known unknowns; that is to say, we know there are some things we do not know. But there are also unknown unknowns — the ones we don’t know, we don’t know.”

DONALD RUMSFELD

“*We do not know. We can only guess*.**”**

KARL POPPER

RESUMO

As doenças neurológicas são altamente prevalentes e impõem uma carga substancial aos pacientes. Este estudo teve como objetivo descrever uma coorte completa de pacientes neurocríticos e estratificados com base nos diagnósticos neurológicos primários e identificar preditores de mortalidade e desfechos desfavoráveis, juntamente com a carga de doença de cada condição na admissão em Unidade de Terapia Intensiva (UTI). Foi realizado um estudo de coorte prospectivo que incluiu consecutivamente pacientes neurológicos admitidos em 36 UTIs de quatro regiões brasileiras e que acompanhados por 30 dias ou até o desfecho da UTI. Dos 4245 pacientes admitidos nas UTIs participantes, 1194 (28,1%) eram neurocríticos e foram incluídos na coorte. Os pacientes neurocríticos apresentaram uma taxa de mortalidade 1,7 vezes maior do que os não neurocríticos (17,21% versus 10,1%, respectivamente). Os diagnósticos neurológicos primários mais frequentes na admissão na UTI foram cuidados pós-operatórios de neurocirurgia eletiva, traumatismo cranioencefálico, acidente vascular cerebral isquêmico e encefalopatia. Idade avançada, admissão de emergência, maior número de possíveis lesões secundárias e piores escores APACHE II, SAPS III, SOFA e Glasgow na admissão na UTI foram preditores independentes de mortalidade e de desfecho desfavorável. O total estimado de anos de vida ajustados por incapacidade (DALY) foi de 4482,94 na coorte geral de pacientes neurocríticos e o diagnóstico neurológico com o maior DALY foi lesão cerebral traumática (1634,42). Os DALYs relativos às desordens neurocríticas foram significativamente impactados pelo diagnóstico neurológico primário, sexo, faixa etária e número de lesões neurológicas secundárias dos pacientes. Descrevemos com maior precisão a epidemiologia de pacientes neurocríticos e estimamos sua carga geral e relativa de doença. Os achados deste estudo são essenciais para orientar as políticas de educação, prevenção e tratamento dos pacientes com doenças neurocríticas graves.

Palavras-chave: Unidade de Terapia Intensiva; Cuidados Críticos; Doenças do Sistema Nervoso; Carga da Doença; Anos de Vida Ajustados pela Incapacidade.

ABSTRACT

Acute neurological emergencies are highly prevalent in intensive care units (ICUs) and impose a substantial burden on patients. This study aims to describe the epidemiology of patients requiring neurocritical care in Brazil, and their differences based on primary acute neurological diagnoses and to identify predictors of mortality and unfavourable outcomes, along with the disease burden of each condition at intensive care unit admission. This prospective cohort study included patients requiring neurocritical care admitted to 36 ICUs in four Brazilian regions who were followed for 30 days or until ICU discharge (Aug-Sep in 2018, 1 month). Of 4245 patients admitted to the participating ICUs, 1194 (28.1%) were patients with acute neurological disorders requiring neurocritical care and were included. Patients requiring neurocritical care had a mean mortality rate 1.7 times higher than ICU patients not requiring neurocritical care (17.21% versus 10.1%, respectively). Older age, emergency admission, higher number of potential secondary injuries, and worse APACHE II, SAPS III, SOFA, and Glasgow coma scale scores on ICU admission are independent predictors of mortality and poor outcome among patients with acute neurological diagnoses. The estimated total DALYs were 4482.94 in the overall cohort, and the diagnosis with the highest DALYs was traumatic brain injury (1634.42). Clinical, epidemiological, treatment, and ICU outcome characteristics vary according to the primary neurologic diagnosis. Advanced age, a lower GCS score and a higher number of potential secondary injuries are independent predictors of mortality and unfavourable outcomes in patients requiring neurocritical care. The findings of this study are essential to guide education policies, prevention, and treatment of severe acute neurocritical diseases.

Keywords: Intensive Care Unit; Critical Care; Nervous System Diseases; Burden of Disease; Disability-Adjusted Life Years

LISTA DE FIGURAS

LISTA DE ABREVIATURAS OU SIGLAS

UTI	-	Unidades de Terapia Intensiva
DALYs	-	*Disability-adjusted Life Years*
CoMIN	-	Comitê de Medicina Intensiva Neurológica
NCB	-	NeuroCríticos Brasil
AMIB	-	Associação de Medicina Intensiva Brasileira
CBMI	-	Congresso Brasileiro de Medicina Intensiva
e-CRF	-	*Eletronic Case Report Form*
CEPETI	-	Centro de Estudos e Pesquisa em Terapia Intensiva
COMIN	-	Congresso de Medicina Intensiva Neurológica
CEP	-	Comitê de Ética em Pesquisa
INC	-	Instituto de Neurologia de Curitiba
SJR	-	*Scimago Journal & Country Rank*
APACHE II	-	*Acute Physiology and Chronic Health Evaluation*
SOFA	-	*Sequential Organ Failure Assessment*

SUMÁRIO

1 INTRODUÇÃO

As Unidades de Terapia Intensiva (UTI) representam um pilar fundamental no espectro do cuidado à saúde, atendendo a pacientes que apresentam quadros críticos e potencialmente reversíveis. Dentre os pacientes que ocupam esses leitos, aqueles com acometimentos neurológicos têm se mostrado frequentes, evidenciando uma crescente demanda por cuidados específicos e especializados. O estudo detalhado da epidemiologia desses pacientes em UTI pode revelar padrões sobre quais doenças são mais prevalentes, quais possuem maior risco de complicações e quais requerem intervenções terapêuticas específicas.

Uma compreensão adequada do impacto que uma doença tem em uma população é um passo crucial para a implementação de medidas preventivas, terapêuticas e de reabilitação. (MENKEN; MUNSAT; TOOLE, 2000) Em contextos globais, as doenças neurológicas representam uma porção significativa da morbidade e mortalidade e impõem uma carga substancial aos pacientes, famílias e sociedade em geral. (FEIGIN; VOS, 2019) Pacientes com distúrbios neurológicos agudos que necessitam de tratamento intensivo (doravante, pacientes neurocríticos) constituem uma parte considerável de todas as internações em unidades de terapia intensiva (UTIs); esses pacientes têm alta morbidade e mortalidade e consomem recursos substanciais de cuidados de saúde, e aqueles que sobrevivem progridem com deficiências relevantes e persistentes. (HALPERN; PASTORES, 2010; RAJ et al., 2018b) No entanto, a distribuição relativa dos pacientes neurocríticos na UTI e sua sobrecarga sobre os serviços de saúde ainda não estão claras. Além disso, é em grande parte desconhecido como esses indivíduos são afetados por suas condições neurológicas específicas.

O impacto destas doenças não se limita à dimensão clínica; traz consigo custos econômicos elevados, sobrecarga emocional para pacientes e familiares e desafios logísticos para os sistemas de saúde. Por isso, avaliar a carga de doença nos pacientes neurocríticos é fundamental para entender não apenas a prevalência ou incidência de desta situação crítica, mas também sua repercussão na qualidade de vida dos indivíduos, na expectativa de vida e no funcionamento social e econômico das comunidades. Em um cenário de recursos limitados, entender essa carga é vital para que os tomadores de decisão possam priorizar intervenções e alocar recursos de maneira eficiente e eficaz.

Existem poucos dados sobre a demografia longitudinal de pacientes neurocríticos. (SILVA et al., 2019) Identificar as tendências e os resultados de admissão desses pacientes pode fornecer metas para otimizar o uso dos recursos disponíveis, apoiar protocolos e processos, impulsionar uma melhor educação médica e melhorar seus resultados gerais. (FEIGIN et al., 2020; ZACHARIA et al., 2012) Para melhor descrever a epidemiologia de pacientes neurocríticos internados em UTIs, foi criado o Estudo NeuroCrítico Brasil (NCB). O objetivo deste estudo foi descrever uma coorte de pacientes neurocríticos e suas diferenças com base em diagnósticos neurológicos primários e identificar preditores de mortalidade e desfecho desfavorável, juntamente com a carga de doença de cada condição neurológica na admissão na UTI.

2 OBJETIVOS

O projeto do Estudo NCB foi desenvolvido com os seguintes objetivos principais:

1. Descrever detalhadamente a epidemiologia da população de pacientes com uma condição neurológica primário que necessitam de cuidados intensivos nas UTIs brasileiras (pacientes neurocríticos), bem como as diferenças com base em diagnósticos neurológicos primários e identificar preditores de mortalidade e desfecho desfavorável.

2. Estimar a carga de doença dos pacientes neurocríticos de forma global e em seus diversos subgrupos definidos pelas condições neurológicas definidas no internamento, traduzida pela métrica de anos de vida perdidos com a doença ajustados pela incapacidade (DALY).

3. Proporcionar uma base sólida para futuras estratégias de educação no manejo clínico, pesquisa e planejamento em saúde pública direcionadas a esta importante população de pacientes internados nas UTIs brasileiras.

3 DESENVOLVIMENTO DO PROJETO NEUROCRÍTICOS BRASIL

A ideia do projeto NeuroCríticos Brasil (NCB) surgiu da paucidade de dados epidemiológicos acerca dos pacientes neurocríticos no Brasil, identificada numa reunião do Comitê de Medicina Intensiva Neurológica (CoMIN) da Associação de Medicina Intensiva Brasileira (AMIB), em novembro de 2016, durante o Congresso Brasileiro de Medicina Intensiva (CBMI), em Porto Alegre, RS. Nos meses subsequentes, o projeto começou a ser construído. Os desafios eram representatividade, acurácia e factibilidade.

Inicialmente, foi idealizado o delineamento, que deveria ser uma coorte multicêntrica de pacientes neurocríticos que fossem internados consecutivamente em UTIs brasileiras.

A fim de descrever a epidemiologia da população de pacientes com um diagnóstico neurológico primário que necessitam de cuidados intensivos nas UTIs brasileiras, estimou-se uma amostra necessária de 608 pacientes, considerando uma proporção de 17,2% de pacientes neurocríticos dentre o total de internados nas UTIs, uma margem de erro de 3% e um nível de confiança de 95%. Esta proporção de 17,2% de pacientes neurocríticos, adveio de um estudo piloto (Estudo Neurocríticos Curitiba) realizado no ano de 2017 em sete hospitais de Curitiba, no qual foram incluídos consecutivamente 9110 pacientes admitidos em UTIs, dos quais 1572 tinham um diagnóstico neurológico primário como causa do internamento. Assim, considerando uma base de 100 internamentos por mês por UTI e a referida proporção de pacientes neurocríticos, seria necessário a inclusão de 36 UTIs no estudo NCB, para a inclusão de 619 participantes, ou seja, pouco mais que a amostra pré-estabelecida.

O período definido de inclusão de pacientes em cada centro foi estabelecido como 30 dias e cada paciente incluído deveria ser acompanhado por até 30 dias (FIGURA 1).

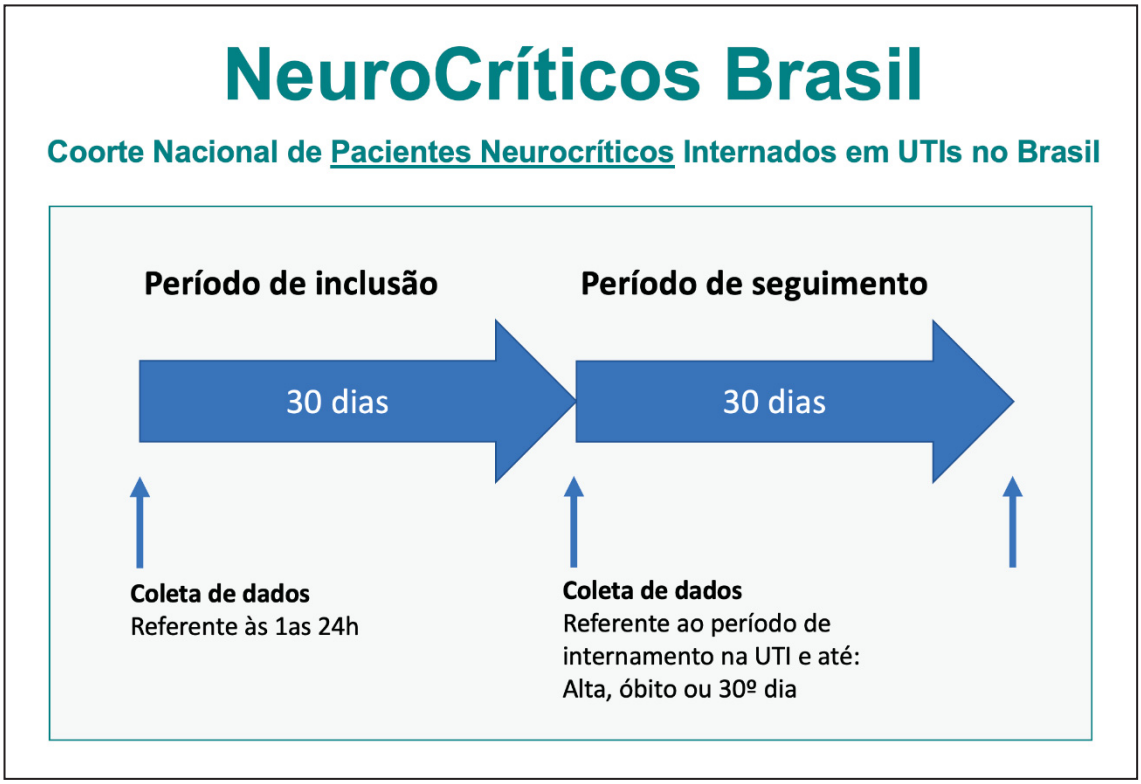

FIGURA 1 - Infográfico do delineamento do Estudo NCB

FONTE: O autor (2018).

Foram estabelecidos os diagnósticos neurológicos primários e os dados a serem coletados de forma sistemática, tanto para a coorte global de pacientes neurocríticos como para cada sub-coorte, representando cada um dos diagnósticos neurológicos primários, a saber: acidente vascular encefálico isquêmico; acidente vascular encefálico hemorrágico; hemorragia subaracnóidea; traumatismo cranioencefálico; traumatismo raquimedular; meningite/ infecção no sistema nervoso central; encefalopatia/coma; crise convulsiva; doença neuromuscular; pós-operatório eletivo de neurocirurgia.

Uma e-CRF (*eletronic Case Report Form*) foi desenvolvida exclusivamente para a coleta sistematizada destes dados para o Estudo NCB. Cada UTI participante preenchia a página com os dados cadastrais e características gerais da UTI (APÊNDICE 1). A seleção de centros contou com ajuda da AMIB-net, uma divisão da AMIB para dar suporte a estudos em UTI. Após o Projeto do Estudo NCB ter sido aprovado em uma reunião no CEPETI, em fevereiro de 2018, nós utilizamos o cadastro de UTIs da AMIB-net para convidar os centros participantes. Uma carta convite foi enviada para as 300 UTIs cadastradas (APÊNDICE 2).

Além disso, fizemos uma apresentação do projeto em um Congresso de Medicina Intensiva Neurológica (COMIN), em São Paulo, em abril de 2018, com distribuição de folders (FIGURA 2). Recebemos 80 respostas com interesse de participar e selecionamos todas as 36 UTIs que possuíam um banco de dados ativo e ao menos um coordenador dedicado para a coleta sistematizada dos dados na e-CRF. O projeto foi aprovado pelo CEP do Instituto de Neurologia de Curitiba (INC) em abril de 2017 sob parecer número 2.024.132.

Das UTIs participantes, 31 incluíram pacientes entre os dias primeiro e 30 de setembro de 2018 e cinco UTIs incluíram pacientes entre os dias primeiro e 30 de outubro de 2018 e os seguiram por até 30 dias após o dia da inclusão. Para cada paciente incluído, foi preenchido o formulário de internamento do paciente e características clínicas de internamento na UTI (APÊNDICE 3), um dos dez formulários referente ao diagnóstico neurológico primário (APÊNDICE 4 a 13) e o formulário de alta da UTI (APÊNDICE 14).

Durante todo esse período, 90 dias, nós monitoramos cotidianamente todos os centros e as anotações das e-CRFs individuais, respondendo questionamentos dos investigadores de cada centro, analisando a coerência das variáveis coletadas e minimizando a ocorrência de dados não preenchidos.

Iniciamos o ano de 2019 consolidando a planilha de dados coletados sistematicamente dos 1194 pacientes neurocríticos das 36 UTIs, representando quatro das cinco regiões brasileiras. Foram mais de 200.000 dados coletados. A tarefa inicial era descrever a população global de pacientes neurocríticos, analisar suas características e explorar inúmeras hipóteses e, depois, descrever a carga de doença para cada paciente individualmente, em termos de DALYs (*Disability-adjusted Life Years*), posteriormente reunidos nos diversos grupos. Começamos a escrever o artigo ainda em 2019, com os dados disponíveis, mas a pandemia de COVID-19, iniciada em março de 2020 e que impactou severamente as UTIs e sua carga de trabalho por cerca de dezoito meses, atrasou a publicação do nosso projeto. Conseguimos finalizar a análise inicial do Estudo NCB em 2022 e escrever o artigo para publicação, o qual, após as devidas revisões, apresentamos nessa tese a seguir. Muitos dados ainda estão sendo analisados e novas publicações, referentes às coortes individuais e com dados adicionais, deverão ser publicadas na sequência.

FIGURA 2 - Folder distribuído no COMIN em São Paulo

FONTE: O autor (2018).

4 ARTIGO CIENTÍFICO - EPIDEMIOLOGY AND DISEASE BURDEN OF PATIENTS REQUIRING NEUROCRITICAL CARE: A BRAZILIAN MULTICENTRE COHORT STUDY

A seguir apresento o trabalho aceito para publicação em outubro de 2023 no periódico *Scientific Reports*, uma revista científica publicada pelo grupo *Nature Portfolio*. É a quinta revista científica mais citada no mundo, classificada como Q1 pela SJR (*Scimago Journal & Country Rank*) e como A1 pelo Qualis da Plataforma Sucupida da CAPES.

O artigo apresentado a seguir também pode ser visualizado na forma de sua publicação no link: https://doi.org/10.1038/s41598-023-44261-w

scientific reports

OPEN

Epidemiology and disease burden of patients requiring neurocritical care: a Brazilian multicentre cohort study

Álvaro Réa-Neto [1,2,3]✉, Rafaella Stradiotto Bernardelli [1,4], Mirella Cristine de Oliveira [1,5], Paula Geraldes David-João [1,6], Amanda Christina Kozesinski-Nakatani [1,7], Antônio Luís Eiras Falcão [8,9], Pedro Martins Pereira Kurtz [10,11,12], Hélio Afonso Ghizoni Teive [13,14] & Neurocritical Brazil Study group *

Acute neurological emergencies are highly prevalent in intensive care units (ICUs) and impose a substantial burden on patients. This study aims to describe the epidemiology of patients requiring neurocritical care in Brazil, and their differences based on primary acute neurological diagnoses and to identify predictors of mortality and unfavourable outcomes, along with the disease burden of each condition at intensive care unit admission. This prospective cohort study included patients requiring neurocritical care admitted to 36 ICUs in four Brazilian regions who were followed for 30 days or until ICU discharge (Aug-Sep in 2018, 1 month). Of 4245 patients admitted to the participating ICUs, 1194 (28.1%) were patients with acute neurological disorders requiring neurocritical care and were included. Patients requiring neurocritical care had a mean mortality rate 1.7 times higher than ICU patients not requiring neurocritical care (17.21% versus 10.1%, respectively). Older age, emergency admission, higher number of potential secondary injuries, and worse APACHE II, SAPS III, SOFA, and Glasgow coma scale scores on ICU admission are independent predictors of mortality and poor outcome among patients with acute neurological diagnoses. The estimated total DALYs were 4482.94 in the overall cohort, and the diagnosis with the highest DALYs was traumatic brain injury (1634.42). Clinical, epidemiological, treatment, and ICU outcome characteristics vary according to the primary neurologic diagnosis. Advanced age, a lower GCS score and a higher number of potential secondary injuries are independent predictors of mortality and unfavourable outcomes in patients requiring neurocritical care. The findings of this study are essential to guide education policies, prevention, and treatment of severe acute neurocritical diseases.

A proper understanding of the impact that a disease has on a population is a crucial step for the implementation of preventive, therapeutic, and rehabilitative m easures[1]. Neurological disorders have an increasingly high prevalence and impose a substantial burden on patients, families, and society in general[2]. Patients who are critically ill with neurological or neurosurgical diseases require neurocritical care to treat the primary insult to the nervous system and prevent or ameliorate secondary neurological and nonneurological injuries. Patients with diverse acute neurological disorders constitute a considerable proportion of all admissions to intensive

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care units (ICUs) worldwide. In Brazil, approximately 10% of ICU admissions are due to neurological causes, according to monitoring data from Brazilian UTIS from 2010 to 2 023[3]. They have high morbidity and mortality and consume substantial health care resources, and those who survive progress with relevant and persistent disabilities[4–6]. However, the relative distribution of patients requiring neurocritical care and their burden on health care services remain unclear

Identifying the proportions, severities, and outcomes of these patients can provide goals to optimize the use of available resources, support protocols and processes, and improve medical education[7,8]. The Neurocritical Brazil Study aimed to better describe the epidemiology of patients requiring neurocritical care in Brazil and their differences based on primary acute neurological disorders and to identify predictors of mortality and poor outcomes, along with an estimate of the disease burden of each acute neurological disorder group identified at ICU admission.

Methods

We conducted a national prospective cohort study including all patients with primary diagnoses of acute neurological conditions admitted to 36 ICUs over 30 consecutive days. After admission, patients were followed for 30 days or until ICU discharge.

The study was approved by the local ethics committee of the Neurological Institute of Curitiba (ethics committee of the coordinating centre) on April 20, 2017 (approval number 2.024.132) and by the local ethics committees at each participating centres. The need for informed consent was waived in all centres, given the noninterventional design of the study and the fact that the data were collected from clinical records and without contact with the participants. All research procedures were conducted in accordance with the ethical standards of the committees on human experimentation of each participating institution and the Declaration of Helsinki (7th revision, 2013). The study results are reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

We invited all 300 ICU members of the ICU network identified in the ICU network of the Brazilian Association of Intensive Care Medicine (AMIBnet) to participate in the study. To participate in the study, each ICU should have an active database of patients, a coordinator willing to follow up on all patients requiring neurocritical care for up to 30 consecutive days, and a team available for data collection. Each ICU should also obtain timely study protocol approval by the institution's ethics committee. In all, 80 ICUs agreed to participate and 36 were included and recruited patients for the study. These ICUs were in four of the five most populous Brazilian regions.

The participating ICUs were distributed across various Brazilian regions. The Supplementary Material S1 presents a complete list of the centres of all participating ICUs and their corresponding investigators, the distribution of participating enrolling centres across Brazil (Supplementary Fig. S1) and the percentage of contribution from each participating centre to the sample (Supplementary Fig. S2).

The study data were collected in 2018 between August 1–30 (31 ICUs) and September 1–30 (5 ICUs). All patients admitted to the participating ICUs during the 30 days of the study were screened, and those with an acute neurological disorder that was the primary cause of ICU admission were consecutively included in the study and followed up for only 30 days or until ICU discharge. The patients were considered eligible for inclusion if they were older than 18 years and were admitted to a participating ICU during the study period.

The patients were subdivided into ten groups according to their primary acute neurological diagnosis on ICU admission (hereafter, diagnostic groups): ischaemic stroke, intracerebral haemorrhage, subarachnoid haemorrhage, encephalopathy, seizures, traumatic brain injury, spinal cord injury, central nervous system infection, neuromuscular disease, and postoperative care of elective neurosurgery. Patients admitted to the participating ICUs with acute neurological diagnoses different than those listed above were excluded from the study. The group of encephalopathies is made up of several entities that affect the entire brain and alter mental function in a diffuse way, such as, septic encephalopathy, brain structural damage (hydrocephalus, tumour, etc.), metabolic encephalopathy, hypoxic-ischaemic encephalopathy, drug-induced encephalopathy, and other aetiologies.

The Center for Study and Research in Intensive Care Medicine (CEPETI) developed a dedicated electronic case report form to capture the study data. We collected the following variables related to the patients and ICU outcomes: age, sex, comorbidities, type of transportation to the hospital, kind of health care coverage (public, private, or complementary), location before transfer to the ICU, worst clinical scores on severity scales (Glasgow Coma Scale [GCS], Acute Physiology and Chronic Health Evaluation [APACHE] II, Simplified Acute Physiology Score [SAPS] III, Sequential Organ Failure Assessment [SOFA]), potential secondary injuries (the "Hs," namely, hypotension, hypoxia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation—the parameters adopted for the definition of each of the Hs, as well as their cut-off points, are described in Table 1) in the first 24 h in the ICU, the results of neurological imaging tests performed on the first day of ICU admission, complications and procedures performed in the ICU, and length of ICU stay during the 30-day study period. We also collected mortality information and calculated the modified Rankin Scale (mRS) during the 30-day ICU observation period, and both were defined as the study outcomes. Patients with mRS scores of 4, 5, or 6 were considered to have an unfavourable outcome, while those with mRS scores of 0, 1, 2, or 3 were considered to have a favourable outcome.

We described these collected variables in the overall cohort and compared their rates in each of the ten diagnostic groups.

Following recommendations from observational studies in critically ill patients[9], we determined a priori the variables to be considered prognostic factors for the two study outcomes. Thus, we evaluated the influence of age, sex, number of secondary injuries (Hs) in the first 24 h in the ICU, and GCS, APACHE II, SAPS III, and SOFA scores on these outcomes. This analysis was performed in the overall cohort and each diagnostic group.

Characteristics	n = 1194
Baseline	
Age, mean ± SD, years	58.9 ± 19.4
Male sex, n (%)	618 (51.8)
Transportation to the hospital[a], n (%)	
Critical care ambulance	376 (31.5)
Ambulance without critical care service	91 (7.6)
Family members	355 (29.7)
Self-driven	370 (31.0)
Coverage of hospitalization costs, n (%)	
Public health insurance	591 (49.5)
Complementary or private insurance	603 (50.5)
Type of ICU admission, n (%)	
Elective	317 (26.6)
Emergency	877 (73.4)
Location before transfer to the ICU, n (%)	
Emergency department	567 (47.5)
Operating room	428 (35.8)
Hospital ward	81 (6.8)
Other	118 (9.9)
Severity scores on ICU admission	
Glasgow Coma Scale, Median (IQR)	14 (9–15)
APACHE II, median (IQR)	11 (7–17)
SAPS III[b], median (IQR)	44 (33–56)
SOFA[c], median (IQR)	2 (1–6)
Comorbidities	
Hypertension, n (%)	603 (50.5)
Cardiopathy, n (%)	177 (14.8)
Chronic obstructive pulmonary disease, n (%)	51 (4.3)
Renal disease, n (%)	83 (7.0)
Diabetes mellitus, n (%)	218 (18.3)
Extracranial neoplasia, n (%)	89 (7.5)
Primary neurological diagnoses, n (%)	
Postoperative care of elective neurosurgery	317 (25.6)
Traumatic brain injury	218 (18,3)
Ischaemic stroke	211 (17.7)
Encephalopathy	155 (13)
Seizures	91 (7.6)
Intracerebral haemorrhage	77 (6.4)
Subarachnoid haemorrhage	70 (5.9)
Central nervous system infection	25 (2.1)
Spinal cord injury	19 (1.6)
Neuromuscular disease	11 (0.9)
Potential secondary injuries (Hs) at ICU admission	
Hypotension (MAP < 65 mmHg or SBP < 90 mmHg), n (%)	267 (22.4)
Hypoxemia (PaO_2 < 60 mmHg or $são_2$ < 90% or SpO_2 < 90%), n (%)	72 (6.0)
Hyperthermia (body temperature > 37.5°C), n (%)	126 (10.6)
Hypercapnia ($PaCO_2$ > 45 mmHg ou RR < 8 ipm), n (%)	115 (9.6)
Hypocapnia ($PaCO_2$ < 35 mmHg), n (%)	213 (19.3)
Hypoglycaemia (venous or capillary glucose values < 60 mg/dL) n (%)	32 (2.7)
Hyponatremia (sodium < 135 mmHg), n (%)	200 (16.8)
Hypothermia (body temperature < 35°C), n (%)	121 (10.1)
Intracranial hypertension (intracranial pressure > 25 mmHg), n (%)	89 (7.5)
Clinical evidence of herniation, n (%)	77 (6.4)
Number of Hs, n (%)	
Zero	500 (41.9)
One	318 (26.6)
Continued	

Characteristics	n = 1194
Two	203 (17.0)
Three or more	173 (14.5)
Imaging tests performed on the first day of ICU admission	
Computed tomography of the head, n (%)	931 (78)
Magnetic resonance of the head, n (%)	208 (17.4)
Cerebral arteriogram, n (%)	87 (7.3)
Procedures performed during the ICU stay	
Urgent neurosurgery, n (%)	199 (16.7)
Placement of an external ventricular drain, n (%)	84 (7.0)
Invasive mechanical ventilation, n (%)	460 (38.5)
Tracheostomy, n (%of patients placed on invasive mechanical ventilation)	146 (31.7)
Noninvasive mechanical ventilation, n (%)	77 (6.4)
Vasoactive drug—vasopressor, n (%)	358 (25.0)
Vasoactive drug—vasodilator, n (%)	82 (6.9)
Renal replacement therapy, n (%)	65 (5.4)
Intracranial pressure monitoring—intraparenchymal, n (%)	55 (4.6)
Intracranial pressure monitoring—intraventricular, n (%)	40 (3.3)
Electroencephalographic monitoring, n (%)	102 (8.5)
Intracranial Doppler monitoring, n (%)	37 (3.1)
Brain tissue oxygen pressure monitoring, n (%)	4 (0.3)
Complications	
Pneumonia, n (%)	203 (17)
Urinary tract infection, n (%)	43 (3.6)
Catheter-related infection, n (%)	35 (2.9)
Primary bloodstream infection, n (%)	27 (2.3)
Neurological infection, n (%)	23 (1.9)
Wound infection, n (%)	15 (1.2)
Clostridium associated diarrhoea, n (%)	2 (0.2)
Renal failure, n (%)	100 (8.4)
Acute respiratory distress syndrome, n (%)	38 (3.2)
Gastrointestinal bleeding, n (%)	15 (1.3)
Intracranial hypertension, n (%)	129 (10.8)
Outcome until the 30th study day, n (%)	
ICU discharge	832 (69.7)
Transfer to another hospital	22 (1.8)
Continued hospitalization on ICU	152 (12.7)
Mortality	188 (15.7)
Brain death[d], n (%)	48 (25.5)
mRS on the day of the ICU outcome or until the 30th study day[e], n (%)	
0. No symptoms at all	283 (23.7)
1. No significant disability despite symptoms; able to carry out all usual duties and activities	201 (16.9)
2. Slight disability; unable to carry out all previous activities, but able to look after own affair without assistance	121 (10.2)
3. Moderate disability; requiring some help (*e.g.*, with shopping/managing affairs) but able to walk without assistance	100 (8.4)
4. Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance	154 (12.9)
5. Severe disability; bedridden, incontinent, and requiring constant nursing care and attention	140 (11.8)
6 Dead	188 (15.8)
Unfavourable outcome (mRS score 4, 5, or 6)[f], n (%)	482 (40.6)
Length of ICU stay until the 30th study day, Median (IQR)	5 (3–16)

Table 1. Baseline characteristics and procedures, complications, and outcomes during ICU stay among patients requiring neurocritical care. *APACHE II* acute physiology and chronic health evaluation, *ICU* intensive care unit, *IQR* interquartile range, *MAP* mean arterial pressure, *mRS* modified Rankin Scale, *n* absolute frequency, $PaCO_2$ partial arterial carbon dioxide pressure, PaO_2 partial arterial oxygen pressure, *RR* respiratory rate, SaO_2 arterial oxygen saturation, *SAPS III* simplified acute physiology score III, *SBP* systolic blood pressure, *SD* standard deviation, *SOFA* sequential organ failure assessment, SpO_2 peripheral oxygen saturation, *%* percentage within column. [a] 2 missing data. [b] 35 missing data. [c] 54 missing data. [d] Percentage calculation considering the 188 deaths from neurological causes in the intensive care unit. In this classification, only patients who had a closed brain death protocol were considered. [e] 7 missing data.

Analysis of disability-adjusted life-years (DALY)

We assessed the disease burden from acute neurocritical disorders using disability-adjusted life-years (DALYs) in accordance with the World Health Organization (WHO) methods and data sources for the global burden of disease estimates 2000–2015[10] and 2000–2019[11]. One DALY represents the loss of 1 year of a "healthy" life. DALYs for a disease or health condition are calculated as the sum of the years of life lost (YLLs) due to premature mortality in the population and the years of life lost due to disability (YLDs) for individuals living with the health condition or its consequences.

The YLLs were calculated from values presented in the complete 2018 mortality table of the Brazilian Institute of Geography and Statistics (IBGE) according to sex and age as the basis for obtaining the standard life expectancy at the age at which death occurs[12]. The YLDs were estimated using disability weights available in the 2017 Global Burden of Disease (GBD) report, considering the mRS classification of patients requiring neurocritical care as parameters for selecting the disability weight[13]. The disability weight was multiplied by the prevalence of individual consequences of the disease. We estimated the population prevalence of each acute neurological disorder by sex and age range (5-year intervals) using the software DisMod-MR 2.1, which is a Bayesian meta-regression tool that was used as the main method to analyse nonfatal data in the GBD project and is recommended by WHO methodological g uidelines[10,11]. For that, sample data related to prevalence rates, fatal cases, mortality, and disease remission for each acute neurocritical disorder and comorbidity relative to the total number of patients requiring neurocritical care were imputed in the software. These YLD values were also corrected for comorbidities by multiplying the weights of the sequelae of acute neurological disorders and the comorbidities presented requiring neurocritical care by each patient participating in the study.

Statistical analysis

Categorical variables are described as absolute (n) and relative (%) frequencies, and numerical variables are described as the mean and standard deviation (SD) or median and interquartile range (IQR).

The nonparametric Mann–Whitney test was used to compare the participating ICUs in terms of the mean numbers of new patients requiring neurocritical care and ICU patients not requiring neurocritical care inpatients during the study period. Student's t test was used to compare the mean SAPS III values and mortality rate among new patients requiring neurocritical care versus ICU patients not requiring neurocritical care an in inpatient. We compared the categorical variables between the ten diagnostic groups using the chi-square test with a subsequent two-by-two comparison with the Bonferroni correction. Given its normal distribution, age was compared between diagnostic groups using one-way analysis of variance (ANOVA) and post hoc least significant difference (LSD). Severity scores and length of ICU stay had skewed distributions and were analysed using the Kruskal–Wallis rank-sum test followed by two-by-two comparisons using Dunn's test.

We performed univariate analysis to explore admission variables related to ICU mortality and unfavourable outcomes. The variables included in the analysis were sex, GCS, SAPS III score, SOFA score, secondary injuries (Hs) within 24 h of ICU admission, and hospitalization covered by the public health system (Brazilian Unified Health System [SUS]). Variables with statistical significance in the univariate analysis were included in the multivariate analysis. Based on results from previous studies, SAPS III was chosen over APACHE II in the multivariate models [4,14,15]. Only three multivariate models are presented, since the variables in SAPS III and SOFA overlap with those in the GCS and Hs. The results of the regression analysis were expressed as odds ratios (ORs) and 95% confidence intervals (CIs), and their statistical significance was assessed by the Wald test. The goodness of fit of the multivariate models, given by their explanatory potential, was expressed by the area under the receiver operating characteristic (ROC) curve of the model's predicted probability for the outcome. The same analysis was performed for each of the ten diagnostic subgroups.

The level of statistical significance was set at 5%. The data were analysed using the statistical software IBM SPSS, version 28.0 (SPSS Inc., Chicago, IL, USA). Missing data were not imputed.

Results

The 36 participating sites had a median of 190 (interquartile range: 136.5 to 309.75) hospital beds and 34 (interquartile range: 20–49) ICU beds. Most participating sites were academic institutions (83.3%) located in large urban centres (63.9% in cities with > 1 million inhabitants), regardless of geographic location. The southeast region, the most populous in Brazil, had 55.5% of the participating centres, 27.8% of the centres were in the south region, 8.3% were in the northeast region and 8.3% were in the central-west region. There were no participating centres in the northern region of Brazil. Critical care physicians assisted patients in 97.2% of the 36 centres. There was a full-time neurosurgical and neurology team available in 94.4% and 83.3% of the participating hospitals, respectively. Furthermore, most centres had an active hospital protocol for treating neurological disorders. The complete profile of the participating hospitals is presented in Supplementary Table S18.

During the study period, 4245 patients were admitted to the 36 participating ICUs over 30 days (median of 98 new patients per ICU), of whom 1194 (28.1%) were patients requiring neurocritical care and 3051 (71.9%) were ICU patients not requiring neurocritical care (Supplementary Fig. S3 and Table S1).

The overall mean ICU mortality rate during the study period was 12.8% ± 8.9%. The mean mortality rate was significantly higher in patients requiring neurocritical care (17.2% ± 12.6%) than in ICU patients not requiring neurocritical care (10.1% ± 8.7%, relative risk 1.7, $p = 0.038$). The difference in mortality rates between neurocritical and ICU patients not requiring neurocritical care was not explained by the differences in the SAPS III results (46.9 ± 4.5 vs. 46.2 ± 12.7, respectively; $p = 0.800$) (Supplementary Table S1).

The study included all 1194 patients requiring neurocritical care consecutively admitted to the 36 participating ICUs over 30 days (Supplementary Fig. S3). The mean age of the patients was 58.9 ± 19.4 years and 51.8% were men. Hospitalization costs were covered by the Brazilian Unified Health System (SUS) in

49.5% (n = 591) of the cases and by complementary or private health care plans in 50.5% (n = 603) of them. The patients were divided into 10 groups according to their primary acute neurological diagnoses. The acute neurocritical condition that most often resulted in ICU admission was postoperative care of elective neurosurgery (26.5%), followed by traumatic brain injury (18.3%). The majority (58.1%) had one or more potential secondary injuries (Hs) on ICU admission. Invasive mechanical ventilation was used by 38.5% of patients, and of these, 31.7% required tracheostomy. Table 1 describes the general characteristics of the overall cohort.

The 10 diagnostic groups differed significantly in terms of patient age, sex, severity scores (GCS, APACHE II, SAPS III, and SOFA), number of potential secondary injuries (Hs) at ICU admission, percentage of patients who required invasive mechanical ventilation and tracheostomy during ICU stay, length of ICU stay, mortality, and mRS classification at the time of the outcome (30 days or day of ICU discharge) (Table 2). Supplementary Table S2 shows the comparison of other baseline characteristics of the patients, the procedures performed during their stay in the intensive care unit, complications, and the outcomes among the 10 acute neurocritical disorders, including the largest group formed of patients with postoperative care of elective neurosurgery. These variables were compared by paired diagnostic groups (pairwise comparison), as shown in Supplementary Fig. S4.

The group of patients with postoperative elective neurosurgery (NPO) care accounted for 25.6% of the sample. This group, when compared to the others, had lower SAPS III (median = 31) and SOFA on admission (median = 1), in addition to a lower prevalence of potential events of secondary injuries on admission and shorter hospital stays (3 days). The comparison of this group with the others is shown in Table 2 and in the supplementary material in Fig. S4 and Table S2. The patients' mean age was the highest and lowest in the ischaemic stroke and spinal cord injury diagnostic groups, respectively. The proportion of men was greater than 70% in the diagnostic groups of central nervous system infection, traumatic brain injury, spinal cord injury, and neuromuscular disease, and the proportion of women in the subarachnoid haemorrhage group was 68.6%. The median GCS score at ICU admission was 10 in patients with intracerebral haemorrhage, subarachnoid haemorrhage, and central nervous system infection, 9 among patients with traumatic brain injury, and ≥ 13 in patients with all other diagnoses. The APACHE II and SAPS III values were highest among patients with central nervous system infection and lowest among those admitted for postoperative care of elective neurosurgery or due to spinal cord injury. The lowest median SOFA value was observed in patients with neuromuscular disease (Table 2 and Supplementary Fig. S4).

One or more secondary injuries (Hs) at ICU admission were present in more than 50% of the patients in the following diagnostic groups: traumatic brain injury, encephalopathy, seizures, intracerebral haemorrhage, subarachnoid haemorrhage, central nervous system infection, and spinal cord injury. The group with central nervous system infection had the highest number of Hs per patient—40% of the patients with this diagnosis had three or more Hs—and the longest ICU stay (Table 2 and Supplementary Fig. S4).

More than 50% of patients with traumatic brain injury, intracerebral haemorrhage, subarachnoid haemorrhage, central nervous system infection and spinal cord injury used invasive mechanical ventilation, a proportion significantly higher than that of the postoperative care of elective neurosurgery, ischaemic stroke, and seizures groups. Among those who were intubated, the highest rate of tracheostomy occurred in the neuromuscular disease group (66.7%), followed by spinal cord injury (58.3%) and intracerebral haemorrhage (46%).

The encephalopathy group (n = 155) was composed of different aetiologies, including: 64 cases of septic encephalopathy, 26 cases of brain structural damage (hydrocephalus, tumour, etc.), 21 cases of metabolic encephalopathy, 19 cases of hypoxic-ischaemic encephalopathy, 13 cases of drug-induced encephalopathy, and 12 cases of other aetiologies. The characteristics of each of the encephalopathy aetiologies are described separately in Supplementary Table S19.

We performed univariate analysis to explore admission variables related to ICU mortality and unfavourable outcomes (mRS score 4, 5, or 6) and found that older age, lower GCS score, higher number of potential secondary injuries (Hs), admission from the emergency department, and hospitalization covered by the public health care system emerged as isolated risk factors for an unfavourable outcome (Table 3). All variables included in the univariate analysis emerged as significant and were selected for the multivariate analysis. Older age, lower GCS score, higher number of potential secondary injuries (Hs), admission from the emergency department, and hospitalization covered by the public health care system emerged as isolated risk factors for an unfavourable outcome and mortality (Table 4).

The same multivariate models were fitted for each diagnostic group (Supplementary Tables S3–S16) with enough cases and events to fit the models (*i.e.,* postoperative care of elective neurosurgery, traumatic brain injury, ischaemic stroke, encephalopathy, seizures, intracerebral haemorrhage, and subarachnoid haemorrhage). In subgroup analyses, older age, lower GCS, higher number of Hs, and higher APACHE II, SAPS III, and SOFA values remained consistently independent risk factors for mortality and unfavourable outcome, especially in the diagnostic groups with larger sample sizes and greater number of outcomes, where a more reliable statistical analysis was possible. Coverage of hospitalization costs by the public health care system was not a risk factor for mortality or unfavourable outcome in the diagnostic groups with traumatic brain injury, ischaemic stroke, encephalopathy, intracerebral haemorrhage, and subarachnoid haemorrhage (Supplementary Tables S6, S8, S10, S14, and S16, respectively).

Regarding disease burden, we identified a total loss of 4482.94 DALYs (4420.022 YLLs and 62.92 YLDs) in the overall cohort. The acute neurocritical disorders analysed in this study had the highest DALYs of any other condition listed for Brazil in the 2017 GBD[16]. Analysing the diagnostic groups individually, we observed that traumatic brain injury was the condition with the most years of "healthy" life lost, followed by encephalopathy and intracerebral haemorrhage (Fig. 1 and Supplementary Table S17).

The acute neurological diagnoses contributed differently to the nonstandardized DALYs in each age group. Indeed, traumatic brain injury contributed the most to the DALYs in patients between the ages of 18–39 years,

while cerebrovascular diseases and encephalopathy had the greatest burden (DALYs) in patients between the ages of 40–69 years. These three diagnostic groups had a similar impact in the age groups above 70 years. When analysed by sex, the impact of traumatic brain injury and encephalopathy on DALYs was greatest in men, while that of cerebrovascular diseases (ischaemic stroke, intracerebral haemorrhage, and subarachnoid haemorrhage) was greatest in women. Furthermore, the estimated DALY was higher among patients who had a greater number of potential secondary injuries (Hs) upon admission to the ICU (Fig. 1 and Supplementary Table S17).

Variables	NPO (n = 317)	TBI (n = 218)	IS (n = 211)	ENC (n = 155)	Seizures (n = 91)	ICH (n = 77)	SAH (n = 70)	SNI (n = 25)	SCI (n = 19)	NMD (n = 11)	p value
Age (years), mean ± SD	53.4 ± 14.7	54.3 ± 22.1	69.3 ± 16.9	65.7 ± 20.2	58.7 ± 22.7	62 ± 15.3	57.6 ± 14.2	55.7 ± 17.6	36.5 ± 18.5	50 ± 20.8	< 0.001[a]
Male sex, n (%)	131 (41.3)	162 (74.3)	107 (50.7)	72 (46.5)	46 (50.5)	37 (48.1)	22 (31.4)	19 (76)	14 (73.7)	8 (72.7)	< 0.001[b]
GCS, median (IQR)	15 (14–15)	9 (3–14)	14 (12–15)	13 (9–14)	14 (11–15)	10 (4–14)	10 (3–14)	10 (4–14)	15 (15—15)	15 (14—15)	< 0.001[c]
APACHE II at ICU admission, median (IQR)	7 (4–10)	14 (10–21)	11 (7–16)	15 (10–25)	10 (6–15)	15 (9–19)	14 (8–20)	20 (12–24)	7 (3–12)	7 (5–10)	< 0.001[c]
SAPS III at ICU admission[d], median (IQR)	31 (24–39)	47 (38–57)	52 (42–58)	57 (47–68)	41 (33–54)	54.5 (44–65.5)	48 (40–60)	59 (44.5–65.5)	35 (27–43)	42 (36–49)	< 0.001[c]
SOFA at ICU admission[e], median (IQR)	1 (0–3)	5 (2–8)	2 (0–4)	4 (2–8)	2 (0–4)	5; 4 (2–7)	4 (2–8)	6 (1.5–9)	3 (1–4)	0 (0–2)	< 0.001[c]
Number of Hs at ICU admission, n (%)											
Zero	162 (51.1)	64 (29.4)	109 (51.7)	47 (30.3)	44 (48.4)	30 (39)	24 (34.3)	6 (24)	8 (42.1)	6 (54.5)	< 0.001[b]
One	96 (30.3)	51 (23.4)	55 (26.1)	39 (25.2)	24 (26.4)	20 (26)	20 (28.6)	5 (20)	5 (26.3)	3 (27.3)	
Two	41 (12.9)	49 (22.5)	30 (14.2)	32 (20.6)	14 (15.4)	13 (16.9)	14 (20)	4 (16)	5 (26.3)	1 (9.1)	
Three or more	18 (5.7)	54 (24.8)	17 (8.1)	37 (23.9)	9 (9.9)	14 (18.2)	12 (17.1)	10 (40)	1 (5.3)	1 (9.1)	
Invasive MV, n (%)	53 (16.7)	139 (63.8)	55 (26.1)	65 (41.9)	24 (26.4)	50 (64.9)	45 (64.3)	14 (56)	12 (63.2)	3 (27.3)	< 0.001[b]
Tracheostomy, n (%)[g]	7 (13.2)	43 (30.9)	18 (32.7)	22 (33.8)	5 (20.8)	23 (46)	15 (33.3)	4 (28.6)	7 (58.3)	2 (66.7)	0.016[b]
Length of ICU stay until 30th day, median (IQR)	3 (2–5)	11 (4–29)	4 (3–11)	6 (3–17.5)	4 (2–9)	16 (6–30)	11.5 (4–22)	13 (4–26)	30 (7.5–30)	4 (3–30)	< 0.001[b]
30-day mortality, n (%)	7 (2.2)	56 (25.7)	24 (11.4)	41 (26.5)	4 (4.4)	22 (28.6)	24 (34.3)	9 (36)	1 (5.3)	0 (0)	< 0.001[b]
mRS on ICU outcome or until 30th day[f], n (%)											
0	121 (38.3)	40 (18.3)	50 (24)	18 (11.6)	36 (40.4)	2 (2.6)	7 (10)	4 (16)	1 (5.3)	4 (36.4)	< 0.001[b]
1	75 (23.7)	30 (13.8)	37 (17.8)	16 (10.3)	16 (18)	11 (14.5)	6 (8.6)	4 (16)	4 (21.1)	2 (18.2)	
2	50 (15.8)	16 (7.3)	17 (8.2)	16 (10.3)	7 (7.9)	8 (10.5)	6 (8.6)	0 (0)	0 (0)	1 (9.1)	
3	29 (9.2)	15 (6.9)	22 (10.6)	16 (10.3)	5 (5.6)	3 (3.9)	7 (10)	1 (4)	2 (10.5)	0 (0)	
4	26 (8.2)	31 (14.2)	34 (16.3)	24 (15.5)	10 (11.2)	13 (17.1)	7 (10)	3 (12)	4 (21.1)	2 (18.2)	
5	8 (2.5)	30 (13.8)	24 (11.5)	24 (15.5)	11 (12.4)	17 (22.4)	13 (18.6)	4 (16)	7 (36.8)	2 (18.2)	
6	7 (2.2)	56 (25.7)	24 (11.5)	41 (26.5)	4 (4.5)	22 (28.9)	24 (34.3)	9 (36)	1 (5.3)	0 (0)	
Unfavourable outcome (mRS score 4, 5, or 6)[f], n (%)	41 (13)	117 (53.7)	82 (39.4)	89 (57.4)	25 (28.1)	52 (68.4)	44 (62.9)	16 (64)	12 (63.2)	4 (36.4)	< 0.001[b]

Table 2. Comparison of the characteristics of patients requiring neurocritical care by 10 acute neurocritical disorders. *APACHE II* acute physiology and chronic health evaluation, *ENC* encephalopathy, *GCS* Glasgow Coma Scale, *ICH* intracerebral haemorrhage, *IQR* interquartile range, *IS* ischaemic stroke, *mRS* modified Rankin Scale, *MV* mechanical ventilation, *n* absolute frequency, *NMD* neuromuscular disease, *NPO* postoperative care of elective neurosurgery, *SAH* subarachnoid haemorrhage, *SAPS III* simplified acute physiology score III, *SCI* spinal cord injury, *SD* standard deviation, *SNI* central nervous system infection, *SOFA* sequential organ failure assessment, *TBI* traumatic brain injury, *%* percentage within column. [a] Significance of the one-way analysis of variance (ANOVA). [b] Significance of the chi-square test. [c] Significance of the Kruskal– Wallis test. [d] Missing data on SAPS III: 3 for NPO, 7 for TBI, 10 for STR, 1 for ENC, 1 for seizures, 5 for ICH, 5 for SAH, 1 for SNI and 2 for SCI. [e] Missing data on SOFA: 6 for NPO, 9 for TBI, 15 for IS, 6 for seizures, 7 for ICH, 6 for SAH, 1 for SNI and 4 for SCI. [f] Missing data on mRS and unfavourable outcome: 1 for NPO, 3 for IS, 2 for seizures, 1 for ICH. [g] Percentage of patients placed on invasive mechanical ventilation.

Factors (n total = 1194)	ICU discharge[a]	Death on ICU[a]	Unadjusted OR (95% CI) for ICU mortality[b]	p value[c]	Favourable outcome (mRS score 1, 2, or 3)[a]	Unfavourable outcome (mRS score 4, 5, or 6)[a]	Unadjusted OR (95% CI) for unfavourable outcome[b]	p value[c]
Age (years)	(n = 1006) 58.5 ± 19	(n = 188) 60.9 ± 21.1	1.006 (0.998–1.014)	0.122	(n = 705) 57.7 ± 18.7	(n = 482) 60.4 ± 20.2	1.007 (1.001–1.013)	0.017
Sex								
Female	519/576 (87)	75/576 (13.0)	Ref		360/572 (62,9)	212/572 (37.1)	Ref	
Male	505/618 (81.7)	113/618 (18.3)	1.494 (1.088–2.052)	0.013	345/615 (56.1)	270/615 (43.9)	1.329 (1.053–1.677)	0.017
GCS	(n = 1006) 14 (11–15)	(n = 188) 7 (3–13)	0.812 (0.784–0.840)	< 0.001	(n = 705) 15 (14–15)	(n = 482) 10 (3–14)	0.764 (0.738–0.792)	< 0.001
APACHE II	(n = 1006) 10 (6–15)	(n = 188) 21.5 (15–27.5)	1.179 (1.151–1.207)	< 0.001	(n = 705) 8 (5–12)	(n = 482)17 (12–23)	1.195 (1.168–1.222)	< 0.001
SAPS III	(n = 984) 42 (32–54)	(n = 175) 60 (47–73)	1.066 (1.054–1.078)	< 0.001	(n = 692) 39 (29–49)	(n = 460) 56 (44–67)	1.075 (1.065–1.086)	< 0.001
SOFA	(n = 968) 2 (1–4)	(n = 172) 8 (5–10)	1.366 (1.302–1.433)	< 0.001	(n = 679) 1 (0–3)	(n = 454) 6 (3–9)	1.434 (1.369–1.503)	< 0.001
Number of Hs								
Zero	478/500 (95.6)	22/500 (4.4)	Ref		380/494 (76.9)	114/494 (23.1)	Ref	
One	283/318 (89)	35/318 (11)	2.687 (1.545–4.672)	< 0.001	207/318 (65.1)	111/318 (34.9)	1.787 (1.309–2.44)	< 0.001
Two	154/203 (75.9)	49/203 (24.1)	6.91 (4.049–11.801)	< 0.001	82/202 (40.6)	120/202 (59.4)	4.878 (3.437–6.924)	< 0.001
Three or more	91/173 (52.6)	82/173 (47.4)	19.578 (11.625–32.972)	< 0.001	36/173 (20.8)	137/173 (79.2)	12.685 (8.313–19.356)	< 0.001
Coverage of hospitalization costs								
Private insurance	552/603 (91.5)	51/603 (8.5)	Ref		432/596 (72.5)	164/596 (27.5)	Ref	
Public insurance	454/591 (76.8)	137/591 (23.2)	3.266 (2.313–4.610)	< 0.001	273/591 (46.2)	318/591 (53.8)	3.068 (2.409–3.908)	< 0.001
Type of admission								
Elective	310/317 (97.8)	7/317 (2.2)	Ref		275/316 (87.0)	41/316 (13.0)	Ref	
Emergency	696/877 (77.4)	181/877 (22.6)	11.517 (5.350–24.793)	< 0.001	430/871 (49.4)	441/871 (50.6)	6.879 (4.828–9.801)	< 0.001

Table 3. Unadjusted odds ratios of prognostic factors for mortality and unfavourable outcome among patients requiring neurocritical care. *APACHE II* acute physiology and chronic health evaluation II, *GCS* Glasgow Coma Scale, *Number of Hs* number of secondary injuries (resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation), *Ref.* reference category, *SAPS III* simplified acute physiology score III, *SOFA* sequential organ failure assessment. [a] Categorical variables (sex, number of Hs, coverage of hospitalization costs, type of admission, and number of deaths) are described as absolute frequencies/total number of cases in the row (percentages), and quantitative variables are described as (number of valid cases) mean and standard deviation (age) or median and interquartile range (all other variables). [b] Odds ratio (OR) and 95% confidence interval (95% IC) of the univariate binary logistic regression model. [c] Wald test p value, results < 0.05 indicate statistical significance.

Discussion

The Neurocritical Brazil Study revealed a comprehensive epidemiology of patients requiring neurocritical care and the impact of ICU admission on this patient population. These patients comprised more than one-quarter of all admissions of critically ill patients (28.1%) and had a 1.7 times higher mortality rate than ICU patients not requiring neurocritical care, a finding that was not explained by severity scores. Other studies have also shown increased mortality among patients requiring neurocritical care compared with other ICU patients[17]. The severity scores seem to discriminate to a similar degree the occurrence of severe disease in ICU patients with and without acute neurological disorders, but the reason why patients with acute neurological disorders have worse outcomes than nonneurocritical ones, despite having similar scores, is due to factors not captured in the first hours of ICU admission when the scores are measured, including longer hospital stay and a greater number of complications and nonneurological organ d ysfunctions[18,19].

The Neurocritical Brazil Study provided a better understanding of the epidemiology of patients requiring neurocritical care than we had b efore[20], not only in terms of their overall and relative prevalence but also in terms of how they differ from each other in terms of demographics, clinical severity, use of ICU resources, and outcomes. Since disease burden is a measure of the prevalence and severity of a disease, it is simply not possible to estimate this measure without knowing the epidemiology of the disease[21]. Although the burden of neurological diseases has been better estimated over the past 20 years[22,23], the burden of neurocritical diseases has remained essentially unknown until n ow[24]. This was the main driving force behind the design of this study, as it was critical to first know the epidemiology of patients requiring neurocritical care before estimating their burden of disease[25].

The most common acute neurological condition for ICU admission in this study was elective neurosurgical postoperative care, which had a relatively small impact on DALYs. In contrast, patients with cerebrovascular diseases, encephalopathy, and particularly traumatic brain injury were also frequently admitted to the ICUs and imposed a substantial impact on DALYs. Traumatic brain injury is the acute critical neurological disorder with the worst impact on DALYs because it affects young patients and causes high mortality (25.7%) and a high

Models	Models for ICU mortality			Models for unfavourable outcome (mRS score 4, 5, 6)		
	n	Adjusted OR (95% CI)[a]	p value[b]	n	Adjusted OR (95% CI)[a]	p value[b]
First multivariate model						
Age (years)	1194	1.022 (1.011–1.032)	0.000	1187	1.021 (1.013–1.03)	0.000
Male sex (ref: female)		1.222 (0.84–1.778)	0.295		1.03 (0.766–1.385)	0.846
GCS		0.895 (0.858–0.934)	0.000		0.835 (0.802–0.868)	0.000
Number of Hs (ref: zero Hs)						
One		1.978 (1.11–3.526)	0.021		1.259 (0.879–1.804)	0.209
Two		3.86 (2.179–6.838)	0.000		2.848 (1.889–4.294)	0.000
Three or more		8.663 (4.912–15.278)	0.000		4.761 (2.924–7.751)	0.000
Public health insurance coverage (ref: private)		2.353 (1.505–3.678)	0.000		2.784 (1.993–3.891)	0.000
Emergency admission (ref: elective)		5.77 (2.567–12.971)	0.000		4.359 (2.899–6.554)	0.000
AUC (95% CI)[c]		0.858 (0.832–0.884)	0.000		0.853 (0.832–0.875)	0.000
Second multivariate model						
Male sex (ref: female)	1194	1.184 (0.81–1.73)	0.384	1187	1.011 (0.754–1.356)	0.941
APACHE II score		1.154 (1.126–1.183)	0.000		1.161 (1.134–1.188)	0.000
Public health insurance coverage (ref: private)		2.828 (1.902–4.206)	0.000		3.383 (2.508–4.563)	0.000
Emergency admission (ref: elective)		4.726 (2.111–10.581)	0.000		4.478 (2.993–6.701)	0.000
AUC (95% CI)[c]		0.867 (0.842–0.891)	0.000		0.849 (0.827–0.871)	0.000
Third multivariate model						
Male sex (ref: female)	1159	1.431 (0.985–2.08)	0.060	1152	1.198 (0.893–1.606)	0.229
SAPS III score		1.056 (1.043–1.069)	0.000		1.07 (1.057–1.082)	0.000
Public health insurance coverage (ref: private)		3.457 (2.367–5.051)	0.000		4.851 (3.572–6.589)	0.000
Emergency admission (ref: elective)		5.455 (2.292–12.982)	0.000		3.614 (2.352–5.553)	0.000
AUC (95% CI)[c]		0.823 (0.793–0.853)	0.000		0.834 (0.81–0.857)	0.000
Fourth multivariate model						
Age (years)	1140	1.015 (1.004–1.025)	0.007	1133	1.014 (1.005–1.022)	0.001
Male sex (ref: female)		1.192 (0.811–1.752)	0.371		1.031 (0.765–1.39)	0.842
SOFA score		1.299 (1.236–1.366)	0.000		1.321 (1.258–1.386)	0.000
Public health insurance coverage (ref: private)		2.396 (1.528–3.757)	0.000		3.006 (2.144–4.214)	0.000
Emergency admission (ref: elective)		8.115 (3.277–20.098)	0.000		5.132 (3.372–7.812)	0.000
AUC (95% CI)[c]		0.855 (0.829–0.882)	0.000		0.846 (0.823–0.869)	0.000

Table 4. Adjusted odds ratios of prognostic factors of mortality and unfavourable outcome for patients requiring neurocritical care. *GCS* Glasgow Coma Scale, *ICU* intensive care unit, *mRS score* modified Rankin Scale score, *number of Hs* number of secondary injuries, *n* number of cases considered in the model, *Ref.* reference category. [a] Odds ratio (OR) and 95% confidence interval (95% IC) of the univariate binary logistic regression model; [b] Wald test p value, results < 0.05 indicate statistical significance. [c] The goodness of fit of the multivariate models, given by their explanatory potential, was expressed by the area under the receiver operating characteristic curve (AUC) of the model's predicted probability for the outcome.

incidence of sequelae within 30 days. As shown in the present study, the DALYs vary significantly with the primary acute neurological diagnosis, sex, age range, and secondary injuries. We also demonstrated a clear negative impact of secondary injuries on prognosis. Of note, the increasing number of secondary injuries progressively increases the risk of a worse prognosis[26,27]. When analysed individually, each secondary neurological injury was associated with worse prognosis and increased DALYs. This indicates a clear window of opportunity to control possible secondary injuries during the first hours of the neurological injury, with an enormous beneficial impact on decreasing the burden of acute severe neurological diseases.

Acute neurocritical disorders are known to heavily burden the developing world. Despite the lack of resources for population-based health in most developing countries, there is a growing demand for resource-intensive strategies for acute neurological care[28]. The present study clearly demonstrated that acute neurocritical disorders are common in ICUs and have very high DALYs. Some strategies that could help efficiently reduce the social and economic impact of acute neurocritical disorders include increased prevention of cerebrovascular diseases, greater safety in traffic to reduce the risk of accidents, and emphasis on the prevention of potential secondary injuries to a severe primary brain injury.

Knowing how these different variables interact to exacerbate the risk of acute neurocritical disorders is essential to implement better education and improved political and social actions to minimize their negative

Figure 1. Nonstandardized DALY estimate for patients with acute neurological disorders by (**a**) primary neurological diagnoses; (**b**) age range; (**c**) age range in females; (**d**) age range in males; (**e**) number of secondary injuries (Hs). *IS* ischaemic stroke, *ICH* intracerebral haemorrhage, *SAH* subarachnoid haemorrhage, *ENC* encephalopathy, *TBI* traumatic brain injury, *SCI* spinal cord injury, *SNI* central nervous system infection, *NMD* neuromuscular disease, *NPO* postoperative care of elective neurosurgery.

consequences and improve results and social health. To achieve these paramount objectives, studies providing better information on the epidemiology of critically ill patients and estimating disease burden are just the beginning[29].

All our patients were admitted to ICUs in Brazil, and different results should be expected in other countries, as demonstrated in the PRINCE S tudy[20,30]. In this study, it was observed that the most prevalent diagnosis on admission was subarachnoid haemorrhage, while in our study, it was postoperative elective neurosurgery followed by traumatic brain i njury[20]. Associated factors, such as independent predictors of mortality, including older age, worse Glasgow Coma Scale and admission from the emergency department were also found[20]. However, compared to the epidemiological profile of the participating ICUs, we realized that we have a greater number of large urban centres when compared to other studies and, consequently, a greater number of participating academic institutions[30]. This may have influenced a different profile of neurological disorders attended.

This study has several limitations. First, the sampling of the participating centres was carried out in a nonrandom manner, and only intensive care units that were part of the network of the Brazilian Association of Intensive Care Medicine (AMIBnet) were invited to participate. Second, participation was voluntary and uncompensated, and it is possible that these factors may have affected the number of participating institutions. In addition, it is expected that among those invited, those who agreed to participate are the ICUs of hospitals that have a more developed research structure. This may have generated an overestimation of the results and may limit the generalizability of the results to all ICUs in Brazil since we cannot infer the manner in which neurocritical care is practised in other hospital settings. Third, the data collection was not monitored. We only monitored and verified incongruous data and outliers. Fourth, the sample size was determined by the number of sites and investigators who volunteered to participate and not by statistical calculations. Thus, it is possible that in the present study, the power was underestimated to detect significant differences in several of the collected variables. Fifth, the data collection took place in the mild months of August and September, and seasonal variation may have influenced the results, although these months are a transition period from winter to spring in Brazil, which must have mitigated this influence. Sixth, the follow-up of our patients was limited to 30 days and only during the ICU period; therefore, their conclusions about DALYs are limited.

Furthermore, it is known that recovery in neurocritical emergencies typically occurs over longer periods, which may overestimate YLDs based on the results of this short period among survivors. Since information about disease burden in critically ill patients is still emerging, many challenges remain to be resolved, and the understanding of these patients' long-term outcomes is fundamental for more accurate estimates[31]. Further studies are also needed to determine which interventions and components of the ICU organization will lead to improved patient-centred outcomes[29,31].

However, despite all these limitations, our study has several strengths. The data were collected prospectively, and the participating centres were distributed across the entire Brazilian territory, except for the North region. The study collected data from different sites across the country, which provides important insight into the global organization of neurocritical care delivery in Brazil. Additionally, most sites comprised large academic institutions located in major cities. In addition, the study provides important information about patients as well as participating centres, which enriches and strengthens the manuscript and allows the reader to assess the external validity of our study at their centre.

The collected data leave some questions to be clarified in new studies. The participation of a larger number of nonacademic institutions, including the northern region, would allow us a more complete and detailed view of the profile of the patients requiring neurocritical care in Brazil. Furthermore, understanding the activities and local practice within each participating ICU could assist in training providers to care for patients requiring neurocritical care and emergencies. All these points are of great importance, and in this study, we presented an accurate description of the epidemiology of patients requiring neurocritical care and estimated their overall and relative disease burden. These are important findings to direct policies regarding education, prevention, and treatment of severe acute neurocritical disorders.

Conclusions

We describe a comprehensive epidemiology of patients requiring neurocritical care treated in ICUs in large urban centres in Brazil and their disease burden in the first 30 days after the acute event. Clinical, epidemiological, treatment, ICU outcomes, and DALY characteristics vary greatly with the primary acute neurological disorder. The study has great potential to guide protocols, education and health policies to minimize the adverse impact of this prevalent condition.

Data availability

The datasets generated and/or analysed during the current study are available in the Zenodo repository, https://doi.org/10.5281/zenodo.74291 81.

Received: 3 March 2023; Accepted: 5 October 2023
Published online: 30 October 2023

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Acknowledgements

We are thankful to all the participating centres and the Neurocritical Brazil Study group for the support and interventions in our study during this challenging period for everyone. We would also like to thank Verônica Barros and Marcelo Martins Junior for their support and collaboration.

Author contributions

A.R.N. and R.S.B. had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: A.R.N., M.C.O., A.L.E.F., P.M.P.K. and H.A.G.T. Acquisition of data: P.D.J. and Neurocritical Brazil Study group. Analysis, or interpretation of data: A.R.N., R.S.B. and A.C.K.N. Statistical analysis: R.S.B. Drafting of the manuscript: A.R.N., R.S.B., M.C.O., P.G.D.J., A.C.K.N., A.L.E.F., P.M.P.K. Critical revision of the manuscript for important intellectual content: A.R.N., R.S.B., M.C.O., P.G.D.J., A.C.C.K., A.L.E.F., P.M.P.K., H.A.G.T. and Neurocritical Brazil Study group. Administrative, technical, or material support: Neurocritical Brazil Study group. Supervision: H.A.G.T. All authors have approved the submitted version and agreed to be personally accountable for its own contributions, and the authors ensure that questions related to the accuracy or integrity of any part of the work, even those ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-023-44261-w.

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4.1 SUPPLEMENTARY MATERIAL

Participating enrolment centres and investigators

Listed below are the representatives from the 36 participating intensive care units that enrolled at least one study patient. The centres are listed in order of enrollment contribution. All study sites were located in Brazil. The names of the centres are accompanied by the city and state in which they are located.

Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo. São Paulo, São Paulo.

Fabíola Prior Caltabeloti

Hospital Beneficência Portuguesa de São Paulo. São Paulo, São Paulo.

Salomon Soriano and Viviane Cordeiro Veiga

Hospital Universitário Cajuru. Curitiba, Paraná.

Luana Alves Tannous and Juliano Gasparetto

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José Arthur Santos Brasil

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Glécia Carla Rocha

Hospital Marcelino Champagnat. Curitiba, Paraná.

Jarbas Motta Junior, Bruna Martins Dzivielevski Câmara, and Livia Rodrigues Figueiredo

Hospital Copa D'Or. Rio de Janeiro, Rio de Janeiro.

Fernando Augusto Bozza, Janaína Oliveira, and William Nascimento Vianna

Hospital Municipal de Cuiabá. Cuiabá, Mato Grosso.

Diogo Roberto Lorenzo Iglesias

Hospital Vita Batel. Curitiba, Paraná.

Rafael Alexandre de Oliveira Deucher

Hospital Barra D'Or. Rio de Janeiro, Rio de Janeiro.

Fernando Augusto Bozza and Gloria Martins

Santa Casa de Misericórdia de Passos. Passos, Minas Gerais.

Marcel Resende Lopes

Fundação Hospitalar do Estado de Minas Gerais. Belo Horizonte, Minas Gerais.

Frederico Bruzzi de Carvalho

Hospital de Clínicas da Universidade Estadual de Campinas. Campinas, São Paulo.

Antônio Luis Eiras Falcão

Santa Casa São João Del Rei. São João Del Rei, Minas Gerais.

Jorge Luiz da Rocha Paranhos

Hospital de Amor. Barretos, São Paulo.

Ulysses Vasconcellos de Andrade e Silva

Hospital Caxias D'Or. Rio de Janeiro, Rio de Janeiro.

Fernando Augusto Bozza and Marco Oliveira Py

Hospital do Trabalhador. Curitiba, Paraná.

Mirella Cristine de Oliveira and Fernanda Baeumle Reese

Hospital São Lucas Copacabana. Rio de Janeiro, Rio de Janeiro.

Marcos Freitas Knibel

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Gustavo Cartaxo Patriota

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Suzana Margareth Ajeje Lobo and Mario Roberto Rezende Guimarães Junior

Hospital São Carlos. Fortaleza, Ceará.

Luciana de Oliveira Neves

Hospital HOME. Brasília, Distrito Federal.

Antônio Aurélio Fagundes

Hospital Israelita Albert Einstein. São Paulo, São Paulo.

Ary Serpa Neto

Hospital Novo Atibaia. Atibaia, São Paulo.

Walter Carlos Girardelli Baptista

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Cintia Magalhães Carvalho Grion

Hospital Universitário do Oeste do Paraná. Cascavel, Paraná.

Péricles Almeida Delfino Duarte

Hospital Quinta D'Or. Rio de Janeiro, Rio de Janeiro.

Fernando Augusto Bozza and Bruno Branco

Hospital das Nações. Curitiba, Paraná.

Luísa da Silva André Salgado and Paula David João

Hospital Copa Star, Rio de Janeiro. Rio de Janeiro.

Pedro Martins Pereira Kurtz and Nívea Melo de Souza Costa

Hospital Santa Casa de Curitiba. Curitiba, Paraná.

Danilo Bastos Pompermayer and Anna Flavia Kaled

Hospital de Força Aérea do Galeão. Rio de Janeiro, Rio de Janeiro.

Rafael Brum

Hospital de Clínicas Antônio Paulino – Pronil. Nilópolis, Rio de Janeiro.

Alessandro Rocha Milan de Souza

Hospital do Câncer UOPECCAN – Filial Umuarama. Umuarama, Paraná.

Jackson Erasmo Fuck

Vitoria Apart Hospital. Serra, Espirito Santo.

Claudio Piras

Figure S1: Distribution of participating enrolling centres across Brazil

Midwest
Distrito Federal:
Hospital de Base do Distrito Federal
Hospital HOME
Mato Grosso:
Hospital Municipal de Cuiabá

Northeast
Bahia:
Hospital da Bahia
Ceará:
Hospital São Carlos
Paraíba:
Hospital Estadual de Emergência e Trauma Senador Humberto Lucena

South
Paraná:
Hospital das Nações
Hospital do Trabalhador
Hospital Marcelino Champagnat
Hospital Santa Casa de Curitiba
Hospital Universitário Cajuru
Hospital Vita Batel
Instituto de Neurologia de Curitiba
Hospital Universitário da Universidade Estadual de Londrina
Hospital do Câncer UOPECCAN – Filial Umuarama
Hospital Universitário do Oeste do Paraná

Southeast
São Paulo:
Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo
Hospital Beneficência Portuguesa de São Paulo
Hospital Israelita Albert Einstein
Hospital de Base de Rio Preto
Hospital de Clínicas da Universidade Estadual de Campinas
Hospital de Amor
Hospital Novo Atibaia
Rio de Janeiro:
Hospital Barra D'Or
Hospital Caxias D'Or
Hospital Copa D'Or
Hospital Copa Star
Hospital Quinta D'Or
Instituto Estadual do Cérebro Paulo Niemeyer
Hospital de Força Aérea do Galeão
Hospital São Lucas Copacabana
Hospital de Clínicas Antônio Paulino – Pronil
Minas Gerais:
Fundação Hospitalar do Estado de Minas Gerais,
Santa Casa de Misericórdia de Passos
Santa Casa São João Del Rei, São João Del Rei
Espírito Santo:
Vitoria Apart Hospital

FIGURE S2: Percentage of contribution from each participating centre to the sample of 1194 patients

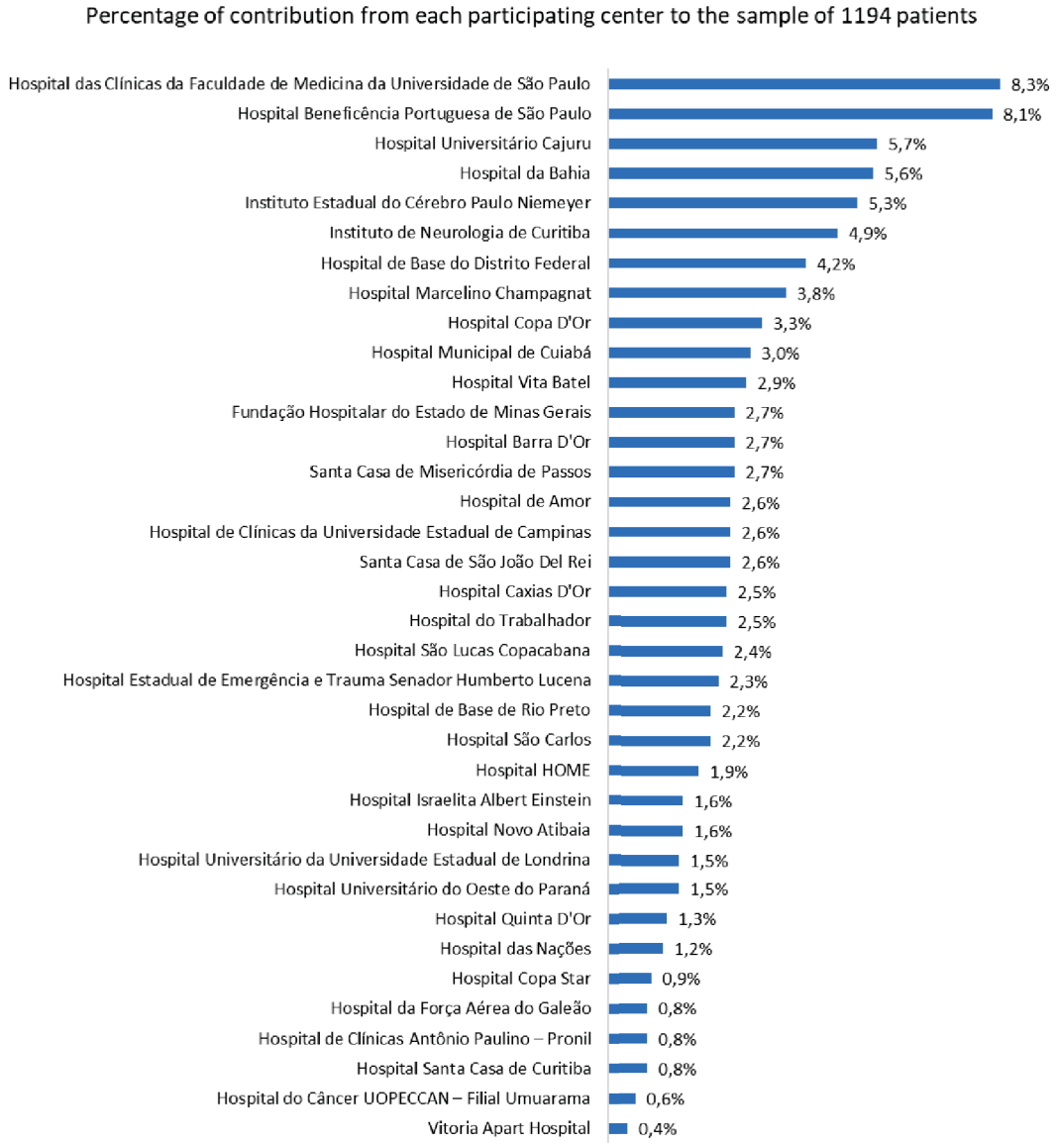
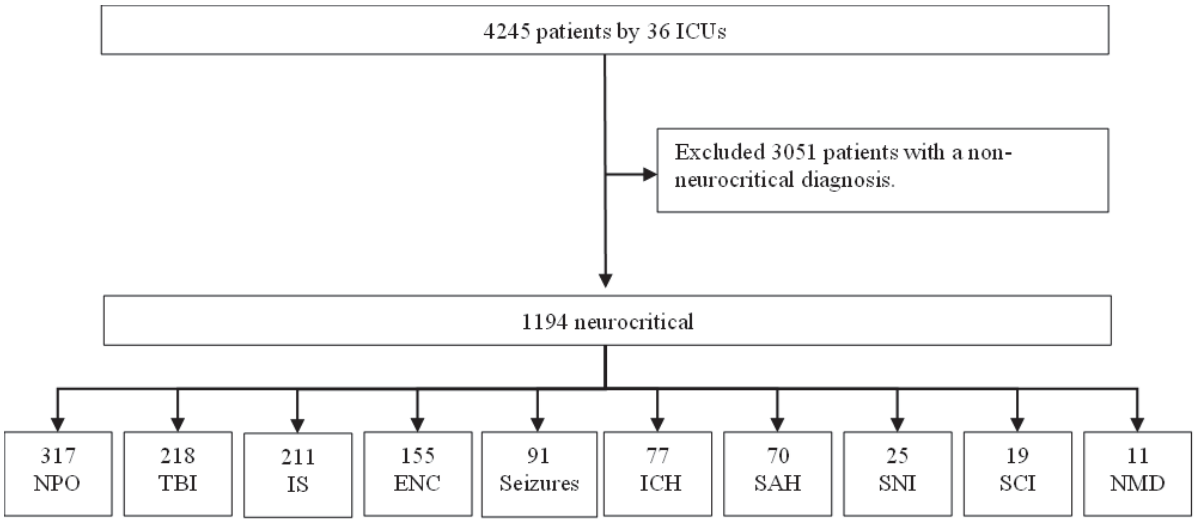
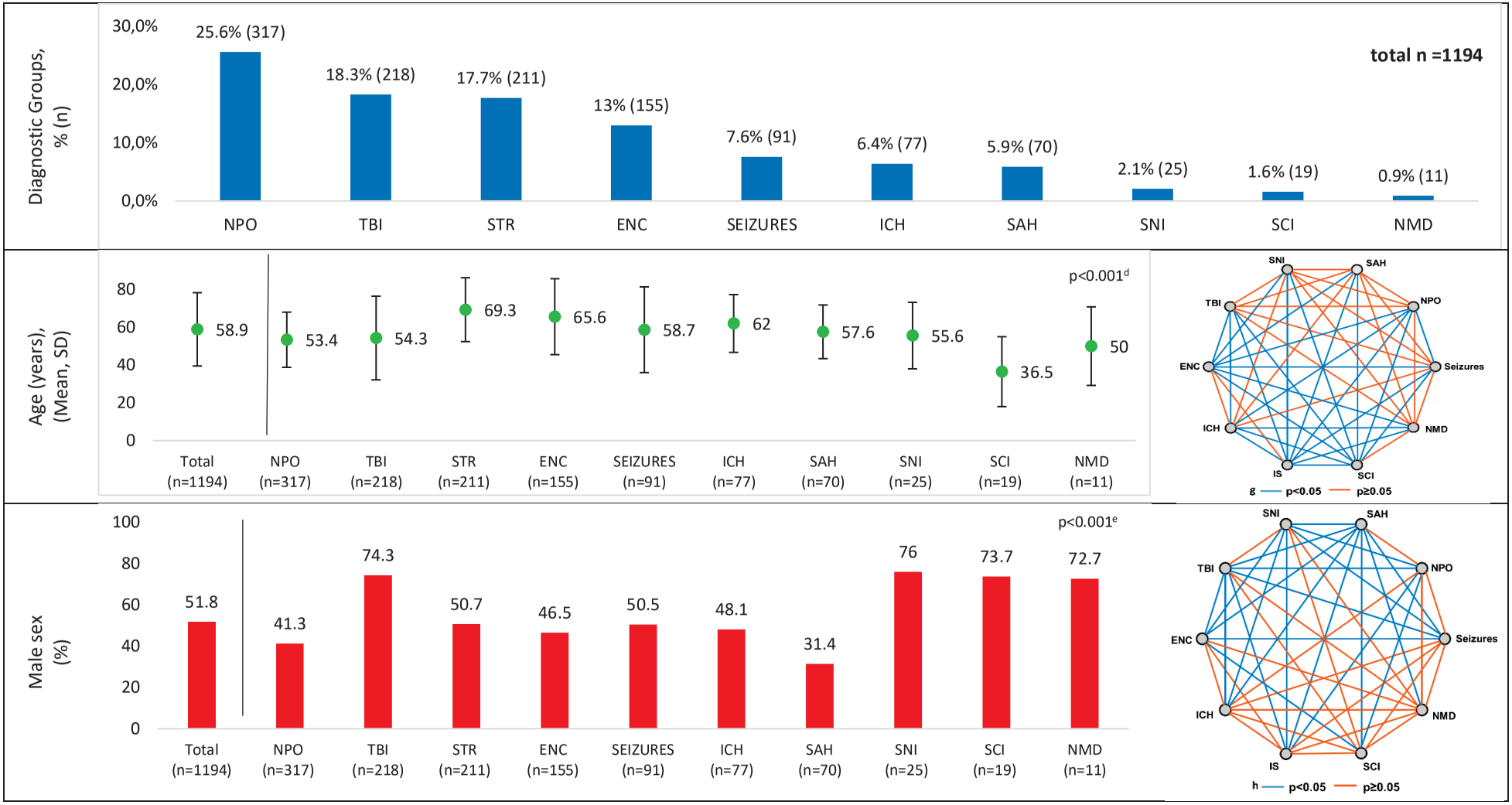


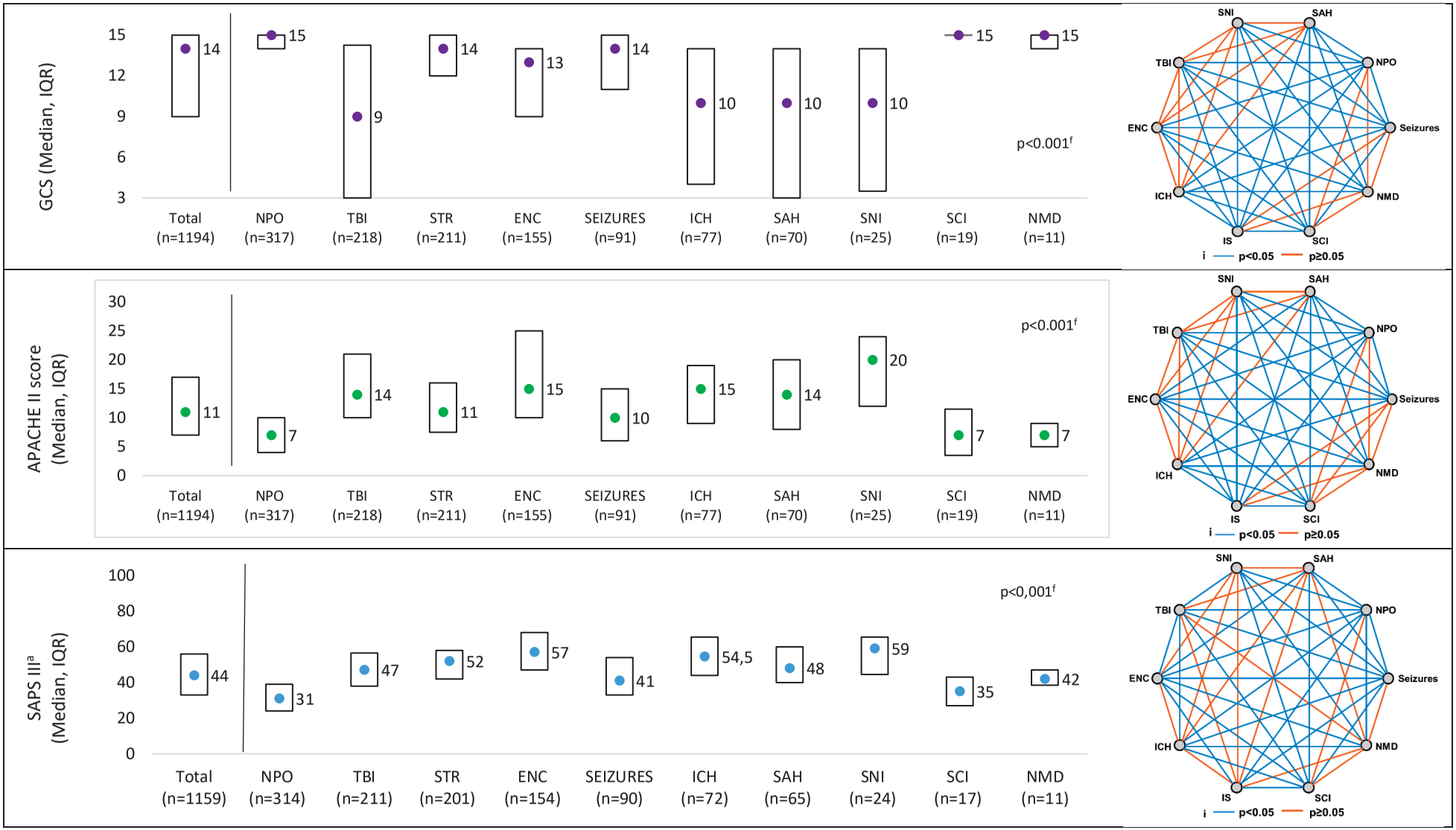
FIGURE S3: Flowchart of study enrolment.

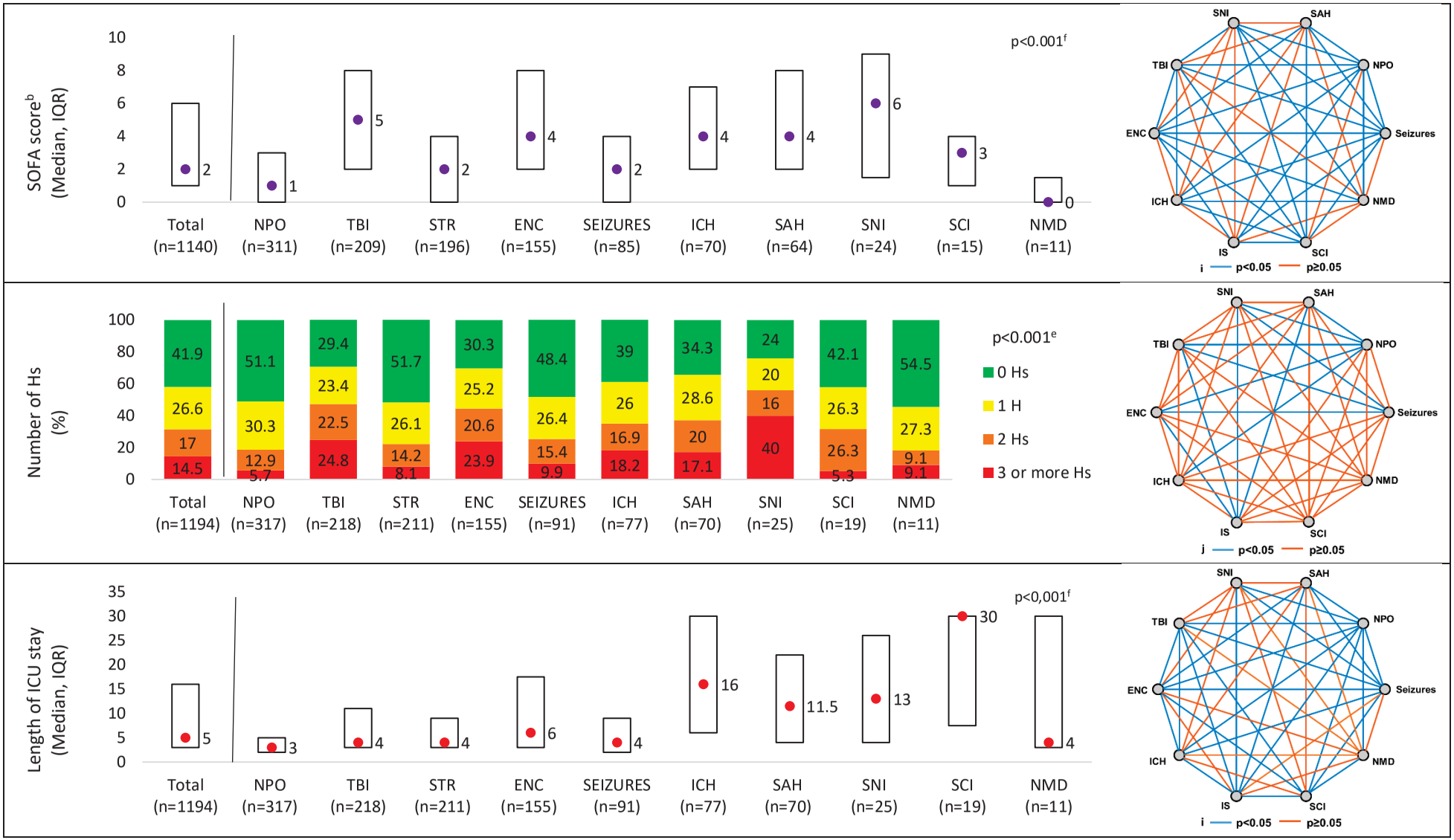


Abbreviations: ICU, intensive care unit; NPO, postoperative care of elective neurosurgery; TBI, traumatic brain injury; IS, ischaemic stroke; ENC, encephalopathy; ICH, intracerebral haemorrhage; SAH, subarachnoid haemorrhage; SNI, central nervous system infection; SCI, spinal cord injury; NMD, neuromuscular disease.

FIGURE S4. Comparison of the characteristics of neurocritical patients admitted to the ICUs in the overall cohort and grouped by 10 neurocritical disorders. The graphs in the right column indicate the results of two-by-two (pairwise) comparisons.




GCS (Median, IQR)
15
12
9
6
3
14
15
9
14
13
14
10
10
10
15
15
p<0.001f
Total (n=1194)
NPO (n=317)
TBI (n=218)
STR (n=211)
ENC (n=155)
SEIZURES (n=91)
ICH (n=77)
SAH (n=70)
SNI (n=25)
SCI (n=19)
NMD (n=11)
SNI
SAH
TBI
NPO
ENC
Seizures
ICH
NMD
IS
SCI
i
p<0.05
p≥0.05
APACHE II score (Median, IQR)
30
25
20
15
10
5
0
11
7
14
11
15
10
15
14
20
7
7
p<0.001f
SAPS III[a] (Median, IQR)
100
80
60
40
20
0
44
31
47
52
57
41
54,5
48
59
35
42
p<0,001f
Total (n=1159)
NPO (n=314)
TBI (n=211)
STR (n=201)
ENC (n=154)
SEIZURES (n=90)
ICH (n=72)
SAH (n=65)
SNI (n=24)
SCI (n=17)
NMD (n=11)


SOFA score[b] (Median, IQR)
p<0.001[f]
Total (n=1140)
NPO (n=311)
TBI (n=209)
STR (n=196)
ENC (n=155)
SEIZURES (n=85)
ICH (n=70)
SAH (n=64)
SNI (n=24)
SCI (n=15)
NMD (n=11)
Number of Hs (%)
p<0.001[e]
0 Hs
1 H
2 Hs
3 or more Hs
Total (n=1194)
NPO (n=317)
TBI (n=218)
STR (n=211)
ENC (n=155)
SEIZURES (n=91)
ICH (n=77)
SAH (n=70)
SNI (n=25)
SCI (n=19)
NMD (n=11)
Length of ICU stay (Median, IQR)
p<0,001[f]
SNI
SAH
TBI
NPO
ENC
Seizures
ICH
NMD
IS
SCI
i p<0.05 p≥0.05
j p<0.05 p≥0.05

Abbreviations: NPO, postoperative care of elective neurosurgery; TBI, traumatic brain injury; IS, ischaemic stroke; ENC, encephalopathy; ICH, intracerebral haemorrhage; SAH, subarachnoid haemorrhage; SNI, central nervous system infection; SCI, spinal cord injury; NMD, neuromuscular disease; GCS, Glasgow

Coma Scale; APACHE II, Acute Physiology and Chronic Health Evaluation; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; m-RS, modified Rankin Scale; n, absolute frequency; %, percentage within column; IQR, interquartile range; SD, standard deviation.

[a] 35 missing data on SAPS III score; [b]54 missing data on SOFA score; [c]7 missing data on m-RS and on Unfavourable outcome.

[d] Significance level, one-way analysis of variance (ANOVA), $p<0.05$.

[e] Significance level, chi-square test, $p<0.05$.

[f] Significance level, Kruskal-Wallis test, $p<0.05$.

[g] Significance level, least significant difference LSD *post hoc* test, $p<0.05$.

[h] Significance level, Fisher's exact test, $p<0.05$.

[i] Significance level, Dunn's *post hoc* test, $p<0.05$.

[j] Significance level, chi-square's test, $p<0.05$.

TABLE S1: Overall admissions to the intensive care units and comparisons between patients with neurocritical and non-neurocritical primary diagnoses.

ICU admissions	Number of ICUs	All patients	Neurocritical patients	Non-neurocritical patients	p value
New ICU admissions in the study period, median (IQR)	30	98 (55–161)	31 (18–39)	70 (23–149)	0.013[a]
ICU mortality rate, mean ± SD	30	12.8 ± 8.9	17.2 ± 12.6	10.1 ± 8.7	0.038[b]
Mean SAPS III in the study period, mean ± SD	20	46.5 ± 7.5	46.9 ± 4.5	46.2 ± 12.7	0.800 [b]

Abbreviations: ICU, intensive care unit; IQR, interquartile range; SD, standard deviation, SAPS III, Simplified Acute Physiology Score

[a] Significance of Mann-Whitney test.

[b] Significance of independent Student *t* test.

TABLE S2: Additional information of baseline characteristics of the patients, procedures performed during stay in the intensive care unit, complications, and outcomes in the overall cohort and in each of the 10 neurocritical diagnoses.

Variables	Total (n=1194)	NPO (n=317)	TBI (n=218)	IS (n=211)	ENC (n=155)	Seizures (n=91)	ICH (n=77)	SAH (n=70)	SNI (n=25)	SCI (n=19)	NMD (n=11)	p value
HOSPITALIZATION DATA												
Ethnicity[c], n (%)												
White	818 (70.2)	220 (69.8)	1450 (72.5)	147 (70)	115 (74.7)	72 (79.1)	43 (55.8)	41 (60.3)	17 (68)	10 (71.4)	8 (72.7)	
Black	96 (8.2)	24 (7.6)	110 (5.5)	21 (10)	11 (7.1)	3 (3.3)	13 (16.9)	7 (10.3)	4 (16)	0 (0)	2 (18.2)	
Mulatto	26 (2.2)	5 (1.6)	70 (3.5)	5 (2.4)	1 (0.6)	1 (1.1)	3 (3.9)	3 (4.4)	1 (4)	0 (0)	0 (0)	0.051[a]
Brown	188 (16.1)	48 (15.2)	330 (16.5)	31 (14.8)	26 (16.9)	10 (11)	16 (20.8)	16 (23.5)	3 (12)	4 (28.6)	1 (9.1)	
Indigenous	2 (0.2)	0 (0)	00 (0)	1 (0.5)	0 (0)	0 (0)	1 (1.3)	0 (0)	0 (0)	0 (0)	0 (0)	
Other	35 (3)	18 (5.7)	40 (2)	5 (2.4)	1 (0.6)	5 (5.5)	1 (1.3)	1 (1.5)	0 (0)	0 (0)	0 (0)	
Transportation to the hospital[d], n (%)												
Critical care ambulance	376 (31.5)	7 (2.2)	134 (61.8)	47 (22.3)	46 (29.7)	20 (22)	45 (58.4)	50 (71.4)	11 (44)	15 (78.9)	1 (9.1)	
Ambulance without critical care service	91 (7.6)	15 (4.7)	20 (9.2)	15 (7.1)	14 (9)	6 (6.6)	8 (10.4)	8 (11.4)	1 (4)	1 (5.3)	3 (27.3)	<0.001[a]
Family members	355 (29.8)	100 (31.6)	37 (17.1)	89 (42.2)	56 (36.1)	37 (40.7)	17 (22.1)	6 (8.6)	7 (28)	3 (15.8)	3 (27.3)	
Self-driven	370 (31)	194 (61.4)	26 (12)	60 (28.4)	39 (25.2)	28 (30.8)	7 (9.1)	6 (8.6)	6 (24)	0 (0)	4 (36.4)	
Source of coverage of hospital costs, n (%)												
Complementary or private health insurance	603 (50.5)	141 (44.5)	66 (30.3)	167 (79.1)	89 (57.4)	79 (86.8)	25 (32.5)	12 (17.1)	14 (56)	2 (10.5)	8 (72.7)	<0.001[a]
Public health insurance (SUS)	591 (49.5)	176 (55.5)	152 (69.7)	44 (20.9)	66 (42.6)	12 (13.2)	52 (67.5)	58 (82.9)	11 (44)	17 (89.5)	3 (27.3)	
Location before transfer to the ICU, n (%)												
Emergency department	567 (47.5)	16 (5)	121 (55.5)	165 (78.2)	94 (60.6)	67 (73.6)	46 (59.7)	28 (40)	15 (60)	9 (47.4)	6 (54.5)	<0.001[a]
Operating room	428 (35.8)	281 (88.6)	73 (33.5)	13 (6.2)	14 (9)	4 (4.4)	15 (19.5)	19 (27.1)	2 (8)	7 (36.8)	0 (0)	
Hospital ward	81 (6.8)	15 (4.7)	5 (2.3)	12 (5.7)	24 (15.5)	13 (14.3)	3 (3.9)	1 (1.4)	3 (12)	1 (5.3)	4 (36.4)	

Other	118 (9.9)	5 (1.6)	19 (8.7)	21 (10)	23 (14.8)	7 (7.7)	13 (16.9)	22 (31.4)	5 (20)	2 (10.5)	1 (9.1)	
Comorbidities												
Hypertension, n (%)	603 (50.5)	134 (42.3)	75 (34.4)	158 (74.9)	79 (51)	37 (40.7)	56 (72.7)	46 (65.7)	10 (40)	5 (26.3)	3 (27.3)	<0.001[a]
Cardiopathy, n (%)	177 (14.8)	22 (6.9)	27 (12.4)	65 (30.8)	39 (25.2)	13 (14.3)	6 (7.8)	0 (0)	2 (8)	0 (0)	3 (27.3)	<0.001[a]
Chronic obstructive pulmonary disease, n (%)	51 (4.3)	14 (4.4)	6 (2.8)	13 (6.2)	7 (4.5)	4 (4.4)	1 (1.3)	4 (5.7)	2 (8)	0 (0)	0 (0)	0.608[a]
Renal disease, n (%)	83 (7)	15 (4.7)	11 (5)	20 (9.5)	20 (12.9)	7 (7.7)	5 (6.5)	2 (2.9)	3 (12)	0 (0)	0 (0)	0.023[a]
Diabetes, n (%)	218 (18.3)	55 (17.4)	24 (11)	74 (35.1)	27 (17.4)	14 (15.4)	13 (16.9)	6 (8.6)	1 (4)	2 (10.5)	2 (18.2)	<0.001[a]
Extracranial neoplasia, n (%)	89 (7.5)	32 (10.1)	9 (4.1)	9 (4.3)	22 (14.2)	10 (11)	3 (3.9)	0 (0)	3 (12)	0 (0)	1 (9.1)	0.001[a]
STATUS AT ADMISSION												
Hypotension, n (%)	267 (22.4)	57 (18)	56 (25.7)	32 (15.2)	61 (39.4)	17 (18.7)	19 (24.7)	14 (20)	7 (28)	4 (21.1)	0 (0)	<0.001[a]
Hypoxemia, n (%)	72 (6)	7 (2.2)	17 (7.8)	12 (5.7)	14 (9)	3 (3.3)	7 (9.1)	8 (11.4)	2 (8)	0 (0)	2 (18.2)	0.008[a]
Hyperthermia, n (%)	126 (10.6)	21 (6.6)	32 (14.7)	17 (8.1)	19 (12.3)	10 (11)	8 (10.4)	5 (7.1)	11 (44)	3 (15.8)	0 (0)	<0.001[a]
Hypercapnia, n (%)	115 (9.6)	14 (4.4)	46 (21.1)	8 (3.8)	17 (11)	7 (7.7)	4 (5.2)	11 (15.7)	2 (8)	4 (21.1)	2 (18.2)	<0.001[a]
Hypocapnia, n (%)	231 (19.3)	44 (13.9)	48 (22)	34 (16.1)	39 (25.2)	15 (16.5)	17 (22.1)	21 (30)	10 (40)	2 (10.5)	1 (9.1)	0.002[a]
Hypoglycaemia, n (%)	32 (2.7)	2 (0.6)	12 (5.5)	6 (2.8)	6 (3.9)	1 (1.1)	0 (0)	2 (2.9)	1 (4)	0 (0)	2 (18.2)	0.002[a]
Hyponatremia, n (%)	200 (16.8)	53 (16.7)	24 (11)	36 (17.1)	34 (21.9)	24 (26.4)	11 (14.3)	7 (10)	7 (28)	4 (21.1)	0 (0)	0.010[a]
Hypothermia, n (%)	121 (10.1)	20 (6.3)	32 (14.7)	13 (6.2)	27 (17.4)	3 (3.3)	8 (10.4)	13 (18.6)	4 (16)	1 (5.3)	0 (0)	<0.001[a]
Intracranial hypertension, n (%)	89 (7.5)	11 (3.5)	44 (20.2)	8 (3.8)	4 (2.6)	1 (1.1)	10 (13)	10 (14.3)	1 (4)	0 (0)	0 (0)	<0.001[a]
Clinical evidence of herniation, n (%)	77 (6.4)	7 (2.2)	38 (17.4)	8 (3.8)	6 (3.9)	0 (0)	11 (14.3)	5 (7.1)	1 (4)	0 (0)	1 (9.1)	<0.001[a]
Imaging tests performed within 24h from admission												
Computed tomography of the head , n (%)	931 (78)	195 (61.5)	194 (89)	195 (92.4)	97 (62.6)	83 (91.2)	65 (84.4)	58 (82.9)	21 (84)	19 (100)	4 (36.4)	<0.001[a]
Magnetic resonance of the head, n (%)	208 (17.4)	46 (14.5)	9 (4.1)	85 (40.3)	16 (10.3)	23 (25.3)	6 (7.8)	5 (7.1)	10 (40)	3 (15.8)	5 (45.5)	<0.001[a]
Cerebral arteriogram, n (%)	87 (7.3)	17 (5.4)	4 (1.8)	24 (11.4)	8 (5.2)	4 (4.4)	4 (5.2)	25 (35.7)	1 (4)	0 (0)	0 (0)	<0.001[a]

PROGRESSION DATA												
REQUIRED PROCEDURES												
Emergency neurosurgery, n (%)	199 (16.7)	18 (5.7)	81 (37.2)	14 (6.6)	7 (4.5)	4 (4.4)	34 (44.2)	30 (42.9)	4 (16)	6 (31.6)	1 (9.1)	<0.001[a]
Placement of external ventricular drain, n (%)	84 (7)	11 (3.5)	21 (9.6)	6 (2.8)	5 (3.2)	2 (2.2)	21 (27.3)	17 (24.3)	1 (4)	0 (0)	0 (0)	<0.001[a]
Invasive mechanical ventilation, n (%)	460 (38.5)	53 (16.7)	139 (63.8)	55 (26.1)	65 (41.9)	24 (26.4)	50 (64.9)	45 (64.3)	14 (56)	12 (63.2)	3 (27.3)	<0.001[a]
Tracheostomy – n (%) of patients placed on invasive mechanical ventilation	146 (31.7)	7 (13.2)	43 (30.9)	18 (32.7)	22 (33.8)	5 (20.8)	23 (46)	15 (33.3)	4 (28.6)	7 (58.3)	2 (66.7)	0.016[a]
Noninvasive ventilation, n (%)	77 (6.4)	10 (3.2)	16 (7.3)	13 (6.2)	17 (11)	7 (7.7)	5 (6.5)	6 (8.6)	0 (0)	1 (5.3)	2 (18.2)	0.062[a]
VAD, n (%)	411 (34.4)	52 (16.4)	109 (50)	55 (26.1)	61 (39.4)	13 (14.3)	49 (63.6)	49 (70)	12 (48)	10 (52.6)	1 (9.1)	<0.001[a]
Vasopressor, n (%) of all the patients who received VAD	358 (87.1)	39 (75)	106 (97.2)	42 (76.4)	60 (98.4)	12 (92.3)	35 (71.4)	41 (83.7)	12 (100)	10 (100)	1 (100)	<0.001[a]
Vasodilator, n (%) of all the patients who received VAD	82 (20)	15 (28.8)	7 (6.4)	16 (29.1)	6 (9.8)	2 (15.4)	22 (44.9)	13 (26.5)	1 (8.3)	0 (0)	0 (0)	<0.001[a]
Dialysis, n (%)	65 (5.4)	2 (0.6)	15 (6.9)	8 (3.8)	17 (11)	4 (4.4)	9 (11.7)	3 (4.3)	6 (24)	1 (5.3)	0 (0)	<0.001[a]
ICP monitoring, n (%)	96 (8)	19 (6)	39 (17.9)	5 (2.4)	2 (1.3)	1 (1.1)	15 (19.5)	14 (20)	1 (4)	0 (0)	0 (0)	<0.001[a]
Intraparenchymal, n (%) of all the patients who underwent ICP monitoring	55 (57.3)	14 (73.7)	30 (76.9)	3 (60)	0 (0)	0 (0)	5 (33.3)	2 (14.3)	1 (100)	0 (0)	0 (0)	<0.001[a]
Intraventricular, n (%) of all the patients who underwent ICP monitoring	40 (41.7)	5 (26.3)	8 (20.5)	2 (40)	1 (50)	1 (100)	10 (66.7)	12 (85.7)	1 (100)	0 (0)	0 (0)	<0.001[a]
Other monitoring measures, n (%)	121 (10.1)	7 (2.2)	24 (11)	28 (13.3)	7 (4.5)	32 (35.2)	9 (11.7)	12 (17.1)	2 (8)	0 (0)	0 (0)	<0.001[a]
EEG, n (%) of all the patients who received other monitoring measures	102 (84.3)	6 (85.7)	16 (66.7)	25 (89.3)	7 (100)	32 (100)	9 (100)	5 (41.7)	2 (100)	0 (0)	0 (0)	<0.001[a]
Intracranial Doppler, n (%) of all the patients who received other monitoring measures	4 (3.3)	2 (28.6)	1 (4.2)	0 (0)	0 (0)	0 (0)	1 (11.1)	0 (0)	0 (0)	0 (0)	0 (0)	<0.001[a]

$PtiO_2$, n (%) of all the patients who received other monitoring measures	37 (30.6)	3 (42.9)	12 (50)	6 (21.4)	0 (0)	3 (9.4)	2 (22.2)	11 (91.7)	0 (0)	0 (0)	0 (0)	0.010[a]
Developed infection, n (%)	292 (24.5)	19 (6)	83 (38.1)	52 (24.6)	41 (26.5)	15 (16.5)	34 (44.2)	24 (34.3)	12 (48)	11 (57.9)	1 (9.1)	<0.001[a]
Pneumonia, n (%) of all the patients who developed infection	203 (69.3)	11 (57.9)	62 (74.7)	36 (67.9)	29 (70.7)	8 (53.3)	25 (73.5)	20 (83.3)	6 (50)	6 (54.5)	0 (0)	0.204[a]
Urinary infection, n (%) of all the patients who developed infection	43 (14.7)	4 (21.1)	8 (9.6)	13 (24.5)	7 (17.1)	4 (26.7)	3 (8.8)	1 (4.2)	2 (16.7)	1 (9.1)	0 (0)	0.222[a]
Catheter-related infection, n (%) of all the patients who developed infection	35 (11.9)	2 (10.5)	12 (14.5)	2 (3.8)	2 (4.9)	2 (13.3)	8 (23.5)	1 (4.2)	4 (33.3)	2 (18.2)	0 (0)	0.043[a]
Primary bacterial infection, n (%) of all the patients who developed infection	27 (9.2)	0 (0)	8 (9.6)	5 (9.4)	4 (9.8)	4 (26.7)	3 (8.8)	1 (4.2)	1 (8.3)	1 (9.1)	0 (0)	0.507[a]
Neurological infection, n (%) of all the patients who developed infection	23 (7.8)	5 (26.3)	4 (4.8)	1 (1.9)	1 (2.4)	1 (6.7)	1 (2.9)	2 (8.3)	7 (58.3)	1 (9.1)	0 (0)	<0.001[a]
Surgical wound infection, n (%) of all the patients who developed infection	15 (5.1)	1 (5.3)	2 (2.4)	5 (9.4)	2 (4.9)	0 (0)	1 (2.9)	2 (8.3)	0 (0)	1 (9.1)	1 (100)	0.004[a]
Clostridium associated diarrhea, n (%) of all the patients who developed infection	2 (0.7)	0 (0)	0 (0)	0 (0)	0 (0)	2 (13.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	<0.001[a]
Renal failure, n (%)	100 (8.4)	3 (0.9)	22 (10.1)	16 (7.6)	26 (16.8)	4 (4.4)	16 (20.8)	6 (8.6)	5 (20)	2 (10.5)	0 (0)	<0.001[a]
Acute respiratory distress syndrome, n (%)	38 (3.2)	4 (1.3)	14 (6.4)	3 (1.4)	3 (1.9)	2 (2.2)	3 (3.9)	3 (4.3)	2 (8)	4 (21.1)	0 (0)	<0.001[a]
Gastrointestinal bleeding, n (%)	15 (1.3)	1 (0.3)	3 (1.4)	2 (0.9)	3 (1.9)	2 (2.2)	1 (1.3)	1 (1.4)	1 (4)	0 (0)	1 (9.1)	0.283[a]
IH, n (%)	129 (10.8)	14 (4.4)	56 (25.7)	8 (3.8)	6 (3.9)	2 (2.2)	21 (27.3)	19 (27.1)	3 (12)	0 (0)	0 (0)	<0.001[a]
Intraparenchymal monitoring in IH, n (%) of all patients who underwent IH	30 (23.3)	8 (57.1)	14 (25)	1 (12.5)	1 (16.7)	0 (0)	4 (19)	2 (10.5)	0 (0)	0 (0)	0 (0)	0.067[a]

IH treatment with mannitol, n (%) of all patients who underwent IH	82 (63.6)	12 (85.7)	32 (57.1)	4 (50)	3 (50)	1 (50)	14 (66.7)	15 (78.9)	1 (33.3)	0 (0)	0 (0)	0.295[a]
IH treatment with decompressive craniectomy, n (%) of all patients who underwent IH	41 (31.8)	5 (35.7)	19 (33.9)	5 (62.5)	0 (0)	0 (0)	7 (33.3)	4 (21.1)	1 (33.3)	0 (0)	0 (0)	0.294[a]
IH treatment with external ventricular drainage, n (%) of all patients who underwent IH	46 (35.7)	5 (35.7)	13 (23.2)	1 (12.5)	2 (33.3)	1 (50)	13 (61.9)	10 (52.6)	1 (33.3)	0 (0)	0 (0)	0.042[a]
IH treatment with surgical drainage, n (%) of all patients who underwent IH	71 (55)	6 (42.9)	39 (69.6)	0 (0)	2 (33.3)	0 (0)	15 (71.4)	7 (36.8)	2 (66.7)	0 (0)	0 (0)	0.001[a]
IH treatment with barbiturate coma therapy, n (%) of all patients who underwent IH	10 (7.8)	1 (7.1)	5 (8.9)	1 (12.5)	0 (0)	1 (50)	1 (4.8)	1 (5.3)	0 (0)	0 (0)	0 (0)	0.478[a]
OUTCOME												
Length of ICU stay until 30th day among survivors[e], median (IQR)	4 (2-9)	3 (1-5)	8 (3-18)	4 (2-8)	5 (3-12)	3.5 (2-6)	8.5 (5-19)	9 (4-14)	4 (3-14)	7 (5-10)	4 (2-4)	<0.001[b]
Length of ICU stay until 30th day among the deceased[f], median (IQR)	8.5 (4-15)	6 (5-18)	8 (3-13.5)	9 (4.5-13.5)	5 (2-15)	11 (9.5-12)	9.5 (4-18)	8.5 (4-14)	13 (11-23)	No deaths until 30th day	No deaths until 30th day	0.250[b]
30-day outcome, n (%)												
Discharge	832 (69.7)	300 (94.6)	113 (51.8)	166 (78.7)	92 (59.4)	75 (82.4)	30 (39)	30 (42.9)	10 (40)	9 (47.4)	7 (63.6)	<0.001[a]
Transference	22 (1.8)	0 (0)	5 (2.3)	3 (1.4)	4 (2.6)	3 (3.3)	2 (2.6)	4 (5.7)	1 (4)	0 (0)	0 (0)	
Death without limitation of life support	117 (9.8)	6 (1.9)	32 (14.7)	15 (7.1)	20 (12.9)	3 (3.3)	15 (19.5)	18 (25.7)	7 (28)	1 (5.3)	0 (0)	
Death with limitation of life support	71 (5.9)	1 (0.3)	24 (11)	9 (4.3)	21 (13.5)	1 (1.1)	7 (9.1)	6 (8.6)	2 (8)	0 (0)	0 (0)	
Continued hospitalization (patient room)	75 (6.3)	5 (1.6)	23 (10.6)	10 (4.7)	8 (5.2)	5 (5.5)	11 (14.3)	5 (7.1)	3 (12)	2 (10.5)	3 (27.3)	
Continued ICU hospitalization	77 (6.4)	5 (1.6)	21 (9.6)	8 (3.8)	10 (6.5)	4 (4.4)	12 (15.6)	7 (10)	2 (8)	7 (36.8)	1 (9.1)	
Cause of death												

Death due to neurological cause[f], n (%) of the total deaths	100 (53.2)	6 (85.7)	38 (67.9)	10 (41.7)	7 (17.1)	2 (50)	14 (63.6)	20 (83.3)	3 (33.3)	0 (0)	0 (0)	<0.001[a]
Brain death protocol[h], n (%) of the total deaths due to neurological cause	48 (48)	3 (50)	27 (71.1)	2 (20)	2 (28.6)	0 (0)	4 (28.6)	9 (45)	1 (33.3)	0 (0)	0 (0)	0.020[a]

Abbreviations: NPO, postoperative care of elective neurosurgery; TBI, traumatic brain injury; IS, ischaemic stroke; ENC, encephalopathy; ICH, intracerebral haemorrhage; SAH, subarachnoid haemorrhage; SNI, central nervous system infection; SCI, spinal cord injury; NMD, neuromuscular disease; ICU, intensive care unit; SUS, Brazilian Unified Health System; VAD, vasoactive drug, ICP, intracranial pressure; EEG, electroencephalogram; $PtiO_2$, brain tissue oxygen pressure; IH, intracranial hypertension; m-RS, modified Rankin scale score; n, absolute frequency; %, percentage within column; IQR, interquartile range; SD, standard deviation.

[a] Significance of the chi-square test.

[b] Significance of the Kruskal-Wallis test.

[c] Missing data on Ethnicity: 29 on Total; 2 on NPO, 18 on TBI, 1 on IS, 1 on ENC, 2 on SAH and 5 on SCI.

[d] Missing data on transportation to the hospital: 2 on Total; 1 on NPO, 1 on TBI.

[e] Considering only those discharged from the ICU, which are: 832 on Total, 300 on NPO, 113 on TBI, 166 on IS, 92 on ENC, 75 on Seizures, 30 on ICH, 30 on SAH, 10 on SNI, 9 on SCI, and 7 on NMD.

[f] Considering only those who died in the ICU until 30th day, which are: 187 on Total, 7 on NPO, 56 on TBI, 24 on IS, 41 on ENC, 4 on Seizures, 22 on ICH, 24 on SAH, 9 on SNI, 0 on SCI, and 0 on NMD.

[g] Considering only deaths due to neurological cause until 30th day, which are: 100 on Total, 6 on NPO, 38 on TBI, 10 on IS, 7 on ENC, 2 on Seizures, 14 on ICH, 20 on SAH, 3 on SNI, 0 on SCI, and 0 on NMD.

TABLE S3: Unadjusted odds ratios of prognostic factors for mortality and unfavourable outcome in the diagnostic group of **postoperative care of elective neurosurgery** in neurocritical patients admitted to intensive care units.

Factors	**ICU discharge[a]**	**Death on ICU[a]**	**Unadjusted OR (95% CI) for ICU Mortality[b]**	**p value[c]**	**Favourable outcome (m-RS score 1, 2, or 3)[a]**	**Unfavourable outcome (m-RS score 4, 5, or 6)[a]**	**Unadjusted OR (95% CI) for Unfavourable outcome[b]**	**p value[c]**
Age (years)	(n=310) 53.4 ± 14.7	(n=7) 56.6 ± 11.4	1.015 (0.964–1.069)	0.566	(n=275) 52.7 ± 14.5	(n=41) 57.8 ± 15	1.024 (1.001–1.048)	0.040
Sex								
Female	182/186 (97.8)	4/186 (2.2)	Ref.		134/141 (100)	7/141 (0)	Ref.	
Male	128/131 (97.7)	3/131 (2.3)	1.066 (0.235–4.846)	0.934	169/176 (93)	7/176 (7)	1.599 (0.828–3.089)	0.162
Glasgow Coma Scale	(n=310) 15 (14–15)	(n=7) 14 (7–15)	0.826 (0.702–0.971)	0.021	(n=275) 15 (14–15)	(n=41) 15 (12–15)	0.889 (0.805–0.982)	0.020
APACHE II	(n=310) 7 (4–10)	(n=7) 13 (9–17)	1.196 (1.062–1.347)	0.003	(n=275) 7 (4–10)	(n=41) 10 (6–14)	1.106 (1.041–1.176)	0.001
SAPS III	(n=308) 31.0 (24–39)	(n=6) 40.5 (32–68)	1.087 (1.03–1.148)	0.002	(n=274) 30 (24–37)	(n=39) 34 (31–46)	1.054 (1.025–1.083)	0.000
SOFA	(n=305) 1 (0–2)	(n=6) 5 (1–8)	1.193 (1.024–1.39)	0.024	(n=271) 1 (0–2)	(n=39) 3 (0–5)	1.163 (1.052–1.284)	0.003
Number of Hs								
Zero	160/162 (98.8)	2/162 (1.2)	Ref.		134/141 (100)	7/141 (0)	Ref.	
One	95/96 (99)	1/96 (1)	0.842 (0.075–9.412)	0.889	169/176 (93)	7/176 (7)	1.186 (0.487–2.888)	0.708
Two	40/41 (97.6)	1/41 (2.4)	2 (0.177–22.612)	0.575	134/141 (100)	7/141 (0)	3.821 (1.533–9.519)	0.004
Three or more	15/18 (83.3)	3/18 (16.7)	16 (2.476–103.381)	0.004	169/176 (93)	7/176 (7)	11.462 (3.877–33.884)	0.000
Coverage of hospitalization costs								
Private insurance	134/141 (100)	7/141 (0)			133/140 (95)	7/140 (5)	Ref.	
Public insurance	169/176 (93)	7/176 (7)	N/A	N/A	142/176 (80.7)	34/176 (19.3)	4.549 (1.95–10.614)	0.000

[a] Categorical variables are described as the absolute number of deaths (percentage of deaths by the total number of cases in the line); age is described as mean ± standard deviation, and the other quantitative variables are described as median (first quartile – third quartile).
[b] Odds ratios and 95% confidence intervals of the univariate binary logistic regression model.
[c] Wald test p value, $p < 0.05$ indicate statistical significance.
Abbreviations: ICU, intensive care unit; m-RS, modified Ranking scale score; OR, odds ratio; ref., reference; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation; N/A, not analysed.

TABLE S4: Adjusted odds ratios of prognostic factors for mortality and unfavourable outcome in the diagnostic group of **postoperative care of elective neurosurgery** in neurocritical patients admitted to intensive care units.

Factors	**Models for ICU mortality**		**Models for Unfavourable outcome (m-RS 4, 5, or 6)**	
First multivariate model	**Adjusted OR (95% CI)[b]**	**p value [c]**	**Adjusted OR (95% CI)[b]**	**p value [c]**
Age (years)	1.021 (0.96–1.087)	0.510	1.033 (1.006–1.06)	0.014
Male sex (ref. female)	1.262 (0.245–6.505)	0.781	2.067 (0.985–4.339)	0.055
Glasgow Coma Scale	0.864 (0.708–1.054)	0.150	0.919 (0.816–1.034)	0.161
Number of Hs (ref. zero Hs)				
One	0.638 (0.055–7.425)	0.719	0.963 (0.382–2.429)	0.936
Two	1.549 (0.132–18.15)	0.727	3.5 (1.343–9.122)	0.010
Three or more	6.649 (0.852–51.859)	0.071	7.229 (2.202–23.734)	0.001
Public health insurance coverage (ref. private)			5.087 (2.026–12.775)	0.001
N included in the model[a]	317		316	
AUC (95% CI) [d]	0.924 (0.861–0.987)	0.000	0.800 (0.731–0.87)	0.000
Second multivariate model	**Adjusted OR (95% CI)[b]**	**p value [c]**	**Adjusted OR (95% CI)[b]**	**p value [c]**
Male sex (ref. female)	1.046 (0.212–5.149)	0.956	1.737 (0.872–3.46)	0.116
APACHE II score	1.191 (1.047–1.355)	0.008	1.098 (1.029–1.171)	0.004
Public health insurance coverage (ref. private)			4.331 (1.832–10.239)	0.001
N included in the model[†]	317		316	
AUC (95% CI) [d]	0.881 (0.812–0.95)	0.001	0.737 (0.67–0.804)	0.000
Third multivariate model	**Adjusted OR (95% CI)[b]**	**p value [c]**	**Adjusted OR (95% CI)[b]**	**p value [c]**
Male sex (ref. female)	0.942 (0.155–5.73)	0.948	1.886 (0.922–3.859)	0.082
SAPS III score	1.083 (1.025–1.145)	0.005	1.057 (1.026–1.088)	0.000
Public health insurance coverage (ref. private)			4.53 (1.89–10.856)	0.001
N included in the model[†]	314		313	
AUC (95% CI) [d]	0.85 (0.726–0.974)	0.003	0.759 (0.687–0.832)	0.000
Fourth multivariate model	**Adjusted OR (95% CI)[b]**	**p value [c]**	**Adjusted OR (95% CI)[b]**	**p value [c]**
Age (years)	1.013 (0.951–1.08)	0.687	1.028 (1.002–1.055)	0.033
Male sex (ref. female)	0.754 (0.13–4.392)	0.754	1.877 (0.923–3.817)	0.082
SOFA score	1.147 (0.978–1.346)	0.092	1.119 (1.008–1.242)	0.035
Public health insurance coverage (ref. private)			4.264 (1.753–10.372)	0.001
N included in the model[†]	311		310	
AUC (95% CI) [d]	0.825 (0.699–0.952)	0.006	0.756 (0.684–0.827)	0.000

[a] Number of cases (n) included in the multivariate model. [b]Odds ratios and 95% confidence intervals of the multivariate binary logistic regression model. [c] Wald test p value, results < 0.05 indicate statistical significance. [d]Area under the receiver operating characteristic curve and 95% confidence interval. Abbreviations: ICU, intensive care unit; m-RS, modified Rankin scale score; 95% CI, 95% confidence interval; ref., reference; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation; AUC, area under the receiver operating characteristic curve

TABLE S5: Unadjusted odds ratios of prognostic factors for mortality and Unfavourable outcome in the diagnostic group of **traumatic brain injury** in neurocritical patients admitted to intensive care units.

Factors	ICU discharge [a]	Death on ICU [a]	Unadjusted OR (95% CI) for ICU Mortality [b]	p value[c]	Favourable outcome (m-RS score 1, 2, or 3) [a]	Unfavourable outcome (m-RS score 4, 5, or 6) [a]	Unadjusted OR (95% CI) for Unfavourable outcome[b]	p value[c]
Age (years)	(n=162) 54.7 ± 21.5	(n=56) 53 ± 24.2	0.997 (0.983–1.01)	0.625	(n=101) 56.9 ± 21.7	(n=117) 52 ± 22.3	0.99 (0.978–1.002)	0.101
Sex								
Female	48/56 (85.7)	8/56 (14.3)			32/56 (57.1)	24/56 (42.9)		
Male	114/162 (70.4)	48/162 (29.6)	2.526 (1.112–5.741)	0.027	69/162 (42.6)	93/162 (57.4)	1.797 (0.972–3.321)	0.061
Glasgow Coma Scale	(n=162) 12.5 (5–15)	(n=56) 4.5 (3–10)	0.868 (0.812–0.928)	0.000	(n=101) 14 (11–15)	(n=117) 5 (3–9)	0.76 (0.709–0.816)	0.000
APACHE II	(n=162) 12 (8–16)	(n=56) 23.5 (15–27.5)	1.212 (1.145–1.282)	0.000	(n=101) 10 (7–14)	(n=117) 18 (14–24)	1.268 (1.186–1.356)	0.000
SAPS III	(n=159) 45 (37–53)	(n=52) 55.5 (44–68)	1.054 (1.029–1.079)	0.000	(n=99) 42 (34–50)	(n=112) 55 (44.5-63.5)	1.073 (1.047–1.101)	0.000
SOFA	(n=158) 3 (1–7)	(n=51) 9 (6–11)	1.353 (1.224–1.497)	0.000	(n=98) 2 (1–4)	(n=111) 8 (5–10)	1.606 (1.417–1.82)	0.000
Number of Hs								
Zero	60/64 (93.7)	4/64 (6.3)			48/64 (74.6)	16/64 (25.4)		
One	46/51 (90.2)	5/51 (9.8)	1.63 (0.414–6.415)	0.484	33/51 (64.5)	18/51 (35.5)	1.636 (0.731–3.664)	0.231
Two	33/49 (67.3)	16/49 (32.7)	7.273 (2.246–23.553)	0.001	14/49 (28.9)	35/49 (71.1)	7.50 (3.240–17.359)	0.000
Three or more	23/54 (42.6)	31/54 (57.4)	20.217 (6.422–63.651)	0.000	6/54 (11.7)	48/54 (88.3)	24.00 (8.654–66.557)	0.000
Coverage of hospitalization costs								
Private insurance	58/66 (87.9)	8/66 (12.1)			50/66 (75.2)	16/66 (24.8)		
Public insurance	104/152 (68.4)	48/152 (31.6)	3.346 (1.482–7.556)	0.004	51/152 (33.6)	101/152 (66.4)	6.189 (3.212–11.926)	0.000

[a] Categorical variables are described as the absolute number of deaths (percentage of deaths by the total number of cases in the line); age is described as mean ± standard deviation, and the other quantitative variables are described as median (first quartile – third quartile).

[b] Odds ratios and 95% confidence intervals of the univariate binary logistic regression model.

[c] Wald test p value, results < 0.05 indicate statistical significance.

Abbreviations: ICU, intensive care unit; m-RS, modified Rankin scale score; OR, odds ratio; ref., reference; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation.

TABLE S6**:** Adjusted odds ratios of prognostic factors for mortality and Unfavourable outcome in the diagnostic group of **traumatic brain injury** in neurocritical patients admitted to intensive care units.

Factors	**Models for ICU mortality**		**Models for Unfavourable outcome (m-RS 4, 5, or 6)**	
First multivariate model	**Adjusted OR (95% CI)[b]**	**p value[c]**	**Adjusted OR (95% CI)[b]**	**p value[c]**
Age (years)	1.017 (0.998–1.036)	0.082	1.023 (1.003–1.043)	0.023
Male sex (ref. female)	2.451 (0.951–6.316)	0.063	1.572 (0.671–3.684)	0.298
Glasgow Coma Scale	0.924 (0.844–1.011)	0.085	0.777 (0.708–0.854)	0.000
Number of Hs (ref. zero)				
One	1.553 (0.385–6.266)	0.537	1.354 (0.53–3.463)	0.527
Two	5.564 (1.574–19.675)	0.008	4.471 (1.65–12.119)	0.003
Three or more	16.255 (4.576–57.743)	0.000	10.88 (3.392–34.906)	0.000
Public health insurance coverage (ref. private)	0.961 (0.301–3.068)	0.947	1.146 (0.392–3.351)	0.803
N included in the model [a]	218		218	
AUC (95% CI) [d]	0.819 (0.754–0.884)	0.000	0.877 (0.831–0.923)	0.000
Second multivariate model	**Adjusted OR (95% CI)[b]**	**p value[c]**	**Adjusted OR (95% CI)[b]**	**p value[c]**
Male sex (ref. female)	2.922 (1.081–7.896)	0.035	1.58 (0.706–3.535)	0.266
APACHE II score	1.221 (1.148–1.298)	0.000	1.244 (1.161–1.334)	0.000
Public health insurance coverage (ref. private)	0.71 (0.259–1.945)	0.505	2.052 (0.921–4.572)	0.079
N included in the model [a]	218		218	
AUC (95% CI) [d]	0.843 (0.786–0.899)	0.000	0.857 (0.808–0.905)	0.000
Third multivariate model	**Adjusted OR (95% CI)[b]**	**p value**	**Adjusted OR (95% CI)[b]**	**p value[c]**
Male sex (ref. female)	2.998 (1.182–7.608)	0.021	1.905 (0.823–4.411)	0.133
SAPS III score	1.061 (1.034–1.088)	0.000	1.093 (1.06–1.128)	0.000
Public health insurance coverage (ref. private)	2.64 (1.098–6.347)	0.030	7.811 (3.538–17.243)	0.000
N included in the model [a]	211		211	
AUC (95% CI) [d]	0.752 (0.679–0.825)	0.000	0.827 (0.772–0.882)	0.000
Fourth multivariate model	**Adjusted OR (95% CI)[b]**	**p value [c]**	**Adjusted OR (95% CI)[b]**	**p value [c]**
Age (years)	1.011 (0.992–1.029)	0.264	1.008 (0.99–1.026)	0.409
Male sex (ref. female)	2.164 (0.85–5.51)	0.105	1.259 (0.541–2.929)	0.593
SOFA score	1.364 (1.221–1.524)	0.000	1.561 (1.362–1.789)	0.000
Public health insurance coverage (ref. private)	1.113 (0.371–3.339)	0.849	1.73 (0.639–4.685)	0.281
N included in the model [a]	209		209	
AUC (95% CI) [d]	0.808 (0.742–0.873)	0.000	0.865 (0.815–0.915)	0.000

[a] Number of cases (n) included in the multivariate model. [b] Odds ratios and 95% confidence intervals of the multivariate binary logistic regression model. [c] Wald test p value, results < 0.05 indicate statistical significance. [d] Area under the receiver operating characteristic curve and 95% confidence interval. Abbreviations: ICU, intensive care unit; m-RS, modified Rankin scale score; OR, odds ratio; 95% CI, 95% confidence interval; ref., reference; AUC, area under the receiver operating characteristic curve; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation.

TABLE S7: Unadjusted odds ratios of prognostic factors for mortality and Unfavourable outcome in the diagnostic group of **ischaemic stroke** in neurocritical patients admitted to intensive care units.

Factors	**ICU discharge** [a]	**Death on ICU** [a]	**Unadjusted OR (95% CI) for ICU Mortality** [b]	**p value**[c]	**Favourable outcome (m-RS score 1, 2, or 3)** [a]	**Unfavourable outcome (m-RS score 4, 5, or 6)** [a]	**Unadjusted OR (95% CI) for Unfavourable outcome**[b]	**p value**[c]
Age (years)	(n=187) 69.2 ± 17	(n=24) 69.7 ± 15.8	1.002 (0.976–1.027)	0.906	(n=126) 68.8 ± 16.8	(n=82) 69.8 ± 17.1	1.003 (0.987–1.02)	0.696
Sex								
Female	92/104 (88.5)	12/104 (11.5)			58/103 (56.3)	45/103 (43.7)		
Male	95/107 (88.8)	12/107 (11.2)	0.968 (0.414–2.266)	0.941	68/105 (64.8)	37/105 (35.2)	0.701 (0.401–1.226)	0.213
Glasgow Coma Scale	(n=187) 15 (13–15)	(n=24) 10.5 (5–13.5)	0.775 (0.699–0.86)	0.000	(n=126) 15 (14–15)	(n=82) 11 (8–14)	0.633 (0.541–0.74)	0.000
APACHE II	(n=187) 10 (7–14)	(n=24) 18.5 (14.5–21.5)	1.206 (1.114–1.307)	0.000	(n=126) 9 (6–12)	(n=82) 15 (10–19)	1.182 (1.116–1.253)	0.000
SAPS III	(n=180) 52 (42–57)	(n=21) 59 (44–67)	1.049 (1.014–1.085)	0.006	(n=122) 48 (41–54)	(n=176) 56 (46–62.5)	1.056 (1.028–1.085)	0.000
SOFA	(n=175) 1 (0–4)	(n=21) 6 (3–9)	1.239 (1.104–1.391)	0.000	(n=118) 1 (0–3)	(n=75) 5 (2–7)	1.332 (1.195–1.486)	0.000
Number of Hs								
Zero	108/109 (99.1)	1/109 (0.9)			82/106 (77.4)	24/106 (22.6)		
One	47/55 (85.5)	8/55 (14.5)	18.383 (2.236–151.155)	0.007	29/55 (52.7)	26/55 (47.3)	3.063 (1.524–6.156)	0.002
Two	23/30 (76.7)	7/30 (23.3)	32.87 (3.855–280.237)	0.001	12/30 (39.4)	18/30 (60.6)	5.125 (2.168–12.117)	0.000
Three or more	9/17 (52.9)	8/17 (47.1)	96 (10.774–855.42)	0.000	3/17 (17.6)	14/17 (82.4)	15.944 (4.228–60.125)	0.000
Coverage of hospitalization costs								
Private insurance	157/167 (94)	10/167 (6)			114/164 (69.5)	50/164 (30.5)		
Public insurance	30/44 (68.2)	14/44 (31.8)	7.327 (2.977–18.031)	0.000	32/44 (27.3)	32/44 (72.7)	6.08 (2.895–12.77)	0.000

[a] Categorical variables are described as the absolute number of deaths (percentage of deaths by the total number of cases in the line); age is described as mean ± standard deviation, and the other quantitative variables are described as median (first quartile – third quartile).
[b] Odds ratio and 95% confidence interval of the univariate binary logistic regression model.
[c] Wald test p value, results < 0.05 indicate statistical significance.
Abbreviations: ICU, intensive care unit; m-RS, modified Rankin scale score; OR, odds ratio; ref., reference; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation.

TABLE S8**:** Adjusted odds ratios of prognostic factors for mortality and Unfavourable outcome in the diagnostic group of **ischaemic stroke** in neurocritical patients admitted to intensive care units.

Factors	**Models for ICU mortality**		**Models for Unfavourable outcome (m-RS 4, 5, or 6)**	
First multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Age (years)	1.033 (0.994–1.074)	0.102	1.007 (0.985–1.03)	0.517
Male sex (ref. female)	1.029 (0.366–2.891)	0.956	0.61 (0.301–1.234)	0.169
Glasgow Coma Scale	0.868 (0.768–0.982)	0.024	0.678 (0.573–0.803)	0.000
Number of Hs (ref. zero)				
One	8.751 (0.993–77.144)	0.051	1.576 (0.678–3.663)	0.291
Two	17.361 (1.901–158.572)	0.011	2.783 (1.005–7.703)	0.049
Three or more	54.814 (5.672–529.691)	0.001	8.944 (2.038–39.258)	0.004
Public health insurance coverage (ref. private)	3.604 (1.041–12.474)	0.043	1.997 (0.73–5.463)	0.178
N included in the model [a]	211		208	
AUC (95% CI) [d]	0.896 (0.841–0.951)	0.000	0.858 (0.804–0.913)	0.000
Second multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Male sex (ref. female)	0.921 (0.348–2.438)	0.868	0.58 (0.3–1.124)	0.107
APACHE II score	1.195 (1.098–1.3)	0.000	1.166 (1.1–1.236)	0.000
Public health insurance coverage (ref. private)	5.878 (2.22–15.566)	0.000	5.42 (2.384–12.323)	0.000
N included in the model [a]	211		208	
AUC (95% CI) [d]	0.857 (0.786–0.928)	0.000	0.804 (0.744–0.864)	0.000
Third multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Male sex (ref. female)	1.049 (0.39–2.819)	0.924	0.594 (0.31–1.141)	0.118
SAPS III score	1.044 (1.01–1.079)	0.011	1.06 (1.029–1.091)	0.000
Public health insurance coverage (ref. private)	6.191 (2.315–16.557)	0.000	7.424 (3.088–17.849)	0.000
N included in the model [a]	201		198	
AUC (95% CI) [d]	0.767 (0.655–0.88)	0.000	0.756 (0.687–0.825)	0.000
Fourth multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Age (years)	1.022 (0.987–1.057)	0.222	1.013 (0.991–1.035)	0.241
Male sex (ref. female)	1.257 (0.456–3.466)	0.659	0.701 (0.359–1.369)	0.298
SOFA score	1.204 (1.064–1.363)	0.003	1.262 (1.129–1.41)	0.000
Public health insurance coverage (ref. private)	5.916 (1.943–18.012)	0.002	4.511 (1.839–11.069)	0.001
N included in the model [a]	197		193	
AUC (95% CI) [d]	0.827 (0.751–0.903)	0.000	0.806 (0.744–0.868)	0.000

[a] Number of cases (n) included in the multivariate model. [b] Odds ratios and 95% confidence intervals of the multivariate binary logistic regression model. [c] Wald test p value, results < 0.05 indicate statistical significance. [d]Area under the receiver operating characteristic curve and 95% confidence interval. Abbreviations: ICU, intensive care unit; m-RS, modified Rankin scale score; OR, odds ratio; 95% CI, 95% confidence interval; ref., reference; AUC, area under the receiver operating characteristic curve; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation

TABLE S9: Unadjusted odds ratios of prognostic factors for mortality and Unfavourable outcome in the diagnostic group of encephalopathy **in neurocritical patients** admitted to intensive care units.

Factors	**ICU discharge** [a]	**Death on ICU** [a]	**Unadjusted OR (95% CI) for ICU Mortality** [b]	**p value**[c]	**Favourable outcome (m-RS score 1, 2, or 3)** [a]	**Unfavourable outcome (m-RS score 4, 5, or 6)** [a]	**Unadjusted OR (95% CI) for Unfavourable outcome**[b]	**p value**[c]
Age (years)	(n=114) 64 ± 20.2	(n=41) 70.2 ± 19.4	1.016 (0.997–1.036)	0.093	(n=66) 63.2 ± 19.9	(n=89) 67.5 ± 20.3	1.011 (0.995–1.027)	0.195
Sex								
Female	66/83 (79.5)	17/83 (20.5)			40/83 (48.2)	43/83 (51.8)		
Male	48/72 (66.7)	24/72 (33.3)	1.941 (0.941–4.004)	0.073	26/72 (36.1)	46/72 (63.9)	1.646 (0.863–3.138)	0.130
Glasgow Coma Scale	(n=114) 13 (10–14)	(n=41) 10 (3–14)	0.872 (0.8–0.95)	0.002	(n=66) 14 (12–14)	(n=89) 11 (8–14)	0.864 (0.789–0.947)	0.002
APACHE II	(n=114) 13.5 (9–20)	(n=41) 27 (20–33)	1.135 (1.083–1.188)	0.000	(n=66) 11 (8–15)	(n=89) 22 (14–28)	1.136 (1.083–1.191)	0.000
SAPS III	(n=113) 54 (44–63)	(n=41) 69 (59–78)	1.074 (1.042–1.106)	0.000	(n=65) 50 (41–57)	(n=89) 64 (55–75)	1.083 (1.051–1.116)	0.000
SOFA	(n=114) 3 (1–7)	(n=41) 9 (5–11)	1.308 (1.175–1.456)	0.000	(n=66) 2 (1–6)	(n=89) 7 (4–10)	1.288 (1.163–1.427)	0.000
Number of Hs								
Zero	44/47 (93.6)	3/47 (6.4)			30/47 (63.8)	17/47 (36.2)		
One	32/39 (82.1)	7/39 (17.9)	3.208 (0.77–13.368)	0.109	18/39 (46.2)	21/39 (53.8)	2.059 (0.866–4.896)	0.102
Two	21/32 (65.6)	11/32 (34.4)	7.683 (1.936–30.488)	0.004	12/32 (37.5)	20/32 (62.5)	2.941 (1.16–7.46)	0.023
Three or more	17/37 (45.9)	20/37 (54.1)	17.255 (4.535–65.657)	0.000	6/37 (16.2)	31/37 (83.8)	9.118 (3.167–26.25)	0.000
Coverage of hospitalization costs								
Private insurance	70/89 (78.7)	19/89 (21.3)			45/89 (50.6)	44/89 (49.4)		
Public insurance	44/66 (66.7)	22/66 (33.3)	1.842 (0.896–3.786)	0.096	21/66 (31.8)	45/66 (68.2)	2.192 (1.128–4.257)	0.021

[a] Categorical variables are described as the absolute number of deaths (percentage of deaths by the total number of cases in the line); age is described as mean ± standard deviation, and the other quantitative variables are described as median (first quartile – third quartile).

[b] Odds ratio and 95% confidence interval of the univariate binary logistic regression model.

[c] Wald test p value, results < 0.05 indicate statistical significance.

Abbreviations: ICU, intensive care unit; m-RS, modified Rankin scale score; OR, odds ratio; ref., reference; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation.

TABLE S10**:** Adjusted odds ratios of prognostic factors for mortality and Unfavourable outcome in the diagnostic group of **encephalopathy** in neurocritical patients admitted to intensive care units.

Factors	**Models for ICU mortality**		**Models for Unfavourable outcome (m-RS 4, 5, or 6)**	
First multivariate model	**Adjusted OR (95% CI)** [b]	**p value**[c]	**Adjusted OR (95% CI)** [b]	**p value**[c]
Age (years)	1.035 (1.009–1.062)	0.008	1.026 (1.005–1.047)	0.013
Male sex (ref. female)	2.827 (1.169–6.838)	0.021	1.766 (0.847–3.68)	0.129
Glasgow Coma Scale	0.915 (0.824–1.017)	0.099	0.905 (0.816–1.005)	0.062
Number of Hs (ref. zero Hs)				
One	2.922 (0.661–12.918)	0.157	1.734 (0.69–4.359)	0.242
Two	7.119 (1.614–31.397)	0.010	2.268 (0.822–6.258)	0.114
Three or more	19.792 (4.447–88.1)	0.000	7.778 (2.444–24.75)	0.001
Public health insurance coverage (ref. private)	1.184 (0.446–3.141)	0.734	1.937 (0.852–4.403)	0.115
N included in the model [a]	155		155	
AUC (95% CI) [d]	0.822 (0.751–0.894)	0.000	0.772 (0.697–0.848)	0.000
Second multivariate model	**Adjusted OR (95% CI)** [b]	**p value**[c]	**Adjusted OR (95% CI)** [b]	**p value**[c]
Male sex (ref. female)	1.872 (0.803–4.367)	0.147	1.436 (0.683–3.018)	0.340
APACHE II score	1.133 (1.081–1.187)	0.000	1.134 (1.081–1.19)	0.000
Public health insurance coverage (ref. private)	1.364 (0.586–3.178)	0.471	2.015 (0.94–4.317)	0.072
N included in the model [a]	155		155	
AUC (95% CI) [d]	0.816 (0.741–0.891)	0.000	0.799 (0.73–0.869)	0.000
Third multivariate model	**Adjusted OR (95% CI)** [b]	**p value**	**Adjusted OR (95% CI)** [b]	**p value**[c]
Male sex (ref. female)	1.809 (0.808–4.052)	0.149	1.462 (0.692–3.089)	0.319
SAPS III score	1.072 (1.04–1.105)	0.000	1.081 (1.049–1.115)	0.000
Public health insurance coverage (ref. private)	1.262 (0.559–2.85)	0.575	1.797 (0.836–3.864)	0.134
N included in the model [a]	154		154	
AUC (95% CI) [d]	0.776 (0.697–0.855)	0.000	0.794 (0.724–0.865)	0.000
Fourth multivariate model	**Adjusted OR (95% CI)** [b]	**p value**[c]	**Adjusted OR (95% CI)** [b]	**p value**[c]
Age (years)	1.025 (1–1.05)	0.053	1.015 (0.995–1.035)	0.137
Male sex (ref. female)	2.011 (0.878–4.606)	0.099	1.513 (0.735–3.116)	0.261
SOFA score	1.297 (1.156–1.455)	0.000	1.261 (1.135–1.401)	0.000
Public health insurance coverage (ref. private)	1.433 (0.561–3.662)	0.452	1.881 (0.841–4.207)	0.124
N included in the model [a]	155		155	
AUC (95% CI) [d]	0.796 (0.716–0.876)	0.000	0.765 (0.69–0.841)	0.000

[a] Number of cases (n) included in the multivariate model. [b] Odds ratios and 95% confidence intervals of the multivariate binary logistic regression model. [c] Wald test p value, results < 0.05 indicate statistical significance. [d] Area under the receiver operating characteristic curve and 95% confidence interval. Abbreviations: ICU, intensive care unit; m-RS, modified Rankin scale score; OR, odds ratio; 95% CI, 95% confidence interval; ref., reference; AUC, area under the receiver operating characteristic curve; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation.

TABLE S11: Unadjusted odds ratios of prognostic factors for mortality and Unfavourable outcome in the diagnostic group of **seizures** in neurocritical patients admitted to intensive care units.

Factors	**ICU discharge** [a]	**Death on ICU** [a]	**Unadjusted OR (95% CI) for ICU Mortality** [b]	**p value**[c]	**Favourable outcome (m-RS score 1, 2, or 3)** [a]	**Unfavourable outcome (m-RS score 4, 5, or 6)** [a]	**Unadjusted OR (95% CI) for Unfavourable outcome**[b]	**p value**[c]
Age (years)	(n=87) 58.8 ± 23.1	(n=4) 56.5 ± 11.4	0.996 (0.953–1.04)	0.841	(n=64) 56.3 ± 23.4	(n=25) 63.1 ± 19.9	1.014 (0.992–1.036)	0.204
Sex								
Female	42/45 (93.3)	3/45 (6.7)			31/43 (72.1)	12/43 (27.9)		
Male	45/46 (97.8)	1/46 (2.2)	0.311 (0.031–3.109)	0.320	33/46 (71.7)	13/46 (28.3)	1.018 (0.403–2.567)	0.970
Glasgow Coma Scale	(n=87) 14 (11–15)	(n=4) 11 (7.5–14)	0.913 (0.735–1.134)	0.411	(n=64) 15 (14–15)	(n=25) 9 (6–14)	0.781 (0.688–0.886)	0.000
APACHE II	(n=87) 10 (5–15)	(n=4) 15.5 (10.5–18)	1.053 (0.936–1.185)	0.392	(n=64) 8 (4–12)	(n=25) 16 (12–19)	1.15 (1.067–1.239)	0.000
SAPS III	(n=86) 41 (33–54)	(n=4) 40 (37.5–53)	1.007 (0.938–1.081)	0.853	(n=64) 39 (31–48.5)	(n=24) 54 (41.5–65)	1.076 (1.034–1.12)	0.000
SOFA	(n=81) 1 (0–4)	(n=4) 6 (3–7.5)	1.399 (0.997–1.964)	0.052	(n=59) 1 (0–3)	(n=24) 4 (3–6.5)	1.639 (1.289–2.084)	0.000
Number of Hs								
Zero	42/44 (95.5)	2/44 (4.5)			32/42 (76.2)	10/42 (23.8)		
One	23/24 (95.8)	1/24 (4.2)	0.913 (0.078–10.62)	0.942	20/24 (83.3)	4/24 (16.7)	0.64 (0.177–2.318)	0.497
Two	13/14 (92.9)	1/14 (7.1)	1.615 (0.135–19.285)	0.705	7/14 (50)	7/14 (50)	3.2 (0.903–11.345)	0.072
Three or more	9/9 (100)	0/9 (0)	N/A	N/A	5/9 (55.6)	4/9 (44.4)	2.56 (0.574–11.408)	0.218
Coverage of hospitalization costs								
Private insurance	78/79 (98.7)	1/79 (1.3)			59/77 (76.6)	18/77 (23.4)		
Public insurance	9/12 (75)	3/12 (25)	0.913 (0.078–10.62)	0.942	5/12 (41.7)	7/12 (58.3)	4.589 (1.298–16.229)	0.018

[a] Categorical variables are described as the absolute number of deaths (percentage of deaths by the total number of cases in the line); age is described as mean ± standard deviation, and the other quantitative variables are described as median (first quartile – third quartile).
[b] Odds ratios and 95% confidence intervals of the univariate binary logistic regression model.
[c] Wald test p value, results < 0.05 indicate statistical significance.
Abbreviations: ICU, intensive care unit; m-RS, modified Rankin scale score; OR, odds ratio; ref., reference; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation; N/A, not analysed.

TABLE S12: Adjusted odds ratios of prognostic factors for mortality and Unfavourable outcome in the diagnostic group of **seizures** in neurocritical patients admitted to intensive care units.

Factors	**Models for ICU mortality**		**Models for Unfavourable outcome (m-RS 4, 5, or 6)**	
First multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Age (years)	N/A	N/A	1.025 (0.996–1.055)	0.089
Male sex (ref. female)	N/A	N/A	0.754 (0.241–2.354)	0.627
Glasgow Coma Scale	N/A	N/A	0.778 (0.672–0.9)	0.001
Number of Hs (ref. zero Hs)		N/A		
One	N/A	N/A	0.548 (0.133–2.266)	0.406
Two	N/A	N/A	1.478 (0.308–7.101)	0.625
Three or more	N/A	N/A	0.776 (0.124–4.873)	0.787
Public health insurance coverage (ref. private)	N/A	N/A	5.028 (0.965–26.187)	0.055
N included in the model [a]	N/A	N/A	89	
AUC (95% CI) [d]	N/A	N/A	0.888 (0.819–0.956)	0.000
Second multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Male sex (ref. female)	0.042 (0.002–1.128)	0.059	0.723 (0.243–2.151)	0.559
APACHE II score	1.062 (0.897–1.257)	0.486	1.149 (1.063–1.241)	0.000
Public health insurance coverage (ref. private)	91.444 (4.383–1907.891)	0.004	4.532 (1.081–19.006)	0.039
N included in the model [a]	91		89	
AUC (95% CI) [d]	0.943 (0.867–1)	0.003	0.835 (0.748–0.922)	0.000
Third multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Male sex (ref. female)	0.06 (0.003–1.295)	0.073	0.911 (0.306–2.706)	0.866
SAPS III score	0.985 (0.896–1.082)	0.750	1.078 (1.033–1.124)	0.000
Public health insurance coverage (ref. private)	102.753 (4.714–2239.75)	0.003	4.193 (0.971–18.095)	0.055
N included in the model [a]	90		88	
AUC (95% CI) [d]	0.863 (0.644–1)	0.014	0.823 (0.724–0.921)	0.000
Fourth multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Age (years)	1.008 (0.937–1.085)	0.822	1.018 (0.99–1.047)	0.209
Male sex (ref. female)	0.064 (0.002–1.795)	0.106	0.713 (0.221–2.305)	0.572
SOFA score	1.318 (0.838–2.073)	0.233	1.595 (1.25–2.036)	0.000
Public health insurance coverage (ref. private)	71.58 (2.584–1983.206)	0.012	3.074 (0.613–15.423)	0.172
N included in the model [a]	85		83	
AUC (95% CI) [d]	0.957 (0.89–1)	0.002	0.846 (0.765–0.927)	0.000

[a] Number of cases (n) included in the multivariate model. [b] Odds ratios and 95% confidence intervals of the multivariate binary logistic regression model. [c] Wald test p value, results < 0.05 indicate statistical significance.

[d] Area under the receiver operating characteristic curve and 95% confidence interval. Abbreviations: N/A, not analysed; ICU, intensive care unit; m-RS, modified Rankin scale score; OR, odds ratio; 95% CI, 95% confidence interval; ref., reference; AUC, area under the receiver operating characteristic curve; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation.

TABLE S13: Unadjusted odds ratios of prognostic factors for mortality and Unfavourable outcome in the diagnostic group of **intracerebral haemorrhage** in neurocritical patients admitted to intensive care units.

Factors	**ICU discharge** [a]	**Death on ICU** [a]	**Unadjusted OR (95% CI) for ICU Mortality** [b]	**p value**[c]	**Favourable outcome (m-RS score 1, 2, or 3)** [a]	**Unfavourable outcome (m-RS score 4, 5, or 6)** [a]	**Unadjusted OR (95% CI) for Unfavourable outcome**[b]	**p value**[c]
Age (years)	(n=55) 63.2 ± 13.5	(n=22) 59 ± 19.2	0.982 (0.951–1.015)	0.280	(n=24) 65.4 ± 13.5	(n=52) 60.2 ± 16	0.977 (0.944–1.01)	0.174
Sex								
Female	27/40 (67.5)	13/40 (32.5)			7/39 (17.9)	32/39 (82.1)		
Male	28/37 (75.7)	9/37 (24.3)	0.668 (0.245–1.816)	0.429	17/37 (45.9)	20/37 (54.1)	0.257 (0.091–0.73)	0.011
Glasgow Coma Scale	(n=55) 11 (4–14)	(n=22) 7 (4–13)	0.916 (0.822–1.021)	0.115	(n=24) 14 (13–15)	(n=52) 7 (3.5–12)	0.732 (0.623–0.86)	0.000
APACHE II	(n=55) 14 (9–19)	(n=22) 18.5 (14–23)	1.086 (1.007–1.171)	0.031	(n=24) 10.5 (7.5–14.5)	(n=52) 18 (14–23)	1.222 (1.097–1.362)	0.000
SAPS III	(n=51) 52 (44–60)	(n=21) 63 (47–69)	1.031 (0.996–1.067)	0.084	(n=22) 42.5 (34–52)	(n=49) 60 (51–69)	1.11 (1.051–1.172)	0.000
SOFA	(n=50) 4 (2–6)	(n=20) 7 (4.5–10)	1.27 (1.071–1.506)	0.006	(n=22) 2 (1–4)	(n=47) 6 (4–8)	1.71 (1.278–2.287)	0.000
Number of Hs								
Zero	24/30 (80)	6/30 (20)			14/29 (48.3)	15/29 (51.7)		
One	16/20 (80)	4/20 (20)	1 (0.243–4.114)	1.000	8/20 (40)	12/20 (60)	1.4 (0.442–4.437)	0.568
Two	9/13 (69.2)	4/13 (30.8)	1.778 (0.405–7.802)	0.446	2/13 (15.4)	11/13 (84.6)	5.133 (0.963–27.363)	0.055
Three or more	6/14 (42.9)	8/14 (57.1)	5.333 (1.334–21.325)	0.018	0/14 (0)	14/14 (100)	All with outcome	
Coverage of hospitalization costs								
Private insurance	19/25 (76)	6/25 (24)			11/24 (45.8)	13/24 (54.2)		
Public insurance	36/52 (69.2)	16/52 (30.8)	1.407 (0.473–4.188)	0.539	13/52 (25)	39/52 (75)	2.538 (0.916–7.034)	0.073

[a] Categorical variables are described as the absolute number of deaths (percentage of deaths by the total number of cases in the line); age is described as mean ± standard deviation, and the other quantitative variables are described as median (first quartile – third quartile).
[b] Odds ratios and 95% confidence intervals of the univariate binary logistic regression model.
[c] Wald test p value, results < 0.05 indicate statistical significance.
Abbreviations: ICU, intensive care unit; m-RS, modified Rankin scale score; OR, odds ratio; ref., reference; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation.

TABLE S14: Adjusted odds ratios of prognostic factors for mortality and Unfavourable outcome in the diagnostic group of the **intracerebral haemorrhage** in neurocritical patients admitted to intensive care units.

Factors	**Models for ICU mortality**		**Models for Unfavourable outcome (m-RS 4, 5, or 6)**	
First multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Age (years)	0.983 (0.948–1.019)	0.353	0.971 (0.919–1.027)	0.307
Male sex (ref. female)	0.759 (0.252–2.288)	0.625	0.156 (0.035–0.697)	0.015
Glasgow Coma Scale	0.978 (0.861–1.11)	0.732	0.731 (0.602–0.887)	0.002
Number of Hs (ref. zero Hs)				
One	1.03 (0.241–4.406)	0.968	2.94 (0.625–13.836)	0.172
Two	1.693 (0.363–7.902)	0.503	5.087 (0.557–46.442)	0.149
Three or more	4.89 (1.113–21.477)	0.036	All with outcome	
Public health insurance coverage (ref. private)	1.208 (0.35–4.169)	0.765	1.301 (0.257–6.589)	0.751
N included in the model [a]	77		76	
AUC (95% CI) [d]	0.693 (0.563–0.824)	0.008	0.903 (0.832–0.975)	0.000
Second multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Male sex (ref. female)	0.812 (0.285–2.317)	0.697	0.302 (0.09–1.009)	0.052
APACHE II score	1.087 (1.005–1.175)	0.036	1.213 (1.088–1.353)	0.001
Public health insurance coverage (ref. private)	1.578 (0.5–4.975)	0.437	3.433 (0.945–12.467)	0.061
N included in the model [a]	77		76	
AUC (95% CI) [d]	0.662 (0.534–0.79)	0.027	0.853 (0.77–0.936)	0.000
Third multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Male sex (ref. female)	0.708 (0.241–2.078)	0.529	0.377 (0.103–1.381)	0.141
SAPS III score	1.029 (0.993–1.066)	0.113	1.109 (1.048–1.173)	0.000
Public health insurance coverage (ref. private)	1.403 (0.447–4.406)	0.562	3.635 (0.96–13.766)	0.058
N included in the model [a]	72		71	
AUC (95% CI) [d]	0.648 (0.504–0.791)	0.050	0.865 (0.774–0.955)	0.000
Fourth multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Age (years)	0.979 (0.943–1.016)	0.258	0.992 (0.944–1.042)	0.740
Male sex (ref. female)	0.585 (0.184–1.858)	0.363	0.272 (0.073–1.01)	0.052
SOFA score	1.258 (1.058–1.497)	0.009	1.619 (1.198–2.188)	0.002
Public health insurance coverage (ref. private)	0.807 (0.22–2.96)	0.746	2.378 (0.52–10.876)	0.264
N included in the model [a]	70		69	
AUC (95% CI) [d]	0.725 (0.584–0.866)	0.003	0.87 (0.773–0.968)	0.000

[a] Number of cases (n) included in the multivariate model. [b] Odds ratios and 95% confidence intervals of the multivariate binary logistic regression model. [c] Wald test p value, results < 0.05 indicate statistical significance. [d] Area under the receiver operating characteristic curve and 95% confidence interval. Abbreviations: ICU, intensive care unit; m-RS, modified Rankin scale score; OR, odds ratio; 95% CI, 95% confidence interval; ref., reference; AUC, area under the receiver operating characteristic curve; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation.

TABLE S15: Unadjusted odds ratios of prognostic factors for mortality and Unfavourable outcome in the diagnostic group of **subarachnoid haemorrhage** in neurocritical patients admitted to intensive care units.

Factors	**ICU discharge** [a]	**Death on ICU** [a]	**Unadjusted OR (95% CI) for ICU Mortality** [b]	**p value**[c]	**Favourable outcome (m-RS score 1, 2, or 3)** [a]	**Unfavourable outcome (m-RS score 4, 5, or 6)** [a]	**Unadjusted OR (95% CI) for Unfavourable outcome**[b]	**p value**[c]
Age (years)	(n=46) 55.2 ± 11.4	(n=24) 62.2 ± 17.9	1.037 (0.999–1.076)	0.059	(n=26) 54.8 ± 10	(n=44) 59.3 ± 16.1	1.024 (0.987–1.062)	0.201
Sex								
Female	32/48 (66.7)	16/48 (33.3)			20/48 (41.7)	28/48 (58.3)		
Male	14/22 (63.6)	8/22 (36.4)	1.143 (0.398–3.285)	0.804	6/22 (27.3)	16/22 (72.7)	1.905 (0.634–5.721)	0.251
Glasgow Coma Scale	(n=46) 14 (8–15)	(n=24) 3 (3–9)	0.784 (0.692–0.888)	0.000	(n=26) 14 (11–15)	7 (3–12)	0.788 (0.691–0.898)	0.000
APACHE II	(n=46) 10.5 (6–16)	(n=24) 20 (17–30)	1.184 (1.085–1.293)	0.000	(n=26) 7 (5–11)	(n=44) 18 (13.5–23)	1.267 (1.129–1.421)	0.000
SAPS III	(n=44) 46 (36.5–48.5)	(n=21) 60 (52–76)	1.062 (1.023–1.102)	0.002	(n=25) 42 (34–48)	(n=40) 54 (45.5–70.5)	1.083 (1.03–1.139)	0.002
SOFA	(n=43) 3 (1–5)	(n=21) 7 (5–9)	1.367 (1.15–1.625)	0.000	(n=25) 2 (0–3)	(n=39) 6 (3–9)	1.412 (1.156–1.724)	0.001
Number of Hs								
Zero	21/24 (87.5)	3/24 (12.5)			13/24 (54.2)	11/24 (45.8)		
One	14/20 (70)	6/20 (30)	3 (0.642–14.023)	0.163	6/20 (30)	14/20 (70)	2.758 (0.791–9.613)	0.111
Two	7/14 (50)	7/14 (50)	7 (1.413–34.682)	0.017	4/14 (28.6)	10/14 (71.4)	2.955 (0.721–12.107)	0.132
Three or more	4/12 (33.3)	8/12 (66.7)	14 (2.547–76.95)	0.002	3/12 (25)	9/12 (75)	3.545 (0.765–16.433)	0.106
Coverage of hospitalization costs								
Private insurance	7/12 (58.3)	5/12 (41.7)			6/12 (50)	6/12 (50)		
Public insurance	39/58 (67.2)	19/58 (32.8)	0.682 (0.191–2.433)	0.555	20/58 (34.5)	38/58 (65.5)	1.9 (0.542–6.661)	0.316

[a] Categorical variables are described as the absolute number of deaths (percentage of deaths by the total number of cases in the line); age is described as mean ± standard deviation, and the other quantitative variables are described as median (first quartile – third quartile).
[b] Odds ratios and 95% confidence intervals of the univariate binary logistic regression model.
[c] Wald test p value, results < 0.05 indicate statistical significance.
Abbreviations: ICU, intensive care unit; m-RS, modified Rankin scale score; OR, odds ratio; ref., reference; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation.

TABLE S16**:** Adjusted odds ratios of prognostic factors for mortality and unfavourable outcome in the diagnostic group of **subarachnoid haemorrhage** in neurocritical patients admitted to intensive care units.

Factors	**Models for ICU mortality**		**Models for Unfavourable outcome (m-RS 4, 5, or 6)**	
First multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Age (years)	1.025 (0.976–1.076)	0.323	1.025 (0.978–1.075)	0.307
Male sex (ref. female)	0.94 (0.236–3.742)	0.930	2.334 (0.624–8.728)	0.208
Glasgow Coma Scale	0.805 (0.688–0.941)	0.006	0.748 (0.62–0.904)	0.003
Number of Hs (ref. zero Hs)				
One	1.978 (0.301–13.002)	0.478	0.968 (0.215–4.363)	0.967
Two	6.252 (0.969–40.359)	0.054	1.724 (0.32–9.281)	0.526
Three or more	4.183 (0.464–37.713)	0.202	0.242 (0.02–2.936)	0.265
Public health insurance coverage (ref. private)	0.408 (0.056–2.949)	0.374	3.808 (0.612–23.703)	0.152
N included in the model [a]	70		70	
AUC (95% CI) [d]	0.844 (0.744–0.944)	0.000	0.821 (0.715–0.928)	0.000
Second multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Male sex (ref. female)	1.066 (0.288–3.946)	0.924	2.825 (0.641–12.446)	0.170
APACHE II score	1.188 (1.087–1.298)	0.000	1.268 (1.129–1.424)	0.000
Public health insurance coverage (ref. private)	0.477 (0.096–2.377)	0.366	3.233 (0.51–20.486)	0.213
N included in the model [a]	70		70	
AUC (95% CI) [d]	0.832 (0.736–0.929)	0.000	0.88 (0.796–0.964)	0.000
Third multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Male sex (ref. female)	1.82 (0.519–6.38)	0.349	3.744 (0.919–15.246)	0.065
SAPS III score	1.068 (1.027–1.111)	0.001	1.094 (1.035–1.156)	0.002
Public health insurance coverage (ref. private)	0.433 (0.101–1.844)	0.257	2.158 (0.498–9.357)	0.304
N included in the model [a]	65		65	
AUC (95% CI) [d]	0.764 (0.642–0.886)	0.001	0.8 (0.691–0.909)	0.000
Fourth multivariate model	**Adjusted OR (95% CI)** [b]	**p value** [c]	**Adjusted OR (95% CI)** [b]	**p value** [c]
Age (years)	1.013 (0.967–1.061)	0.587	1.018 (0.971–1.066)	0.460
Male sex (ref. female)	1.373 (0.368–5.123)	0.637	1.826 (0.483–6.905)	0.375
SOFA score	1.376 (1.143–1.655)	0.001	1.379 (1.124–1.692)	0.002
Public health insurance coverage (ref. private)	0.377 (0.063–2.256)	0.285	2.977 (0.504–17.575)	0.229
N included in the model [a]	64		64	
AUC (95% CI) [d]	0.82 (0.715–0.925)	0.000	0.812 (0.696–0.928)	0.000

[a] Number of cases (n) included in the multivariate model. [b] Odds ratios and 95% confidence intervals of the multivariate binary logistic regression model. [c] Wald test p value, results < 0.05 indicate statistical significance. [d] Area under the receiver operating characteristic curve and 95% confidence interval. Abbreviations: ICU, intensive care unit; m-RS, modified Rankin scale score; OR, odds ratio; 95% CI, 95% confidence interval; ref., reference; AUC, area under the receiver operating characteristic curve; APACHE II, Acute Physiology and Chronic Health Evaluation II; SAPS III, Simplified Acute Physiology Score III; SOFA, Sequential Organ Failure Assessment; Hs, number of secondary injuries, resulting from the sum of the presence of hypotension, hypoxemia, hyperthermia, hypercapnia, hypocapnia, hypoglycaemia, hyponatremia, hypothermia, intracranial hypertension, and clinical evidence of herniation.

TABLE S17: Non-standardized Disability-adjusted life-years (DALYs), years of life lost (YLLs), and years lost due to disability (YLDs) in the overall cohort of neurocritical patients and in patients grouped by main diagnosis.

Neurocritical patients	**N**	**DALYs**	**YLLs**	**YLDs**
Total neurocritical patients	1194	4482.94	4420.022	62.92
Traumatic brain injury	218	1634.42	1618.800	15.62
Encephalopathy	155	709.66	703.510	6.15
Subarachnoid haemorrhage	70	559.01	557.426	1.58
Intracerebral haemorrhage	77	557.31	554.420	2.89
Ischaemic stroke	211	421.72	406.567	15.16
Central nervous system infection	25	237.13	236.589	0.54
Postoperative status of elective neurosurgery	317	195.78	180.360	15.42
Seizures	91	110.20	106.849	3.35
Spinal cord injury	19	57.54	55.500	2.04
Neuromuscular disease	11	0.17	0	0.17

TABLE S18**:** Characteristics of registered sites according to available resources

Caracteristics of sites	**n=36**
Located in cities with > 1 million inhabitants, n(%)	23 (63,9%)
Active hospital beds, median (IQR)	190 (136,5 - 309,75)
Adult ICU active beds, median (IQR)	34 (20 - 49)
Type of institution, n(%)	
Only public	11 (30,6%)
Only private	22 (61,1%)
Public and private	3 (8,3%)
Academic hospital, n(%)	30 (83,3%)
Availability of Cranial Tomography, n(%)	
24/7	34 (94,4%)
Elective	2 (5,6%)
Availability of Cranial Magnetic Resonance, n(%)	
24/7	19 (52,8%)
Elective	7 (19,4%)
Not available	10 (27,8%)
Availability of Cerebral Arteriography, n(%)	
24/7	22 (61,1%)
Elective	10 (27,8%)
Not available	4 (11,1%)
Hospital with surgical centre, n(%)	36 (100%)
Titled intensivist, n(%)	37 (97,2%)
Neurologist available 24/7 at the Hospital, n(%)	30 (83,3%)
Neurosurgeon available 24/7 at the Hospital, n(%)	34 (94,4%)
Professionals available in the ICU	
Dedicated Doctor, n(%)	36 (100%)
Dedicated Nurse, n(%)	36 (100%)
Dedicated Physiotherapist, n(%)	36 (100%)
Pharmacist, n(%)	32 (88,9%)
Psychologist, n(%)	31 (86,1%)
Speech therapist, n(%)	32 (88,9%)
Nutritionist, n(%)	36 (100%)
Dentist, n(%)	18 (50%)
Active care protocols in the hospital/ICU:	
Ischaemic stroke, n(%)	25 (69,4%)
Subarachnoid haemorrhage, n(%)	21 (58,3%)
Hemorrhagic stroke, n(%)	22 (61,1%)
Traumatic brain injury, n(%)	18 (50%)
External ventricular drain care, n(%)	24 (66,7%)

Deep vein thrombosis, n(%)	32 (88,9%)
Seizures, n(%)	21 (58,3%)
Bundle Ventilator-associated pneumonia, n(%)	33 (91,7%)
Bundle Urinary Infection related to urinary catheter, n(%)	33 (91,7%)
Bundle Central catheter-related infection, n(%)	32 (88,9%)
Availability EV Thrombolysis 24/7, n(%)	32 (88,9%)

Abbreviations: ICU, intensive care unit; IQR, interquartile range; n, absolute frequency; %, percentage within column.

TABLE S19: Comparison of the characteristics of patients with a primary diagnosis of encephalopathy, stratified by etiologies.

Variables	septic encephalo-pathy (n=64)	brain structural damage (n=26)	metabolic encephalo-pathy (n=21)	hypoxic-ischaemic encephalo-pathy (n=19)	drug-induced encephalo-pathy (n=13)	other etiologies (n=12)
Age (years), mean ± SD	74.2 ± 15.9	53 ± 17.6	68.9 ± 19.3	61 ± 19.1	44.4 ± 21.9	72.4 ± 17.1
Male Sex, n (%)	33 (51.6)	10 (38.5)	5 (23.8)	16 (84.2)	4 (30.8)	4 (33.3)
GCS, Median (IQR)	12 (10 - 14)	14 (10 - 15)	13 (9 - 14)	12 (3 - 14)	6 (4 - 13)	14 (12.5-14.5)
APACHE II at ICU admission, Median (IQR)	17 (13 - 25)	9 (7 - 11)	20 (11 - 26)	30 (20 - 35)	12 (4 - 22)	11 (8.5-17.5)
SAPS III at ICU admission[a], Median (IQR)	60 (52 - 71)	49 (43 - 58)	55 (50 - 62)	67 (49 - 86)	49.5 (38 - 66.5)	52 (46 - 60)
SOFA at ICU admission, Median (IQR)	6 (3 - 8)	2 (1 - 4)	5 (3 - 9)	9 (7 - 12)	4 (1 - 7)	2 (0.5 - 2.5)
Number of Hs at ICU admission, n (%)						
Zero	17 (26.6)	13 (50)	4 (19)	3 (15.8)	5 (38.5)	5 (41.7)
One	14 (21.9)	3 (11.5)	7 (33.3)	3 (15.8)	6 (46.2)	6 (50)
Two	16 (25)	6 (23.1)	6 (28.6)	2 (10.5)	1 (7.7)	1 (8.3)
Three or more	17 (26.6)	4 (15.4)	4 (19)	11 (57.9)	1 (7.7)	0 (0)
Length of ICU stay until 30th day, Median (IQR)	5.5 (3 - 12)	8 (5 - 15)	3 (2 - 17)	6 (4 - 12)	3.5 (1.5 - 15.5)	3 (2 - 4)
30-day mortality, n (%)	20 (31.3)	5 (19.2)	3 (14.3)	11 (57.9)	1 (7.7)	1 (8.3)
m-RS on ICU outcome or until 30th day, n (%)						
0	6 (9.4)	2 (7.7)	4 (19)	0 (0)	4 (30.8)	2 (16.7)
1	6 (9.4)	2 (7.7)	3 (14.3)	0 (0)	3 (23.1)	2 (16.7)
2	4 (6.3)	7 (26.9)	1 (4.8)	0 (0)	1 (7.7)	3 (25)
3	9 (14.1)	1 (3.8)	2 (9.5)	2 (10.5)	1 (7.7)	1 (8.3)
4	10 (15.6)	6 (23.1)	2 (9.5)	3 (15.8)	2 (15.4)	1 (8.3)
5	9 (14.1)	3 (11.5)	6 (28.6)	3 (15.8)	1 (7.7)	2 (16.7)
6	20 (31.3)	5 (19.2)	3 (14.3)	11 (57.9)	1 (7.7)	1 (8.3)
Unfavourable outcome (m-RS score 4, 5, or 6), n (%)	39 (60.9)	14 (53.8)	11 (52.4)	17 (89.5)	4 (30.8)	4 (33.3)

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation; ENC, encephalopathy; GCS, Glasgow Coma Scale; ICH, intracerebral haemorrhage; IQR, interquartile range; IS, ischaemic stroke; m-RS, modified Rankin Scale; n, absolute frequency; NMD, neuromuscular disease; NPO, postoperative care of elective neurosurgery; SAH, subarachnoid haemorrhage; SAPS III, Simplified Acute Physiology Score III; SCI, spinal cord injury; SD, standard deviation; SNI, central nervous system infection; SOFA, Sequential Organ Failure Assessment; TBI, traumatic brain injury; %, percentage within column.

[a] Missing data on SAPS III: 1 on drug-induced encephalopathy.

5 DISCUSSÃO

O Estudo Neurocrítico Brasil revelou uma epidemiologia abrangente de pacientes neurocríticos e o impacto da internação em UTI sobre essa população de pacientes. Esses pacientes representaram mais de um quarto de todas as internações de pacientes críticos (28,1%) e apresentaram uma taxa de mortalidade 1,7 vezes maior do que os pacientes não neurocríticos, achado que não foi explicado pelos escores de gravidade. Outros estudos também mostraram aumento da mortalidade entre pacientes neurocríticos em comparação com outros pacientes de UTI. (MAYR et al., 2006) Os escores de gravidade parecem discriminar em grau semelhante a ocorrência de doença grave em pacientes neurocríticos e não neurocríticos, mas a razão pela qual os pacientes neurocríticos apresentam piores desfechos do que os não neurocríticos, apesar de apresentarem escores (GLASGOW Scale, APACHE II e SOFA) semelhantes, deve-se a fatores não captados nas primeiras horas de internação na UTI, quando esses escores são medidos, incluindo maior tempo de internação hospitalar e maior número de complicações e disfunções de órgãos não neurológicos. (VINCENT; MORENO, 2010; ZYGUN et al., 2006)

Temos hoje um melhor conhecimento da epidemiologia de pacientes neurocríticos do que tínhamos antes, (VENKATASUBBA RAO et al., 2020) não apenas em relação à sua prevalência total e relativa, mas também em relação à forma como diferem de outros pacientes críticos em termos demográficos, gravidade clínica, uso de recursos de UTI e desfechos. Como a carga de doença é uma medida da prevalência e gravidade de uma doença, simplesmente não é possível estimar essa medida sem conhecer a epidemiologia da doença. (STEENLAND; ARMSTRONG, 2006) Embora a carga de doenças neurológicas tenha sido melhor estimada nos últimos 20 anos, (DEUSCHL et al., 2020; FEIGIN et al., 2021) a carga de doenças neurocríticas permaneceu essencialmente desconhecida até o momento. (ADHIKARI et al., 2010) Essa foi a principal força motriz por trás do desenho do Estudo Neurocríticos Brasil; foi fundamental conhecer primeiro a epidemiologia de pacientes neurocríticos antes de estimar sua carga de doença. (“Epidemiology is a science of high importance.”, 2018)

A condição neurológica mais comum para a internação na UTI neste estudo foi o cuidado pós-operatório de neurocirurgia eletiva, que teve um impacto relativamente pequeno nos DALYs. Em contraste, pacientes com doenças cerebrovasculares,

encefalopatia e, particularmente, traumatismo cranioencefálico também foram frequentemente admitidos nas UTIs e impuseram um impacto substancial nos DALYs. A lesão cerebral traumática é a condição neurológica crítica com pior impacto nos DALYs durante e após a internação na UTI. Como mostrado no presente estudo, os DALYs variam significativamente com o diagnóstico neurológico primário, sexo, faixa etária e lesões secundárias. Também demonstramos um claro impacto negativo das lesões secundárias no prognóstico. É importante ressaltar que o aumento do número de lesões secundárias aumenta progressivamente o risco de pior prognóstico. (FONTAINE et al., 2020; VOLPI et al., 2018) Quando analisada individualmente, cada lesão neurológica secundária esteve associada a pior prognóstico e aumento dos DALYs. Isso indica uma clara janela de oportunidade para o controle de possíveis lesões secundárias durante as primeiras horas da lesão neurológica, com um enorme impacto benéfico na diminuição da carga de doenças neurológicas agudas graves.

As condições neurocríticas são conhecidas por sobrecarregar fortemente o mundo em desenvolvimento. Apesar da falta de recursos para a saúde de base populacional na maioria dos países em desenvolvimento, há uma demanda crescente por estratégias intensivas em recursos para cuidados neurológicos agudos. (MATEEN, 2011) O presente estudo demonstrou claramente que as condições neurocríticas são comuns em UTIs e apresentam DALYs muito elevados. Algumas estratégias que poderiam ajudar a reduzir eficientemente o impacto social e econômico de doenças neurocríticas incluem maior prevenção de doenças cerebrovasculares, maior segurança no trânsito para reduzir o risco de acidentes e ênfase na prevenção de possíveis lesões secundárias a uma lesão cerebral primária grave.

Conhecer como essas diferentes variáveis interagem para exacerbar o risco de doenças neurocríticas é essencial para implementar uma melhor educação e melhores ações políticas e sociais para minimizar suas consequências negativas e melhorar os resultados e a saúde social. Para alcançar esses objetivos primordiais, estudos que forneçam melhores informações sobre a epidemiologia de pacientes críticos e estimem a carga de doença são apenas o começo. (CERRO; CHECKLEY, 2014)

Este estudo apresenta algumas limitações importantes. Todos os nossos pacientes foram admitidos em UTIs no Brasil, e resultados diferentes devem ser esperados em outros países, como demonstrado no Estudo PRINCE. (SUAREZ et al., 2020; VENKATASUBBA RAO et al., 2020) O seguimento de nossos pacientes foi limitado

a 30 dias, e alguns pacientes permaneceram na UTI por um período mais longo; assim, sua mortalidade estimada e DALYs podem ter sido menores do que as reais. Como as informações sobre a carga da doença em pacientes críticos ainda estão surgindo, muitos desafios ainda precisam ser resolvidos, e a compreensão dos resultados a longo prazo desses pacientes é fundamental para estimativas mais precisas. Mais estudos também são necessários para determinar quais intervenções e componentes da organização da UTI levarão a melhores resultados centrados no paciente e na sociedade.

6 CONCLUSÃO

1. O Estudo NeuroCríticos Brasil descreve de forma detalhada, acurada e abrangente a epidemiologia dos pacientes neurocríticos internados em UTIs brasileiras. Tanto a população global de pacientes neurocríticos, quanto suas divisões em dez diferentes condições neurocríticas, foram descritas e analisadas sistematicamente com relação a suas características demográficas, condições clínicas iniciais, evolução durante o internamento, intervenções recebidas e desfechos até 30 dias do internamento;

2. Conhecida a epidemiologia, foi possível aferir a carga de doença dos pacientes neurocríticos, analisar suas diferenças relativas e estimar o impacto individual e social dessa importante condição clínica;

3. Assim, o Estudo NeuroCríticos Brasil atinge o objetivo da sua força motriz original de fornecer uma base epidemiológica confiável para a desenvolvimento de programas mais eficientes de educação dos profissionais de saúde, no delineamento de melhores pesquisas clínicas e na promoção de políticas públicas que minimizem os graves efeitos das doenças neurológicas agudas.

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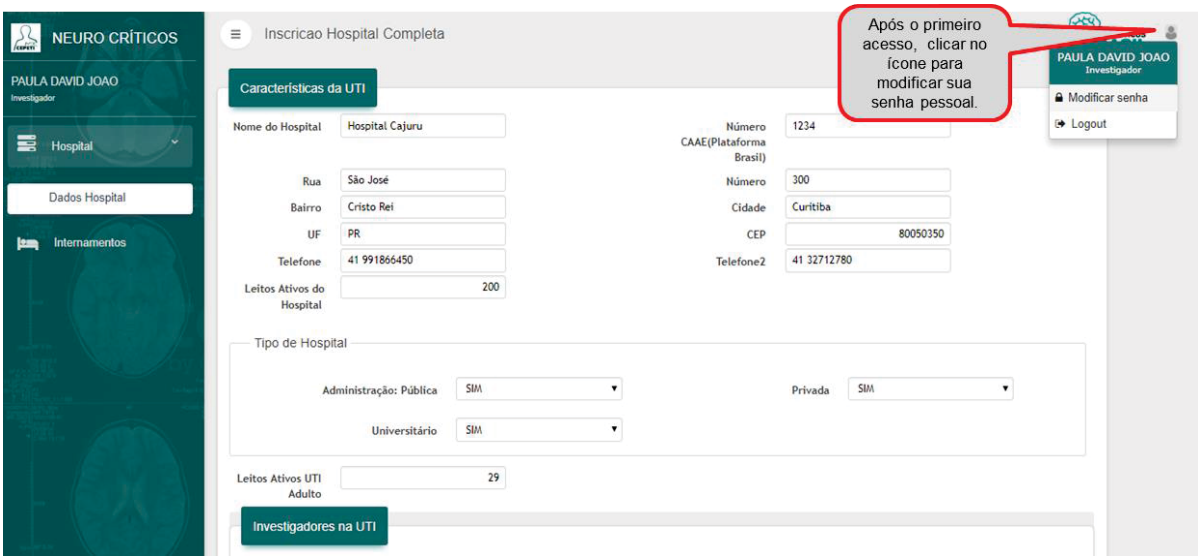
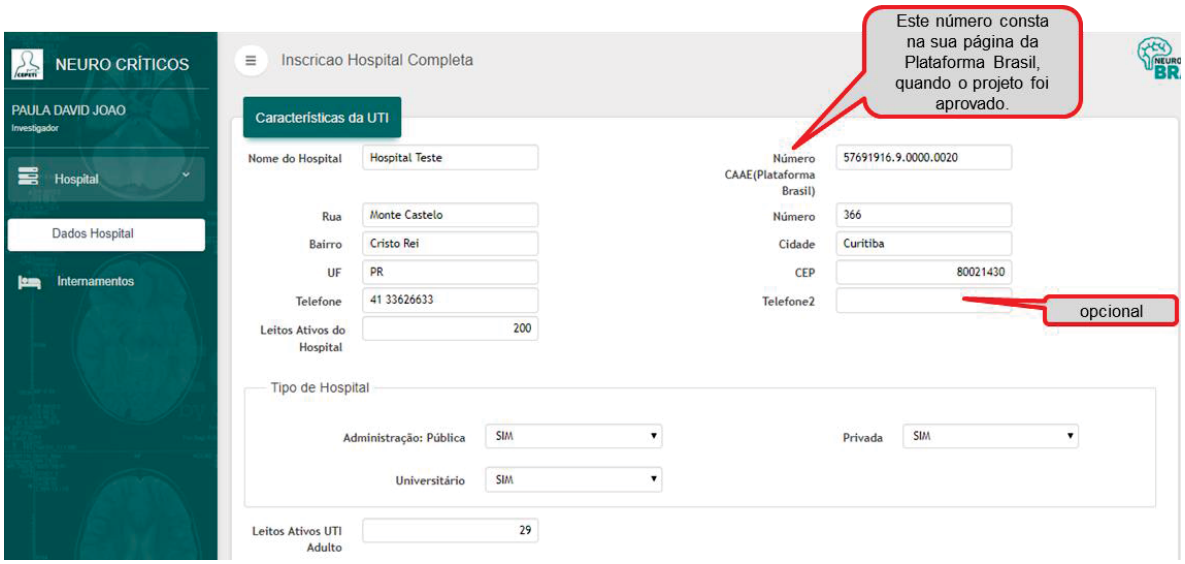
APÊNDICE 1 – FORMULÁRIO DE CADASTRO DAS UTIS PARTICIPANTES NA E-CRF DO ESTUDO NCB




Alterar Minha Senha
Alterar Senha
Usuário
paula_gdj@yahoo.com.br
Senha Atual
Nova Senha
Confirmar Nova Senha
CONFIRMAR
FECHAR
Repetir a senha do primeiro acesso
Escolher uma senha de preferência pessoal e depois CONFIRMAR


Alterar Minha Senha
Alterar Senha
Usuário
paula_gdj@yahoo.com.br
Senha Atual
Nova Senha
Confirmar Nova Senha
FECHAR
Após esta mensagem aparecer no canto superior direito da tela, clique em FECHAR.


NEURO CRÍTICOS
PAULA DAVID JOAO
Investigador
Hospital
Dados Hospital
Internamentos
Inscricao Hospital Completa
Este número consta na sua página da Plataforma Brasil, quando o projeto foi aprovado.
Características da UTI
Nome do Hospital
Hospital Teste
Número CAAE(Plataforma Brasil)
57691916.9.0000.0020
Rua
Monte Castelo
Número
366
Bairro
Cristo Rei
Cidade
Curitiba
UF
PR
CEP
80021430
Telefone
41 33626633
Telefone2
opcional
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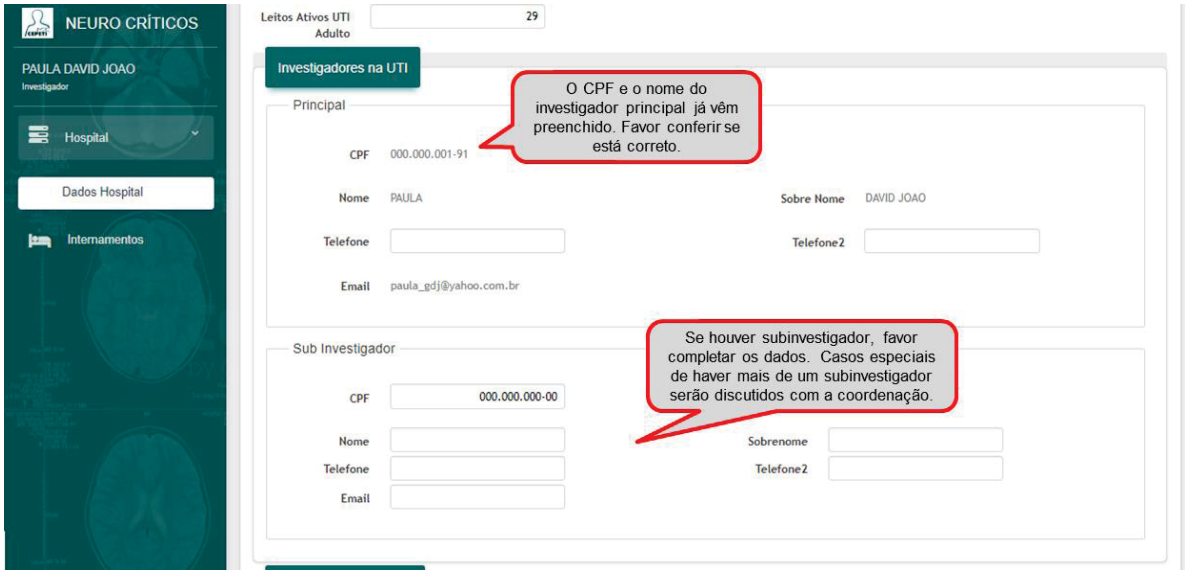
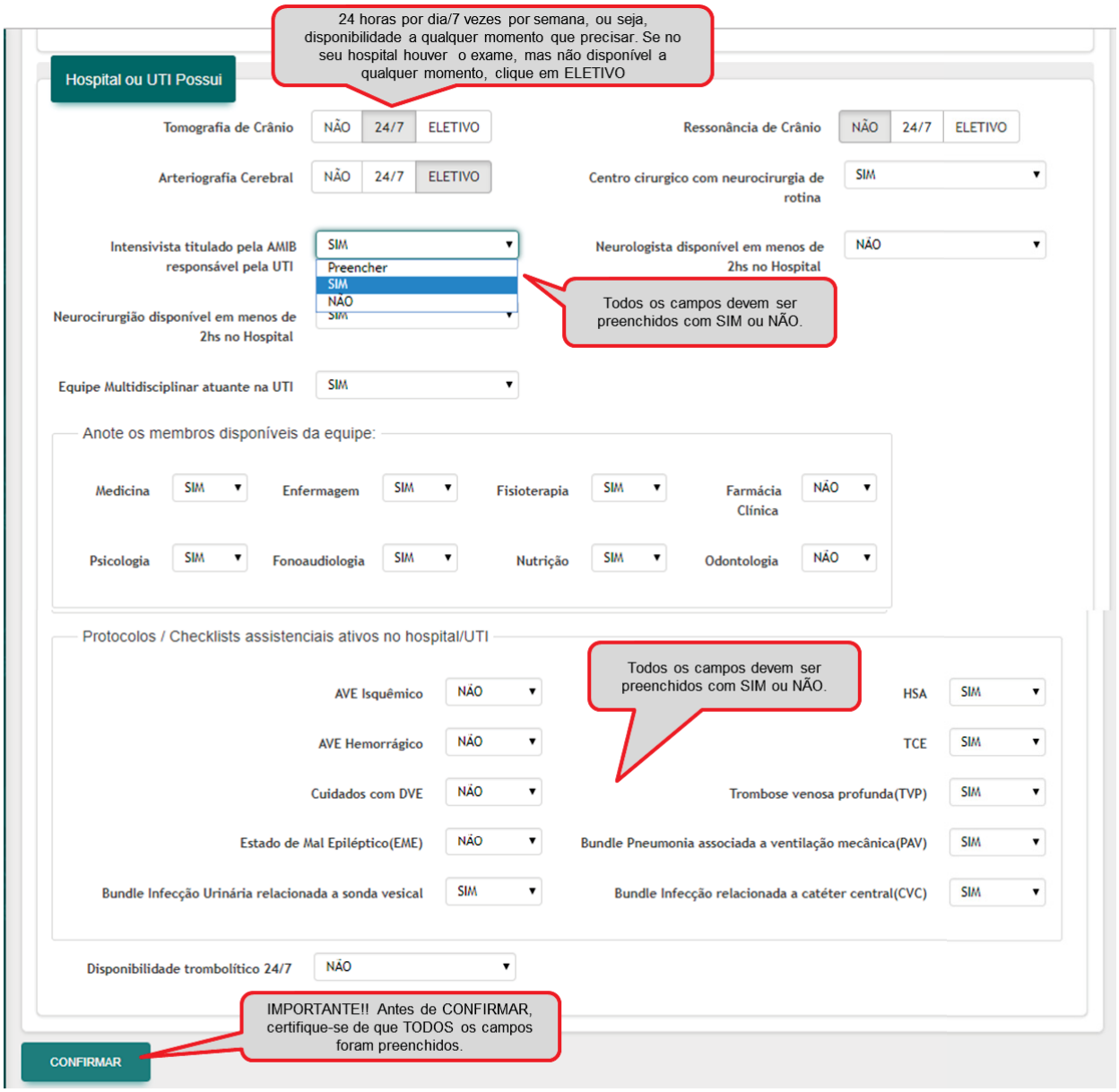
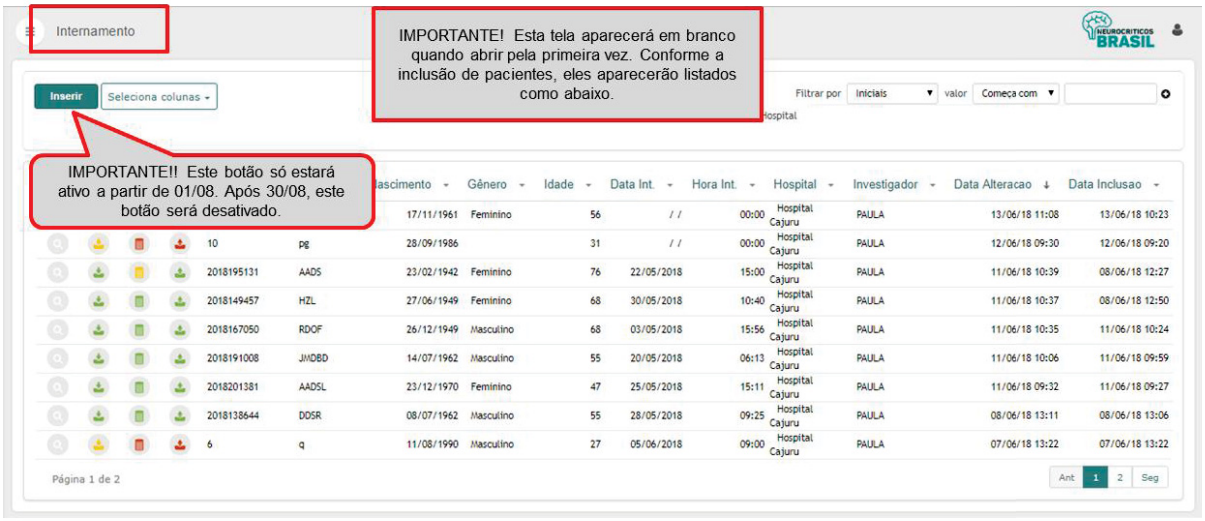
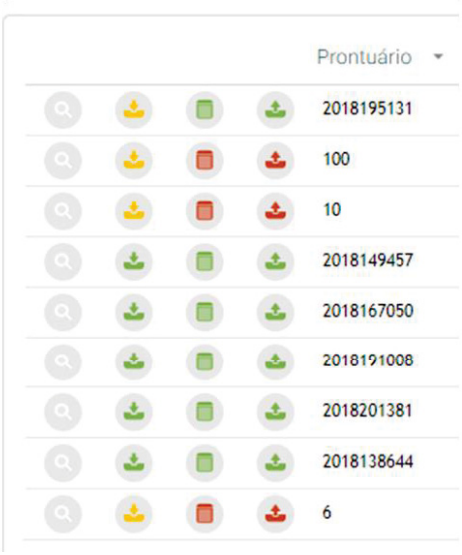
Tipo de Hospital
Administração: Pública
SIM
Privada
SIM
Universitário
SIM
Leitos Ativos UTI Adulto
29


NEURO CRÍTICOS
PAULA DAVID JOAO
Investigador
Hospital
Dados Hospital
Internamentos
Leitos Ativos UTI Adulto
29
Investigadores na UTI
Principal
O CPF e o nome do investigador principal já vêm preenchido. Favor conferir se está correto.
CPF
000.000.001-91
Nome
PAULA
Sobre Nome
DAVID JOAO
Telefone
Telefone2
Email
paula_gdj@yahoo.com.br
Sub Investigador
Se houver subinvestigador, favor completar os dados. Casos especiais de haver mais de um subinvestigador serão discutidos com a coordenação.
CPF
000.000.000-00
Nome
Sobrenome
Telefone
Telefone2
Email


24 horas por dia/7 vezes por semana, ou seja, disponibilidade a qualquer momento que precisar. Se no seu hospital houver o exame, mas não disponível a qualquer momento, clique em ELETIVO
Hospital ou UTI Possui
Tomografia de Crânio
NÃO
24/7
ELETIVO
Ressonância de Crânio
NÃO
24/7
ELETIVO
Arteriografia Cerebral
NÃO
24/7
ELETIVO
Centro cirurgico com neurocirurgia de rotina
SIM
Intensivista titulado pela AMIB responsável pela UTI
SIM
Preencher
SIM
NÃO
Neurologista disponível em menos de 2hs no Hospital
NÃO
Neurocirurgião disponível em menos de 2hs no Hospital
Todos os campos devem ser preenchidos com SIM ou NÃO.
Equipe Multidisciplinar atuante na UTI
SIM
Anote os membros disponíveis da equipe:
Medicina
SIM
Enfermagem
SIM
Fisioterapia
SIM
Farmácia Clínica
NÃO
Psicologia
SIM
Fonoaudiologia
SIM
Nutrição
SIM
Odontologia
NÃO
Protocolos / Checklists assistenciais ativos no hospital/UTI
Todos os campos devem ser preenchidos com SIM ou NÃO.
AVE Isquêmico
NÃO
HSA
SIM
AVE Hemorrágico
NÃO
TCE
SIM
Cuidados com DVE
NÃO
Trombose venosa profunda(TVP)
SIM
Estado de Mal Epiléptico(EME)
NÃO
Bundle Pneumonia associada a ventilação mecânica(PAV)
SIM
Bundle Infecção Urinária relacionada a sonda vesical
SIM
Bundle Infecção relacionada a catéter central(CVC)
SIM
Disponibilidade trombolítico 24/7
NÃO
IMPORTANTE!! Antes de CONFIRMAR, certifique-se de que TODOS os campos foram preenchidos.
CONFIRMAR





Vermelho: nenhum preenchimento

Amarelo: ficha incompleta

Verde: ficha completa

APÊNDICE 2 – CONVITE ENVIADO ÀS UTIS CADASTRADAS NA AMIB-NET

Curitiba, 21 de fevereiro de 2018.

Prezado(a) colega,

Gostaríamos de convidá-lo(a) a participar do seguinte estudo:

Coorte Nacional de Pacientes Neurocríticos Internados em Unidades de Terapia Intensiva no Brasil (NeuroCríticos Brasil)

Este é um estudo de coorte, multicêntrico, com o objetivo de conhecer os pacientes neurocríticos internados nos hospitais brasileiros.

Descrever e analisar a distribuição dos pacientes neurocríticos no Brasil, os seus principais diagnósticos primários, os recursos utilizados no seu tratamento e a suas respectivas evoluções, serão fundamentais para conhecer a magnitude do problema e dirigir educação e investimento nesta importante área da Medicina Intensiva.

Todos os centros participantes do Brasil, no mesmo período, coletarão dados de todos os pacientes internados na UTI no período 30 dias consecutivos (provavelmente em abril de 2018), cujo motivo de internação seja um diagnóstico neurológico primário, tendo acompanhamento por 30 dias ou até a alta hospitalar ou óbito. O projeto já foi aprovado pelo Comitê de Ética em Pesquisa do Hospital Instituto de Neurologia de Curitiba (Parecer nº 2.059.086), o qual é vinculado ao centro coordenador CEPETI - Centro de Estudos e Pesquisas em Terapia Intensiva, em Curitiba.

Os investigadores de todos os centros participantes (dois a três por instituição) serão listados ao final da publicação ou em material suplementar, dependendo da política editorial de cada periódico. A listagem ocorrerá por ordem alfabética dos centros.

Caso aceite participar do estudo, favor realizar cadastro no site: www.neurocriticosbrasil.com.br e para qualquer informação adicional, contatar: contato@neurocriticosbrasil.com.br

Sua contribuição será muito valiosa para o sucesso desse projeto.

Atenciosamente,

Investigador Principal

Dr. Álvaro Réa-Neto

Professor Adjunto de Medicina do Departamento de Clínica Médica da UFPR

Diretor do CEPETI - Centro de Estudos e Pesquisas em Emergências e Terapia Intensiva

Consultores

Dr. Antônio Luís Eiras Falcão

Coordenador da Disciplina de Fisiologia e Metabologia Cirúrgica da FCM-UNICAMP

UTI/HC/UNICAMP

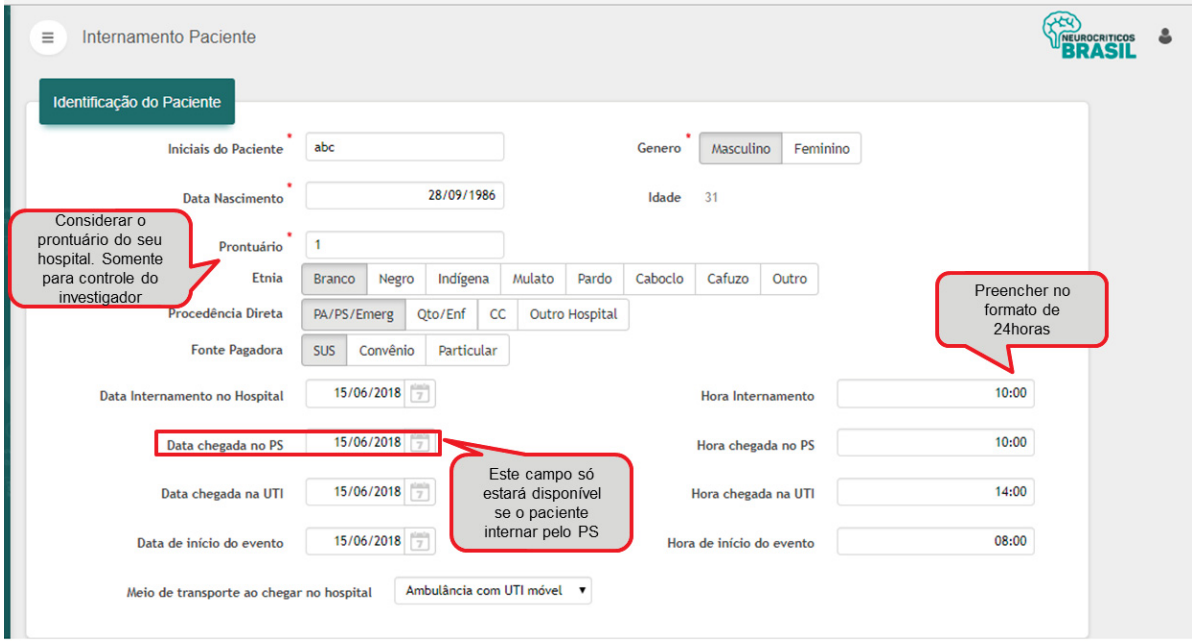
Dr. Pedro Kurtz

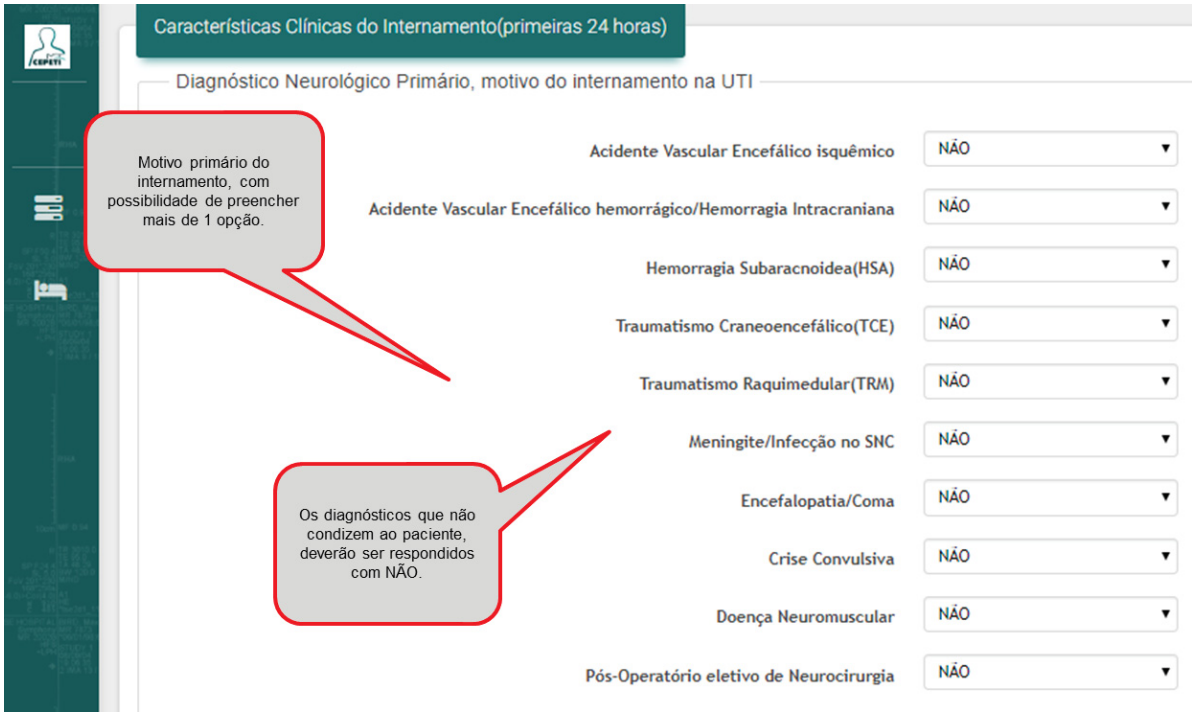
Diretor Clínico e Supervisor da Neuro UTI do Instituto Estadual do Cérebro Paulo Niemeyer (IECPN)

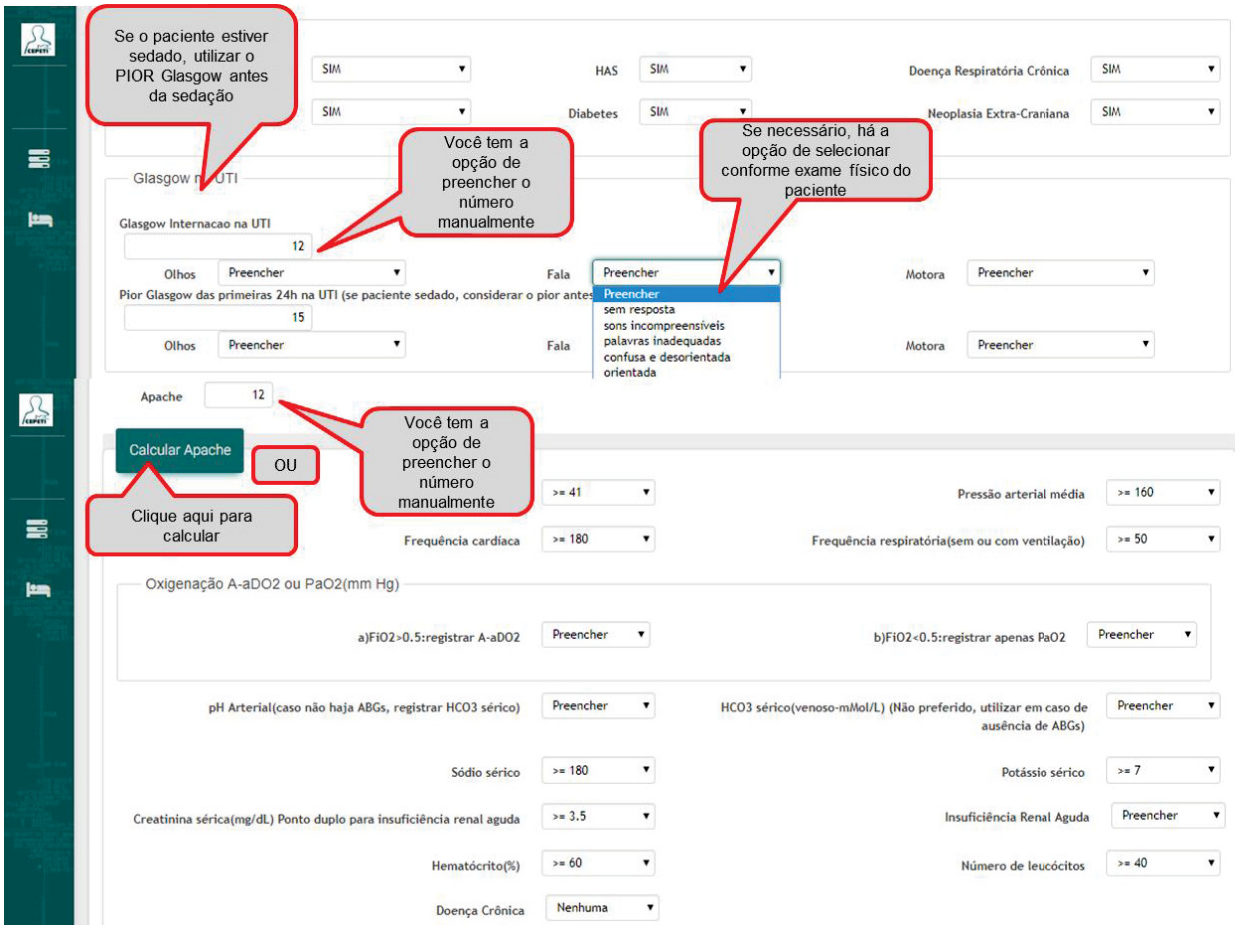
Realização:

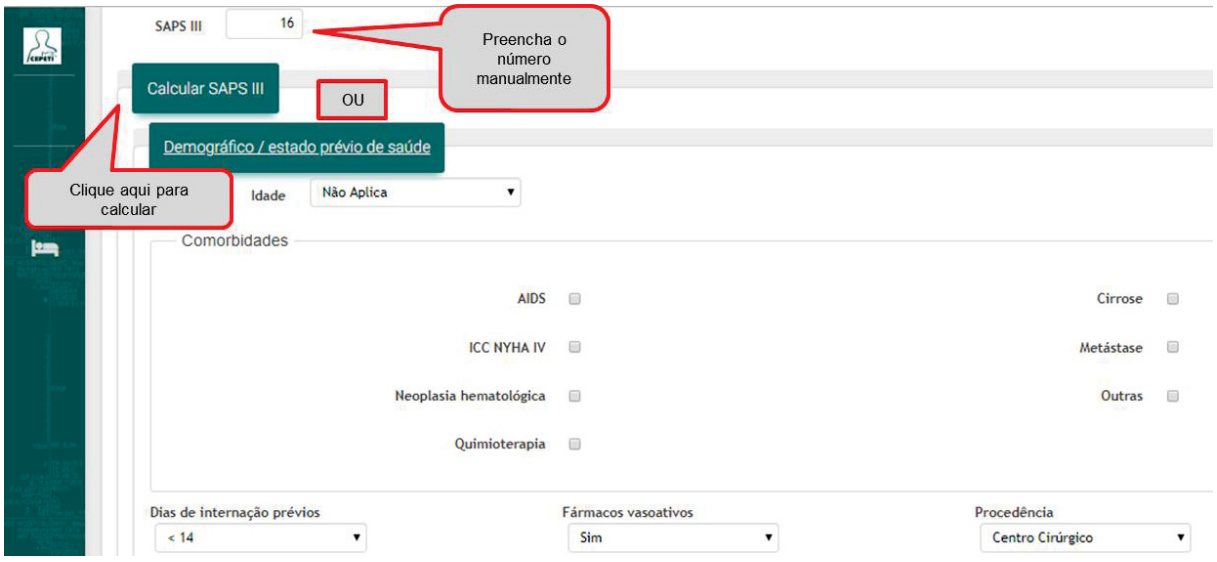
Apoio:

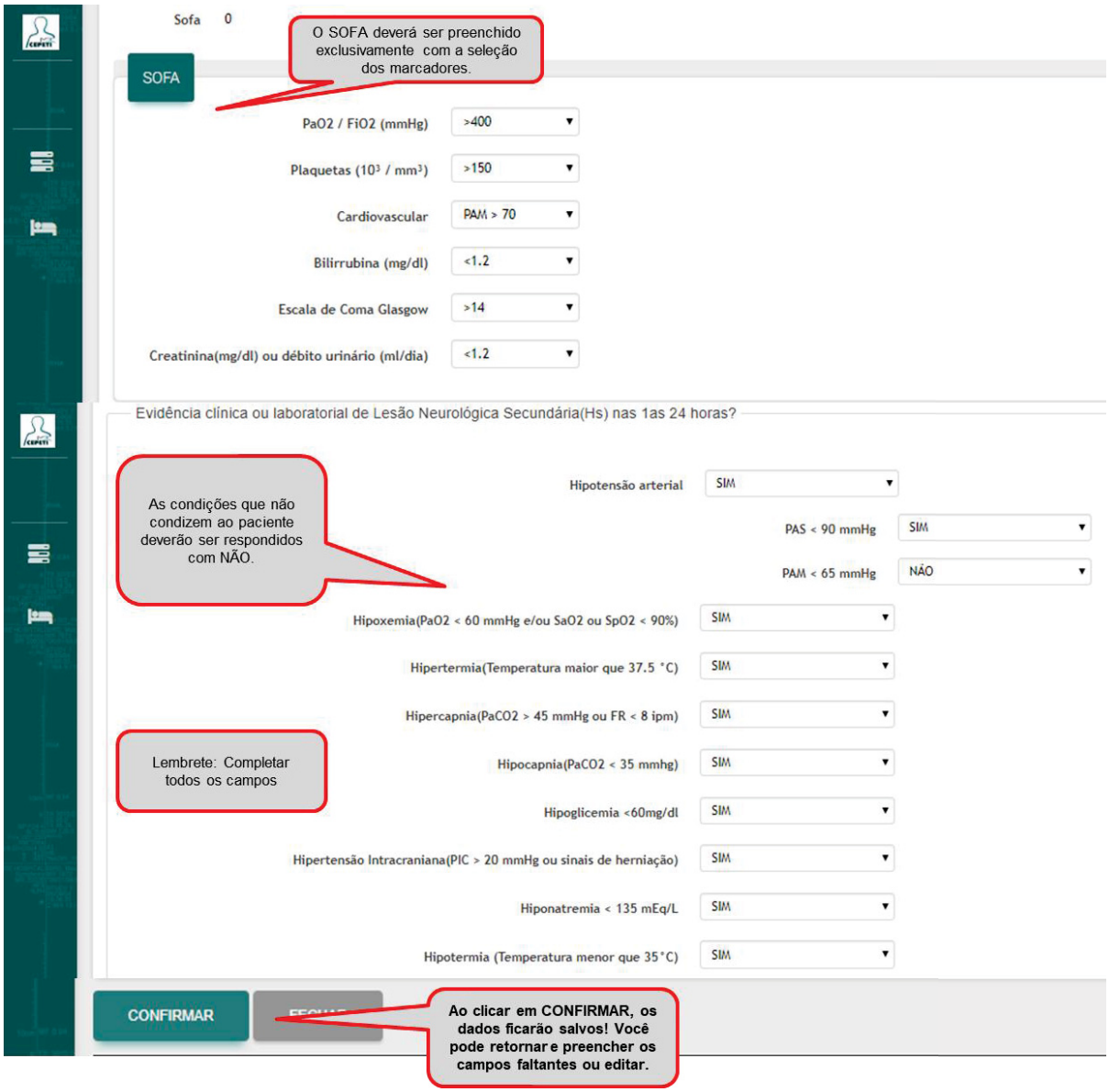
APÊNDICE 3 – FORMULÁRIO DE INTERNAMENTO DO PACIENTE E CARACTERÍSTICAS CLÍNICAS DE INTERNAMENTO NA UTI



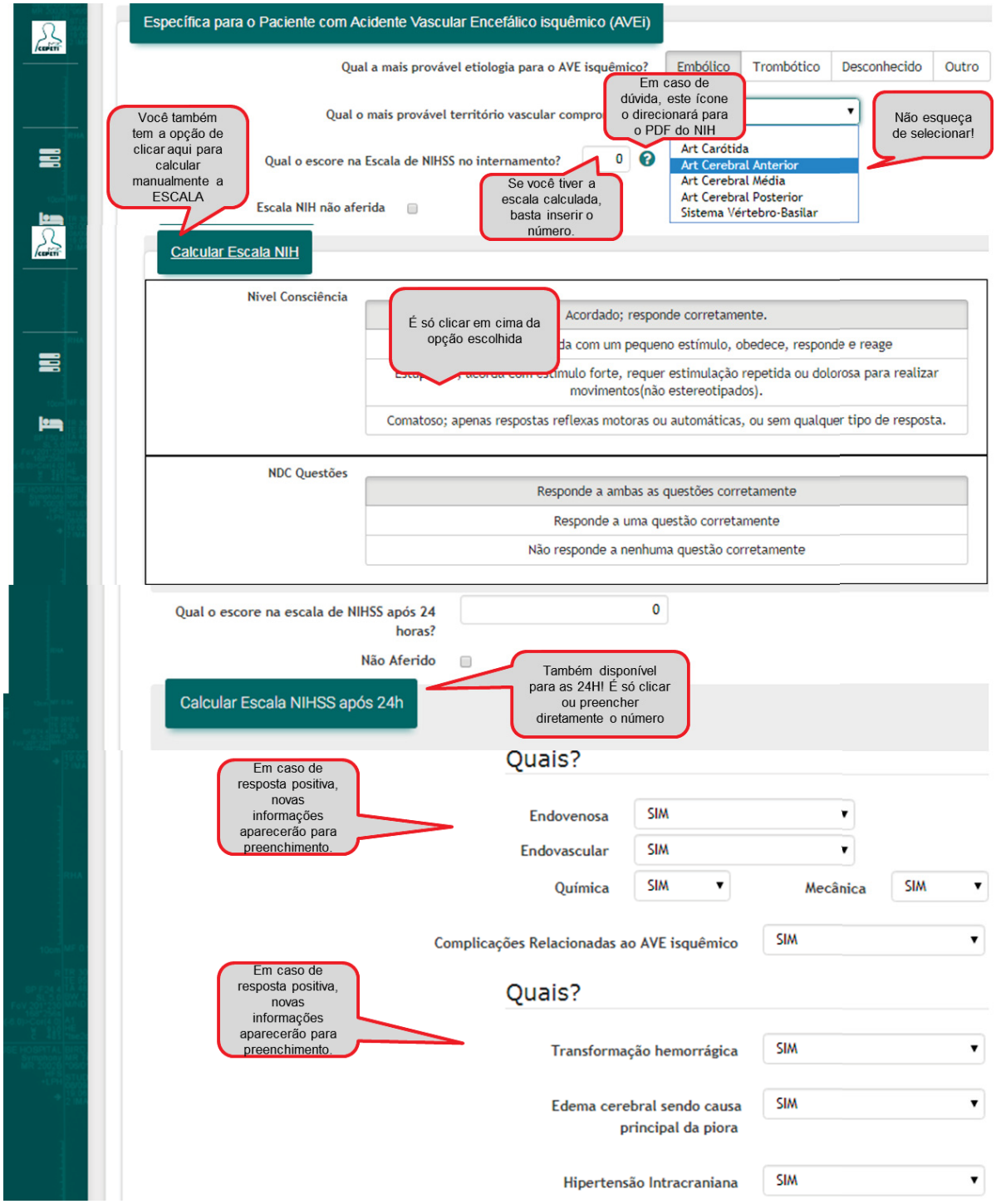



Se o paciente estiver sedado, utilizar o PIOR Glasgow antes da sedação
Você tem a opção de preencher o número manualmente
Se necessário, há a opção de selecionar conforme exame físico do paciente
Glasgow Internacao na UTI
12
Olhos
Preencher
Fala
Preencher
sem resposta
sons incompreensíveis
palavras inadequadas
confusa e desorientada
orientada
Motora
Pior Glasgow das primeiras 24h na UTI (se paciente sedado, considerar o pior antes
15
Apache
12
Calcular Apache
OU
Você tem a opção de preencher o número manualmente
Clique aqui para calcular
Pressão arterial média
Frequência cardíaca
Frequência respiratória(sem ou com ventilação)
Oxigenação A-aDO2 ou PaO2(mm Hg)
a)FiO2>0.5:registrar A-aDO2
b)FiO2<0.5:registrar apenas PaO2
pH Arterial(caso não haja ABGs, registrar HCO3 sérico)
HCO3 sérico(venoso-mMol/L) (Não preferido, utilizar em caso de ausência de ABGs)
Sódio sérico
Potássio sérico
Creatinina sérica(mg/dL) Ponto duplo para insuficiência renal aguda
Insuficiência Renal Aguda
Hematócrito(%)
Número de leucócitos
Doença Crônica
Nenhuma

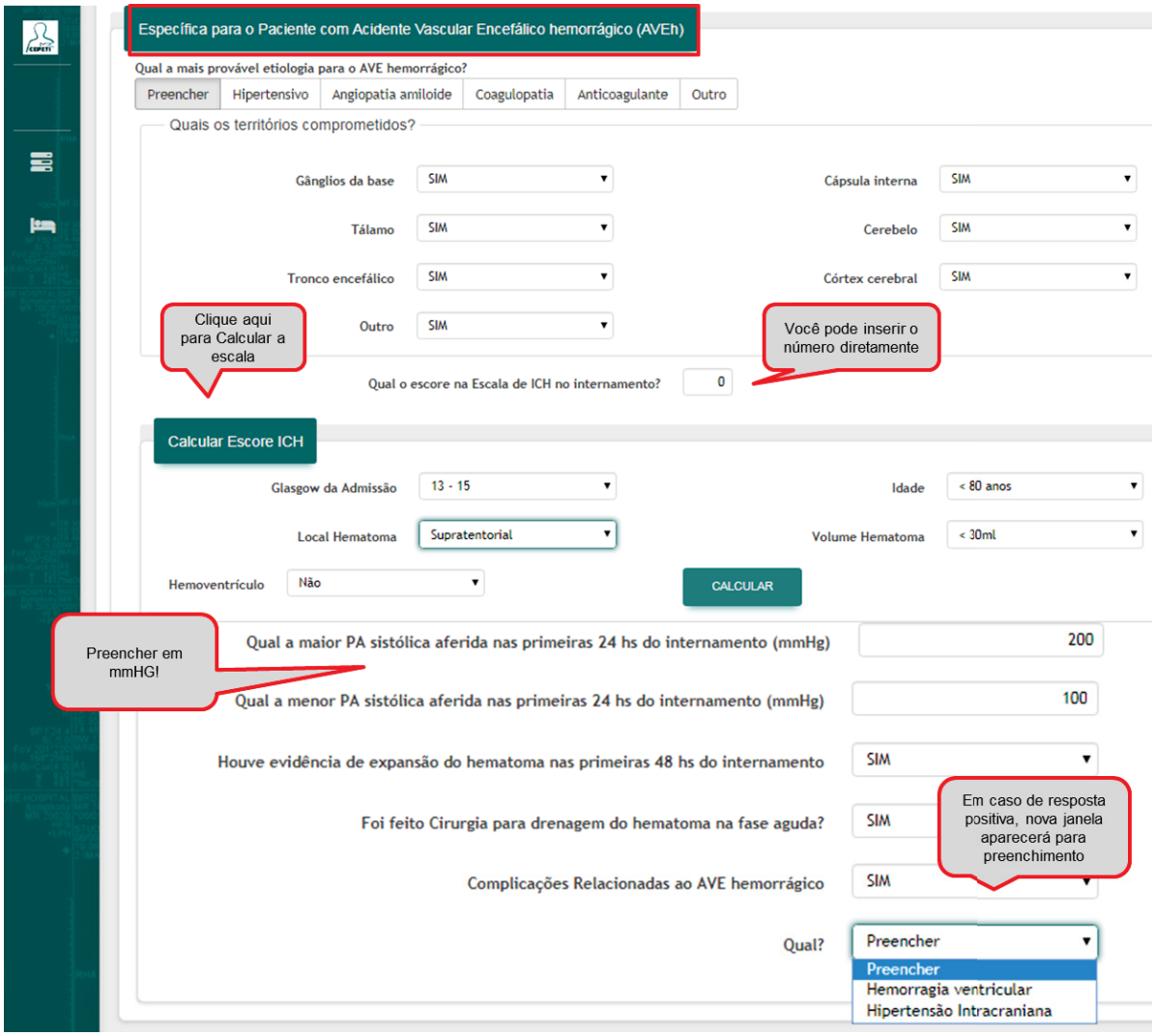

SAPS III
16
Preencha o número manualmente
Calcular SAPS III
OU
Demográfico / estado prévio de saúde
Clique aqui para calcular
Idade
Não Aplica
Comorbidades
AIDS
Cirrose
ICC NYHA IV
Metástase
Neoplasia hematológica
Outras
Quimioterapia
Dias de internação prévios
< 14
Fármacos vasoativos
Sim
Procedência
Centro Cirúrgico


Sofa 0
O SOFA deverá ser preenchido exclusivamente com a seleção dos marcadores.
SOFA
PaO2 / FiO2 (mmHg) >400
Plaquetas (10³ / mm³) >150
Cardiovascular PAM > 70
Bilirrubina (mg/dl) <1.2
Escala de Coma Glasgow >14
Creatinina(mg/dl) ou débito urinário (ml/dia) <1.2
Evidência clínica ou laboratorial de Lesão Neurológica Secundária(Hs) nas 1as 24 horas?
As condições que não condizem ao paciente deverão ser respondidos com NÃO.
Hipotensão arterial SIM
PAS < 90 mmHg SIM
PAM < 65 mmHg NÃO
Hipoxemia(PaO2 < 60 mmHg e/ou SaO2 ou SpO2 < 90%) SIM
Hipertermia(Temperatura maior que 37.5 °C) SIM
Hipercapnia(PaCO2 > 45 mmHg ou FR < 8 ipm) SIM
Lembrete: Completar todos os campos
Hipocapnia(PaCO2 < 35 mmhg) SIM
Hipoglicemia <60mg/dl SIM
Hipertensão Intracraniana(PIC > 20 mmHg ou sinais de herniação) SIM
Hiponatremia < 135 mEq/L SIM
Hipotermia (Temperatura menor que 35°C) SIM
CONFIRMAR
Ao clicar em CONFIRMAR, os dados ficarão salvos! Você pode retornar e preencher os campos faltantes ou editar.

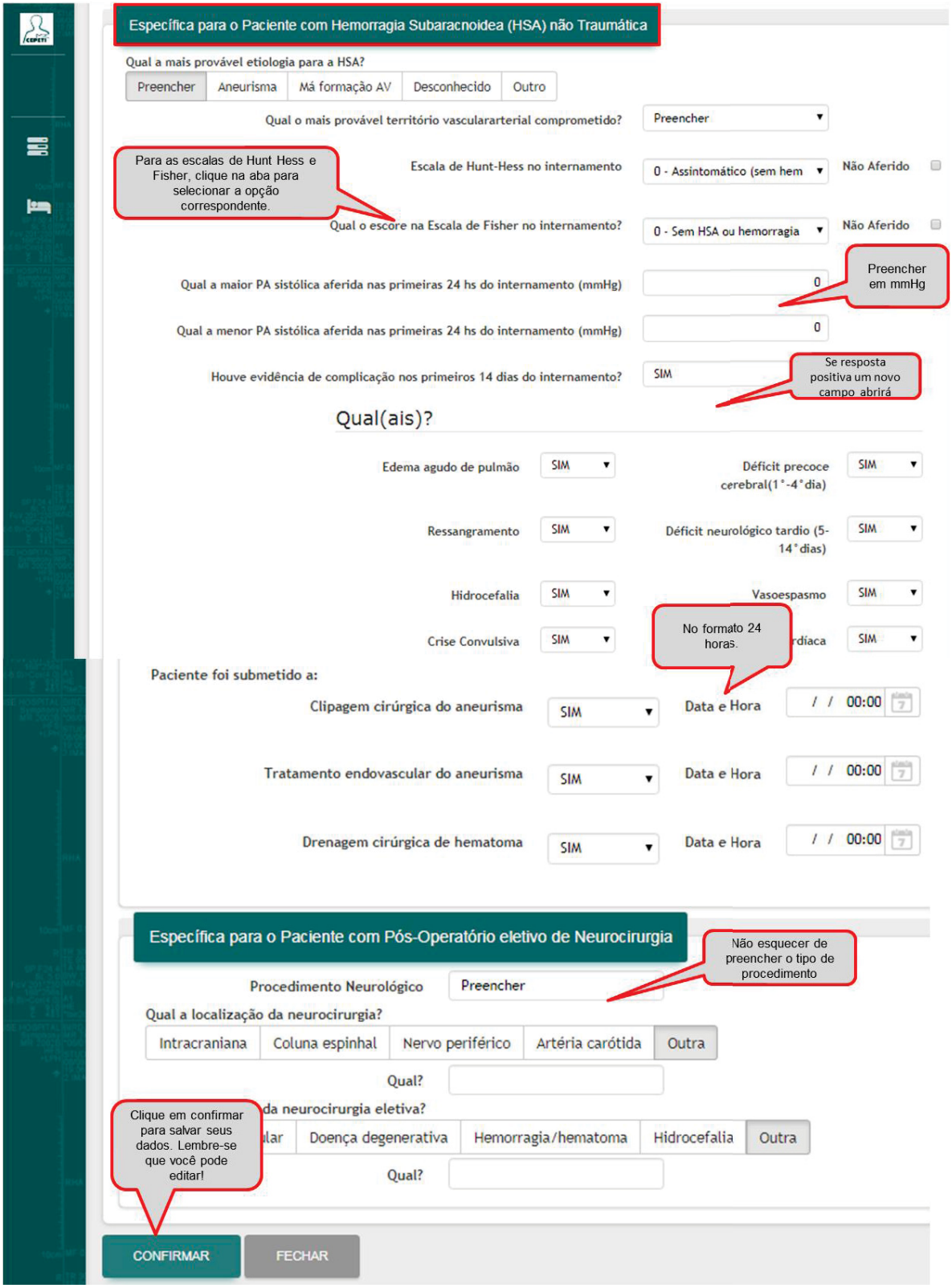
APÊNDICE 4 – FORMULÁRIO PARA PARTICIPANTES COM DIAGNÓSTICO PRIMÁRIO DE ACIDENTE VASCULAR ENCEFÁLICO ISQUÊMICO



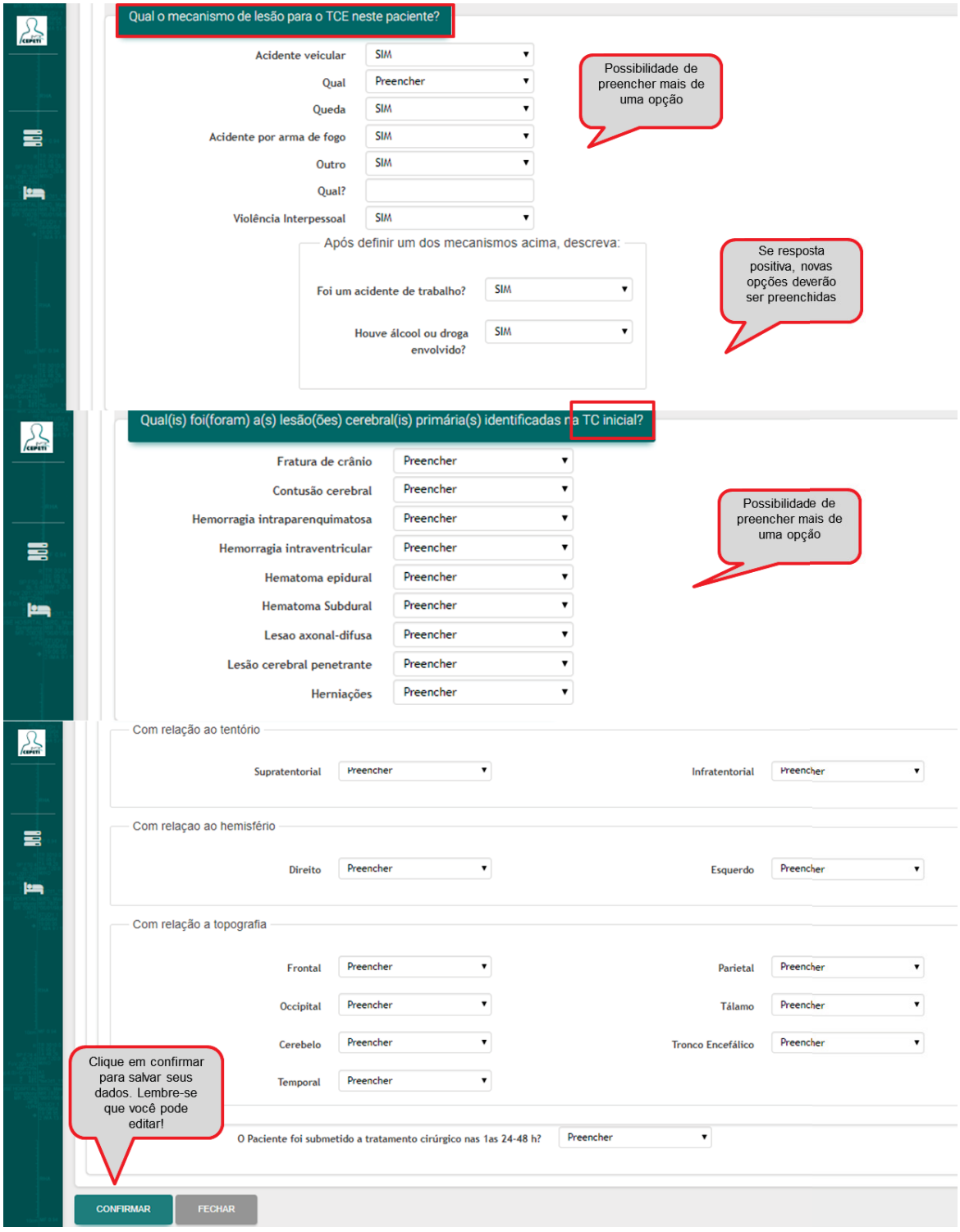
APÊNDICE 5 – FORMULÁRIO PARA PARTICIPANTES COM DIAGNÓSTICO PRIMÁRIO DE ACIDENTE VASCULAR ENCEFÁLICO HEMORRÁGICO



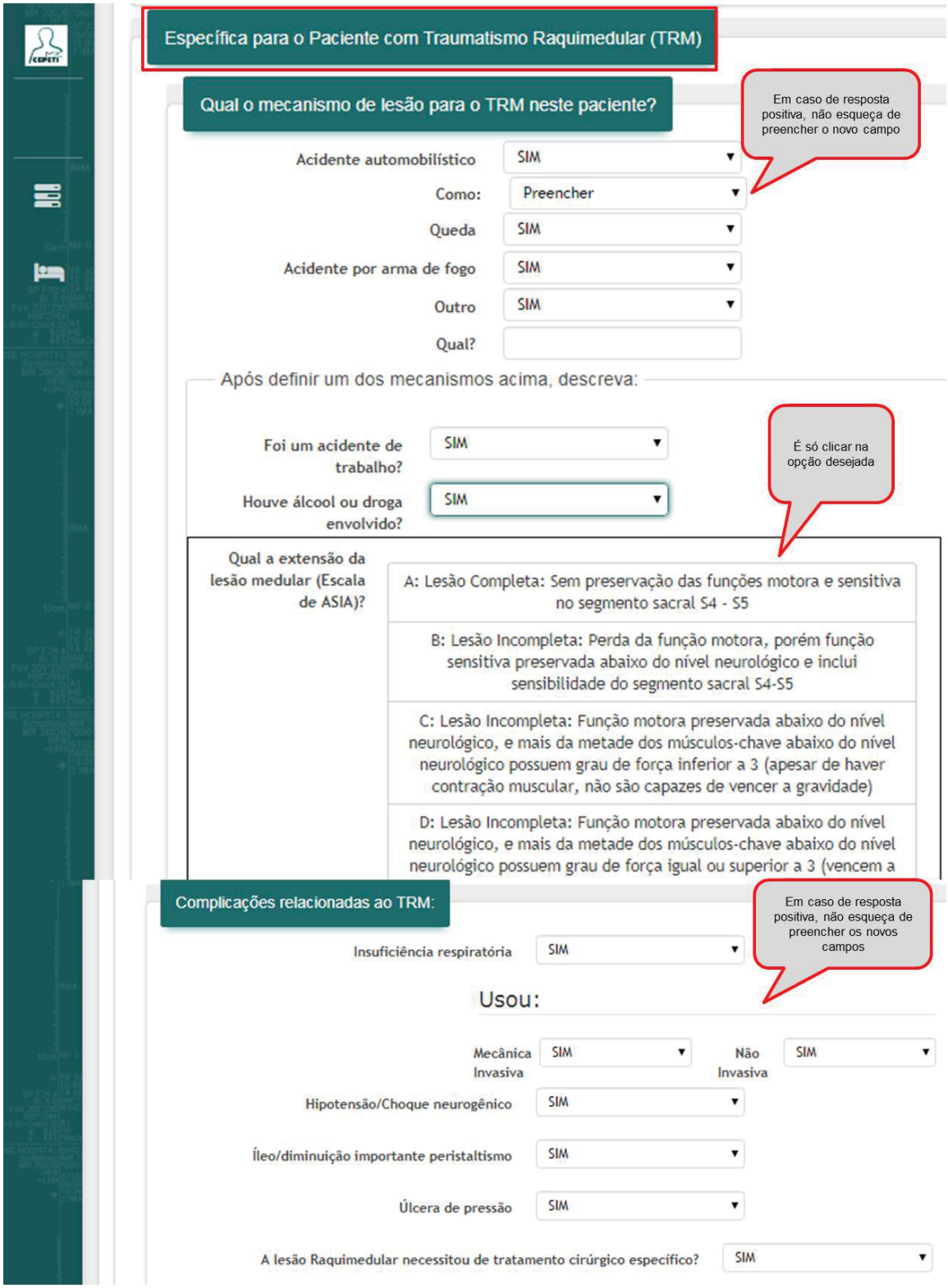
APÊNDICE 6 – FORMULÁRIO PARA PARTICIPANTES COM DIAGNÓSTICO PRIMÁRIO DE HEMORRAGIA SUBARACNOIDEA



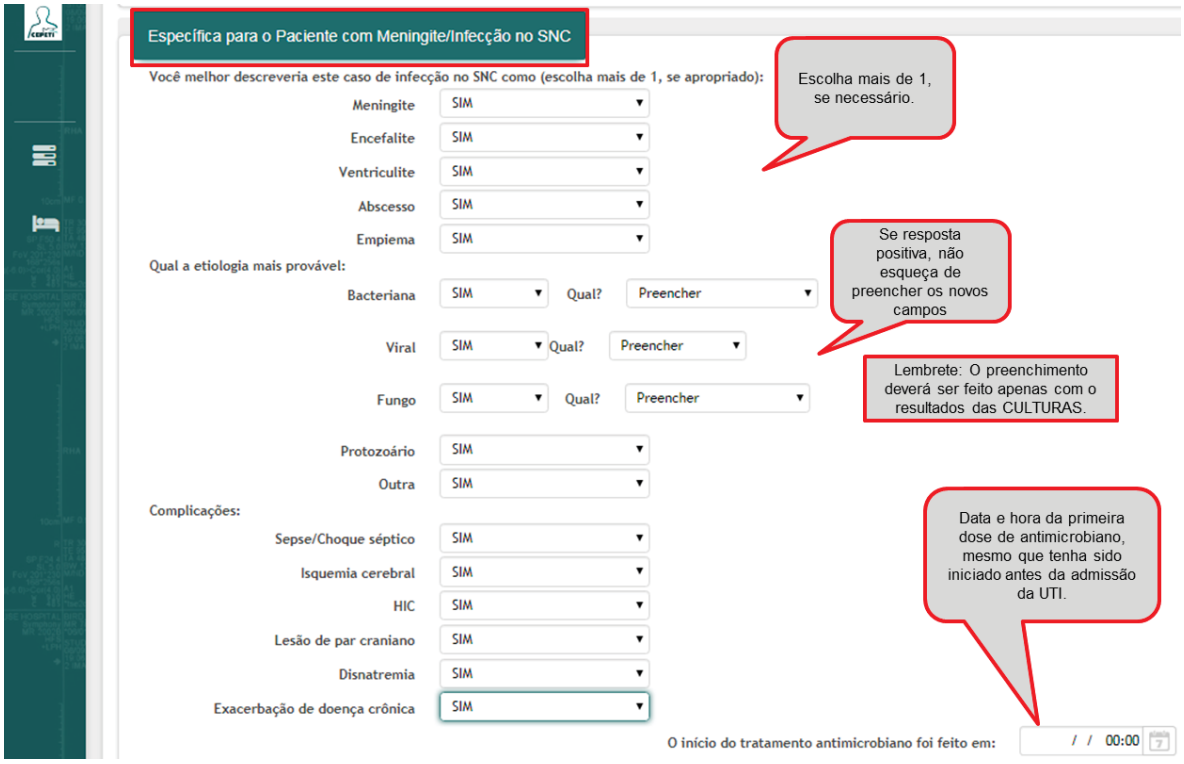
APÊNDICE 7 – FORMULÁRIO PARA PARTICIPANTES COM DIAGNÓSTICO PRIMÁRIO DE TRAUMATISMO CRANIOENCEFÁLICO



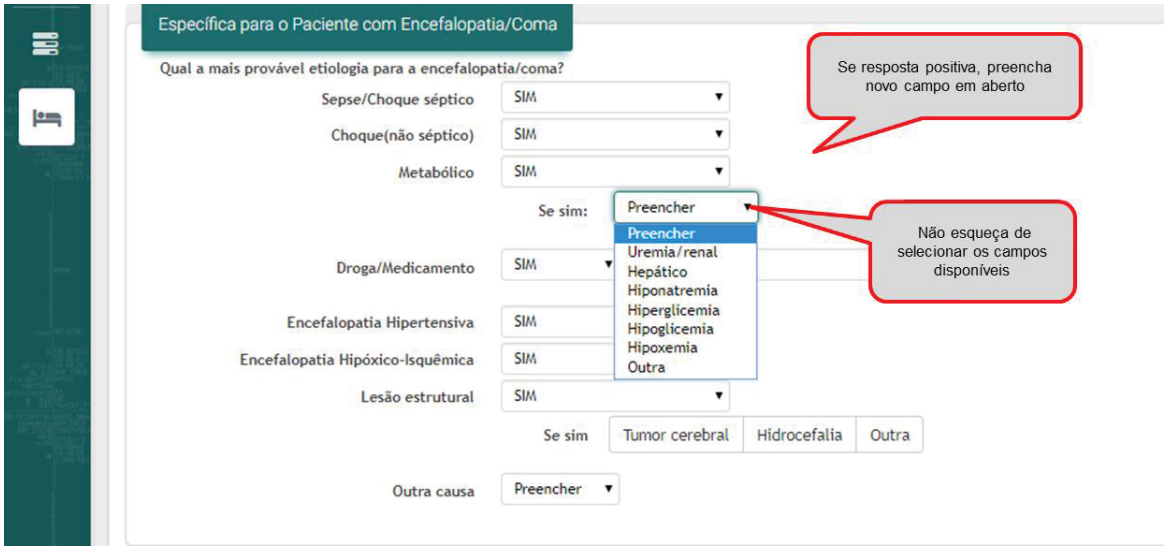
APÊNDICE 8 – FORMULÁRIO ESPECÍFICO PARA PARTICIPANTES INTERNADOS NA UTI COM DIAGNÓSTICO PRIMÁRIO DE TRAUMATISMO RAQUEMEDULAR



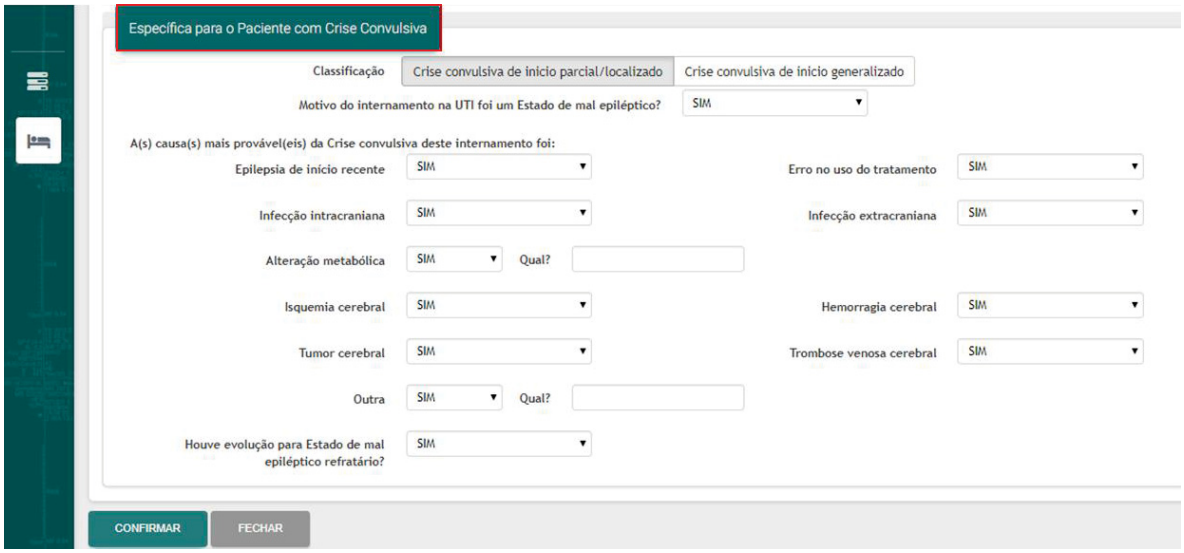
APÊNDICE 9 – FORMULÁRIO PARA PARTICIPANTES COM DIAGNÓSTICO PRIMÁRIO DE MENINGITE/ INFECÇÃO NO SISTEMA NERVOSO CENTRAL



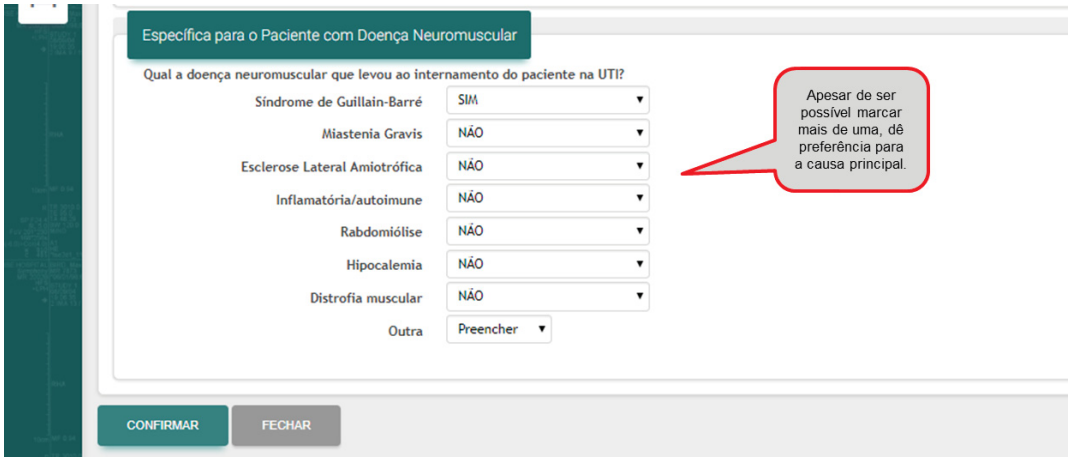
APÊNDICE 10 – FORMULÁRIO PARA PARTICIPANTES COM DIAGNÓSTICO PRIMÁRIO DE ENCEFALOPATIA



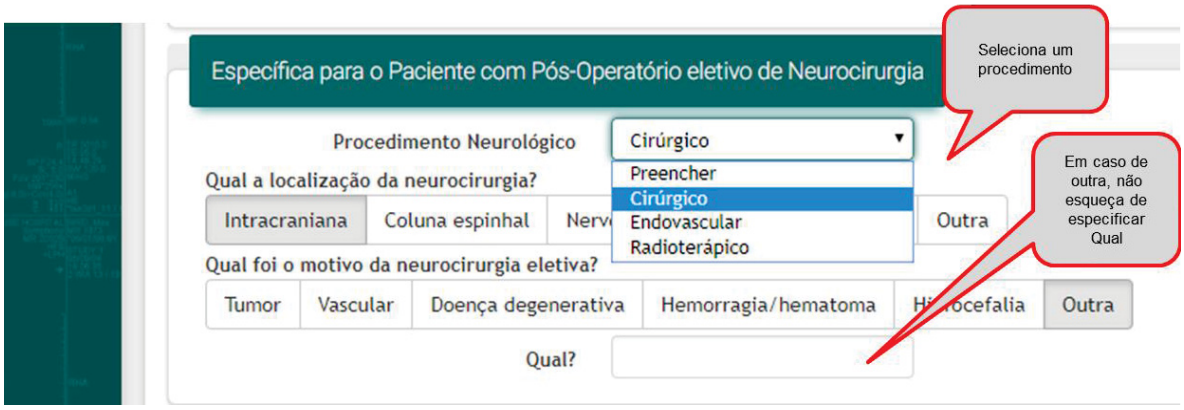
APÊNDICE 11 – FORMULÁRIO PARA PARTICIPANTES COM DIAGNÓSTICO PRIMÁRIO DE CRISE CONVULSIVA



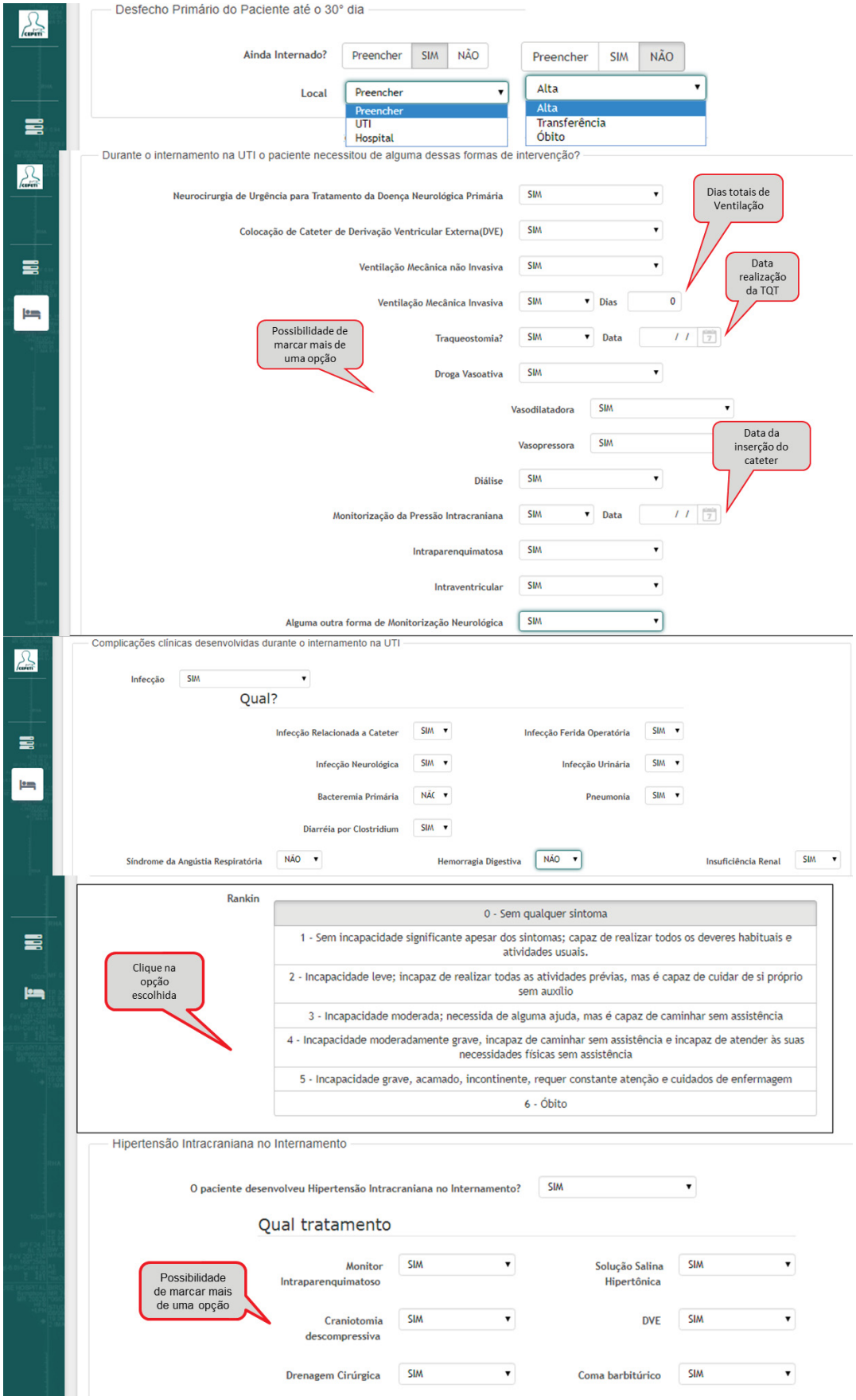
APÊNDICE 12 – FORMULÁRIO PARA PARTICIPANTES COM DIAGNÓSTICO PRIMÁRIO DE DOENÇA NEUROMUSCULAR



APÊNDICE 13 – FORMULÁRIO PARA PARTICIPANTES COM DIAGNÓSTICO PRIMÁRIO DE PÓS-OPERATÓRIO ELETIVO DE NEUROCIRURGIA



APÊNDICE 14 – FORMULÁRIO DE ALTA (DESFECHO) DA UTI



APÊNDICE 15 – RESULTADOS ADICIONAIS DE DALY POR 1000 PACIENTES INTERNADOS EM UTI

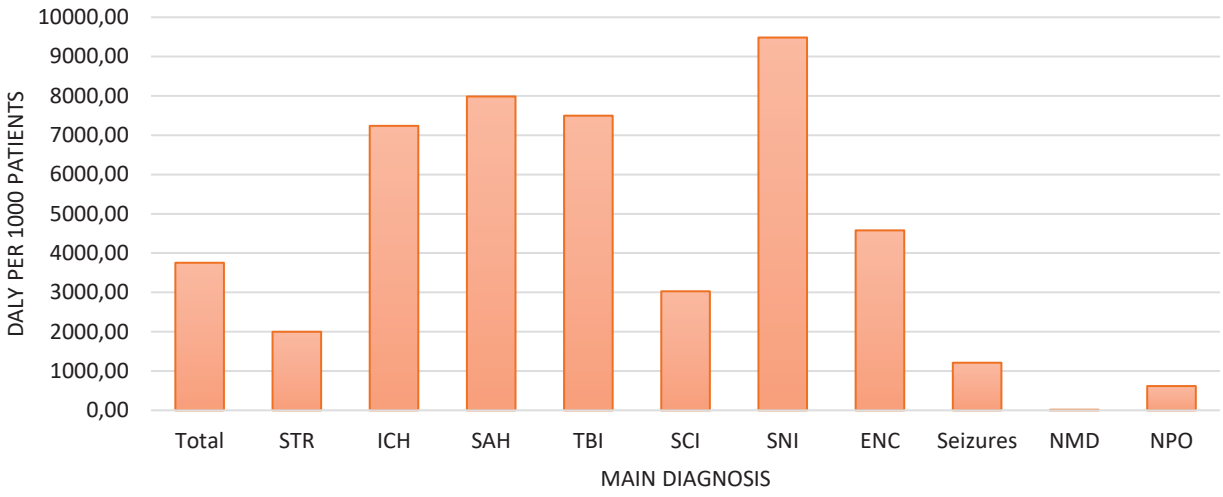


Figure 1 – DALY per 1000 patients admitted to the ICU for each primary neurological diagnosis.

Table 1 - DALYs, YLLs, and YLDs per 1,000 ICU patients for the total neurocritical patient cohort and for each primary neurological diagnosis.

Neurocritical patients	DALYs per 1000 ICU patients	YLLs per 1000 ICU patients	YLDs per 1000 ICU patients
Total neurocritical patients	3754.56	3701.86	52.70
Traumatic brain injury	7497.34	7425.69	71.65
Encephalopathy	4578.45	4538.77	39.68
Subarachnoid haemorrhage	7985.86	7963.23	22.57
Intracerebral haemorrhage	7237.79	7200.26	37.53
Ischaemic stroke	1998.67	1926.86	71.85
Central nervous system infection	9485.20	9463.56	21.60
Postoperative status of elective neurosurgery	617.60	568.96	48.64
Seizures	1210.99	1174.16	36.81
Spinal cord injury	3028.42	2921.05	107.37
Neuromuscular disease	15.45	0.00	15.45

APÊNDICE 16 – RESULTADOS ADICIONAIS DE DALY ESTRAPORPOR 1000 PACIENTES INTERNADOS EM UTI

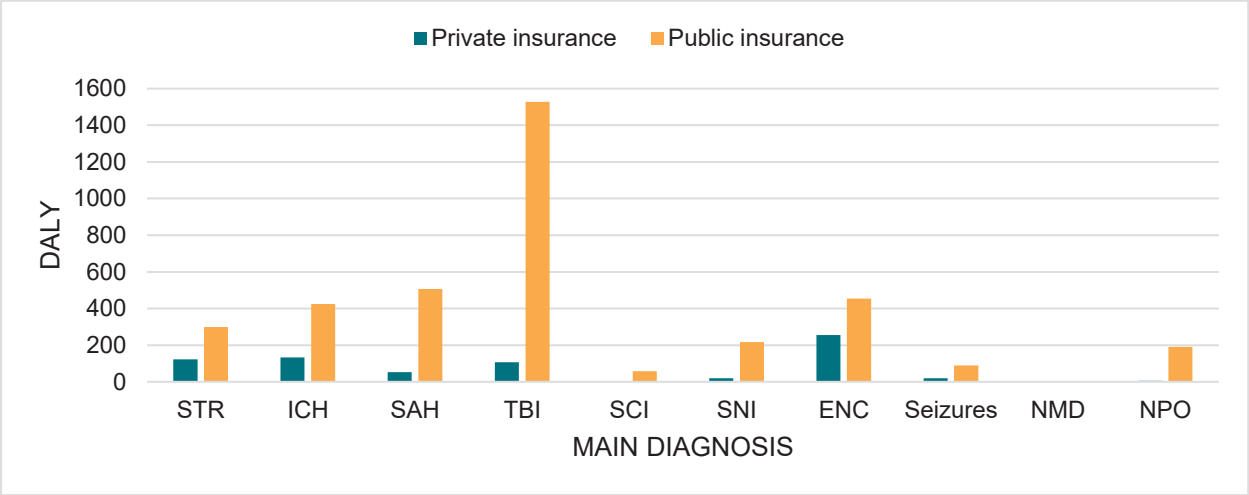


Figure 1 – DALYs for the total neurocritical patient cohort and for each primary neurological diagnosis by private and public insurance.

Table 1 - DALYs for the total neurocritical patient cohort and for each primary neurological diagnosis by private and public insurance.

Neurocritical patients	Private insurance		Public insurance	
	n	DALYs	n	DALYs
Total	603	715.883	591	3767.059
Ischaemic stroke	167	121.938	44	299.785
Intracerebral haemorrhage	25	133.336	52	423.976
Subarachnoid haemorrhage	12	52.892	58	506.116
Traumatic brain injury	66	106.833	152	1527.586
Spinal cord injury	2	0.171	17	57.369
Central nervous system infection	14	20.035	11	217.094
Encephalopathy	89	255.503	66	454.159
Seizures	79	20.228	12	89.974
Neuromuscular disease	8	0.105	3	0.063
Postoperative status of elective neurosurgery	141	4.842	176	190.937

ANEXO 1 – PARECER DE APROVAÇÃO DO COMITÊ DE ÉTICA EM PESQUISA EM SERES HUMANOS – CEPSH-INC

INSTITUTO DE NEUROLOGIA DE CURITIBA

Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Coorte Nacional de Paciente Neurocríticos Internados em Unidades de Terapia Intensiva no Brasil (NeuroCríticos Brasil).

Pesquisador: Álvaro Réa Neto

Área Temática:

Versão: 2

CAAE: 63301416.4.1001.5227

Instituição Proponente: CEPETI - CENTRO DE ESTUDOS E DE PESQUISA EM TERAPIA INTENSIVA

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 2.024.132

Apresentação do Projeto:

O estudo visa a descrição dos pacientes internados com um diagnóstico primário neurológico nas Unidades de Terapia Intensiva (UTIs) brasileiras. Trata-se de um um estudo prospectivo, observacional, multicêntrico, que consiste na identificação de pacientes internados com um diagnóstico primário neurológico nas Unidades de Terapia Intensiva de diversas regiões do Brasil.

Objetivo da Pesquisa:

Objetivo primário: Descrição dos pacientes internados com um diagnóstico primário neurológico nas UTIs brasileiras.

Objetivo Secundário: Identificação da frequência, epidemiologia e evolução dos pacientes neurocríticos nas UTIs Brasileiras.

Avaliação dos Riscos e Benefícios:

No projeto os riscos e benefícios estão contemplados de forma adequada.

Comentários e Considerações sobre a Pesquisa:

Pesquisa observacional, com aspectos éticos observados de forma adequada.

Considerações sobre os Termos de apresentação obrigatória:

Os termos estão apresentados de forma correta, com a ressalva de que o TCLE apresenta seu primeiro parágrafo confuso, dando margem à interpretação dúbia. Sugerimos a modificação do

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Bairro: Campo Comprido **CEP:** 81.210-310
UF: PR **Município:** CURITIBA
Telefone: (41)3028-9570 **Fax:** (41)3028-8580 **E-mail:** cep@inc-neuro.com.br

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referido tópico do texto.

Recomendações:

Sugerimos a modificação do primeiro parágrafo do texto do TCLE, conforme referido acima.

Conclusões ou Pendências e Lista de Inadequações:

projeto adequado sob o ponto de vista ético.

Considerações Finais a critério do CEP:

Projeto aprovado, com a solicitação de que apresente ao cep a modificação solicitada no TCLE.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_845460.pdf	29/03/2017 17:01:46		Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TERMODECONSENTIMENTOLIVREESCLARECIDONEUROCRITICOS.pdf	29/03/2017 16:55:49	Álvaro Réa Neto	Aceito
Projeto Detalhado / Brochura Investigador	PROJETO_NEUROCRITICOSBRASIL_V1_1de28demarcode2017.pdf	29/03/2017 16:55:30	Álvaro Réa Neto	Aceito
Folha de Rosto	FolhadeRostoassinada.pdf	23/12/2016 14:23:29	Álvaro Réa Neto	Aceito
Declaração de Pesquisadores	Autorizacao_INC.pdf	23/12/2016 11:14:50	Álvaro Réa Neto	Aceito
Declaração de Pesquisadores	Autorizacao_Erasto.pdf	23/12/2016 11:14:28	Álvaro Réa Neto	Aceito
Projeto Detalhado / Brochura Investigador	PROJETO_NEUROCRITICOSBRASIL_V10.pdf	23/12/2016 11:14:03	Álvaro Réa Neto	Aceito
Projeto Detalhado / Brochura Investigador	PROJETO_NEUROCRITICOSBRASIL_V10.docx	23/12/2016 11:13:43	Álvaro Réa Neto	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	Dispensa_TCLE.pdf	23/12/2016 09:55:21	Álvaro Réa Neto	Aceito
Projeto Detalhado / Brochura Investigador	NeuroCriticosBrasil_fichacoletadedados_V1_0.pdf	23/12/2016 09:54:42	Álvaro Réa Neto	Aceito
Projeto Detalhado / Brochura Investigador	NeuroCriticosBrasil_fichacoletadedados_V1_0.docx	23/12/2016 09:53:16	Álvaro Réa Neto	Aceito

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Bairro: Campo Comprido **CEP:** 81.210-310
UF: PR **Município:** CURITIBA
Telefone: (41)3028-9570 **Fax:** (41)3028-8580 **E-mail:** cep@inc-neuro.com.br

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DE CURITIBA

Continuação do Parecer: 2.024.132

Declaração de Pesquisadores	Termo_Confidencialidade.pdf	22/12/2016 17:20:41	Álvaro Réa Neto	Aceito
Declaração de Pesquisadores	Termo_Compromisso_Dados.pdf	22/12/2016 17:20:26	Álvaro Réa Neto	Aceito
Declaração de Pesquisadores	Declarao_Uso_Especifico_Dados.pdf	22/12/2016 17:19:34	Álvaro Réa Neto	Aceito
Declaração de Pesquisadores	Declaracao_Resultados_Publicos.pdf	22/12/2016 17:19:21	Álvaro Réa Neto	Aceito
Declaração de Pesquisadores	Declaracao_Responsabilidade_Investigador.pdf	22/12/2016 17:18:52	Álvaro Réa Neto	Aceito
Declaração de Pesquisadores	Carta_encaminhamento_CEP.pdf	22/12/2016 17:14:51	Álvaro Réa Neto	Aceito
Declaração de Pesquisadores	Analise_de_Merito_CEP.pdf	22/12/2016 17:14:00	Álvaro Réa Neto	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

CURITIBA, 20 de Abril de 2017

Assinado por:
Samanta Fabricio Blattes da Rocha
(Coordenador)

Endereço: Rua Jeremias Maciel Perreto, 300
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ANEXO 2 – SEGUNDO ARTIGO PUBLICADO

Com o objetivo de satisfazer o pré-requisito de obtenção do grau de doutor pelo PPGMICS da UFPR, adiciono o segundo artigo publicado, em conjunto com meu orientador, Prof. Hélio Afonso Ghizone Teive, na BMC Neurology, em fevereiro de 2023, intitulado “Epidemiological and clinical characteristics predictive of ICU mortality of patients with traumatic brain injury treated at a trauma referral hospital – a cohort study”.

O artigo apresentado a seguir também pode ser visualizado na forma de sua publicação no link: https://doi.org/10.1186/s12883-023-03145-2

BMC Neurology

https://doi.org/10.1186/s12883-023-03145-2

RESEARCH Open Access

Epidemiological and clinical characteristics predictive of ICU mortality of patients with traumatic brain injury treated at a trauma referral hospital – a cohort study

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Abstract

Background Traumatic brain injury (TBI) has substantial physical, psychological, social and economic impacts, with high rates of morbidity and mortality. Considering its high incidence, the aim of this study was to identify epidemiological and clinical characteristics that predict mortality in patients hospitalized for TBI in intensive care units (ICUs).

Methods A retrospective cohort study was carried out with patients over 18 years old with TBI admitted to an ICU of a Brazilian trauma referral hospital between January 2012 and August 2019. TBI was compared with other traumas in terms of clinical characteristics of ICU admission and outcome. Univariate and multivariate analyses were used to estimate the odds ratio for mortality.

Results Of the 4816 patients included, 1114 had TBI, with a predominance of males (85.1%). Compared with patients with other traumas, patients with TBI had a lower mean age (45.3 ± 19.1 versus 57.1 ± 24.1 years, $p < 0.001$), higher median APACHE II (19 versus 15, $p < 0.001$) and SOFA (6 versus 3, $p < 0.001$) scores, lower median Glasgow Coma Scale (GCS) score (10 versus 15, $p < 0.001$), higher median length of stay (7 days versus 4 days, $p < 0.001$) and higher mortality (27.6% versus 13.3%, $p < 0.001$). In the multivariate analysis, the predictors of mortality were older age (OR: 1.008 [1.002–1.015], $p = 0.016$), higher APACHE II score (OR: 1.180 [1.155–1.204], $p < 0.001$), lower GCS score for the first 24 h (OR: 0.730 [0.700–0.760], $p < 0.001$), greater number of brain injuries and presence of associated chest trauma (OR: 1.727 [1.192–2.501], $p < 0.001$).

Conclusion Patients admitted to the ICU for TBI were younger and had worse prognostic scores, longer hospital stays and higher mortality than those admitted to the ICU for other traumas. The independent predictors of mortality were older age, high APACHE II score, low GCS score, number of brain injuries and association with chest trauma. **Keywords** Traumatic brain injury, Craniocerebral trauma, Intensive care unit, Trauma

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Introduction

Among traumatic injuries, traumatic brain injury (TBI) is associated with increased morbidity and mortality among adults worldwide, leading often disabling to physical and psychological consequences [1–3]. According to data from the Global Burden of Disease [4], the overall incidence of TBI in 2016 was 369 per 100,000 inhabitants, with a 4% increase in the incidence rate between 1990 and 2016. In comparison, in Brazil, the incidence of TBI in 2016 was similar to the global incidence, with 383 per 100,000 inhabitants, with a percentage increase of 5.6 [4]. Furthermore, between 2008 and 2012, TBI accounted for 9,700 hospital deaths per year, overwhelming the public health system [5].

In addition to the high incidence, a European study revealed that almost half of hospitalized patients with TBI require admission to an intensive care unit duo to the risks of secondary brain injuries and complications [6]. These patients evolve to death on average in 15% of cases or require prolonged periods of hospitalization [7].

Detailed and contextualized epidemiological and clinical information on individuals with TBI admitted to the ICU are important for understanding the risks associated with morbidity and mortality. In addition, such information can contribute to the development of therapeutic and preventive measures that can be applied during hospitalization.

Despite the consequences of TBI on public health, in Brazil, there are still few studies detailing clinical and epidemiological characteristics that predict outcomes for these patients in the ICUs [1, 8–10]. Thus, the aim of this study was to identify epidemiological and clinical characteristics predictive of ICU mortality among patients admitted for TBI in a trauma referral hospital.

Materials and methods

This retrospective cohort study consecutively included patients with TBI over 18 years of age treated in the ICU between January 1, 2012, and August 31, 2019, in a trauma referral hospital in the city of Curitiba/PR, Brazil. The Complexo Hospitalar do Trabalhador is a level 1 trauma center according to the American Trauma Society classification, with a tertiary care facility available to the public health system and capable of providing comprehensive care for all aspects of injuries [11]. Patients are referred by the public health system center and the hospital follows the recommendations of the Brain Trauma Foundation [12]. All patients with an altered Glasgow Coma Scale or any acute abnormality on CT and who had an indication of full support at hospital admission were admitted to the ICU.

Patients who were hospitalized for late sequelae of TBI and those for whom there ware no data on age, sex, and type of TBI on the CT or ICU outcome recorded in the electronic medical record and in the daily medical follow-up sheets at the bedside were excluded.

The study was approved by the local ethics committee of the Instituto de Neurologia de Curitiba under protocol number 5.663.561 (Project title: Factors associated with mortality and hospital time in patients with traumatic brain (TBI) in intensive care units (ICU) in a trauma reference hospital in the city of Curitiba/PR, Brazil between 2012 and 2019; CAAE:61409122.9.0000.5227) and the need for informed consent was waived given the noninterventional study design and data collection was performed only in clinical records, without contact with the participants. All research procedures were conducted in accordance with the ethical standards of the institutional committee on human experimentation and with the Helsinki Declaration of 1975 and Resolution 466/12 of the National Health Council (Conselho Nacional de Saúde - CNS). The STROBE guidelines were used to ensure the reporting of this study.

Using electronic medical records and daily bedside medical tracking forms, data were collected on the sex and age of the patient and on the mechanism of trauma (e.g., gunshot wound (GSW); stab wound (SW); physical aggression; being run over; bicycle accident; collisions; motorcycle accident; and falling from the same level (SLF) and/or falling from a height (OLF). In addition, information was collected on the presence of polytrauma and/or skull trauma, and injuries identified on cranial CT were recorded as follows: subarachnoid haemorrhage (SAH), subdural haematoma (SDH), epidural haematoma (EDH), diffuse axonal injury (DAI), intraparenchymal haemorrhage (IPH), cerebral contusion, skull depression, skull fracture, intraventricular haemorrhage, ischaemia, cerebral oedema and/or pneumocephalus.

Data were also collected on the type and number of TBI-associated injuries, which may present as injuries to chest, abdomen, pelvis, spine, limbs and/or face and neck. The types of interventions ware recorded: conservative treatment, intracranial pressure monitoring (ICPm), craniectomy, hematoma drainage, external ventricular shunt(EVD) and correction of depression and/ or fracture correction. Last, the following data for ICU admission were collected: SOFA (Sequential Organ Failure Assessment) score, APACHE II (Acute Physiology and Chronic Health Evaluation) score and Glasgow Coma Scale (GCS) scores and outcome (length of hospitalization, discharge or death, reason for death and GCS score at discharge).

Statistical analysis

The results for categorical variables are presented as absolute and relative frequencies, and the results for quantitative variables are presented as the mean and standard deviation, median and minimum and maximum values.

For quantitative variables, comparisons between 2 groups were performed using Student's t test or the nonparametric Mann–Whitney test for data with a nonnormal distribution. The association between 2 categorical variables was performed using the chi-square test, and when both were dichotomous, Fisher's exact test was applied.

Simple and multiple binary logistic regression models of the following factors alone and/or adjusted were used to estimate odds ratios and 95% confidence intervals for mortality: age,

trauma mechanisms, APACHE II score, GCS score, SOFA score in the first 24 h, associated injuries, number of injuries on cranial CT and presence of each brain injury on CT, compared with the absence of any injury. The significance of each of the variables in the models was evaluated using the Wald test.The level of statistical significance was set at 5%, and the data were analysed using the statistical analysis software IBM SPSS, version 28.0 (SPSS Inc., Chicago, IL, USA). Imputation of missing data was not performed.

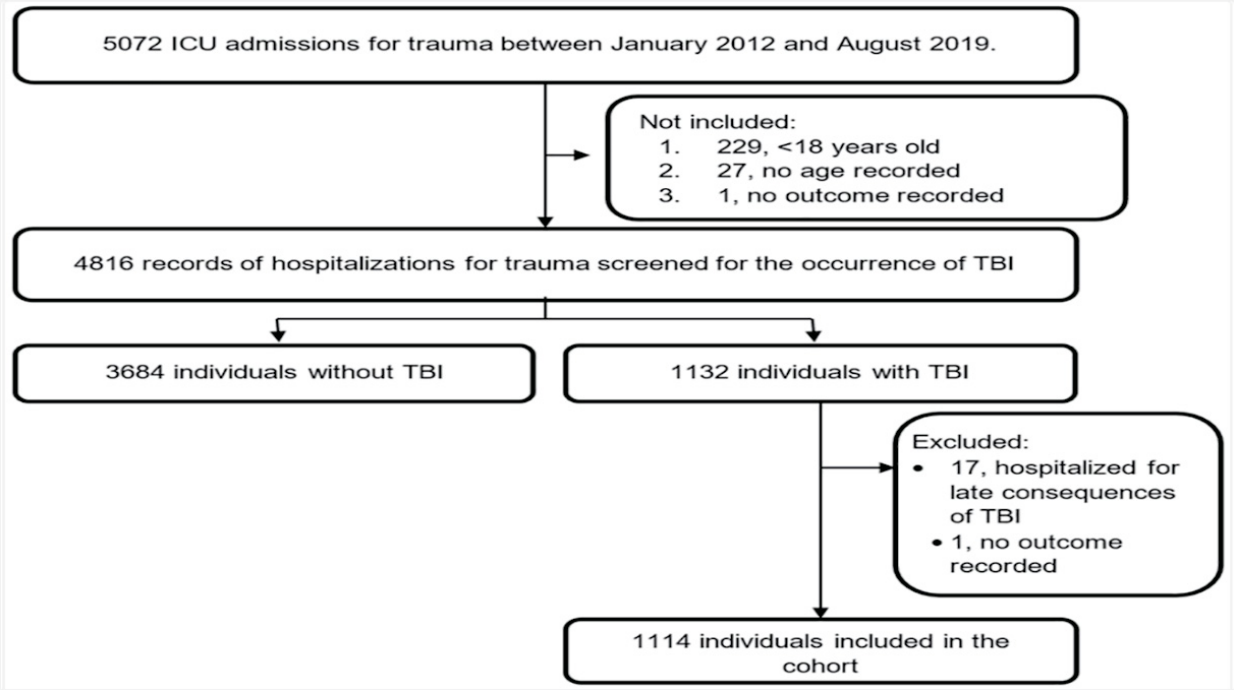

Fig. 1 Process of selection of the study sample
Abbreviations: ICU, intensive care unit; TBI, traumatic brain injury

Results

Between January 2012 and August 2019, 5,072 trauma victims were admitted to the ICU. Of these, 4816 patients older than 18 years at the time of ICU admission were screened for TBI, of which 23.5% were diagnosed with a TBI (n = 1132). We excluded 17 patients hospitalized for late sequelae of TBI and 1 who was transferred to the ICU of another hospital, making it impossible to determine the outcome. Thus, 1,114 patients made up the cohort of this study (Fig. 1).

Comparing the profile of the 1,114 individuals with TBI with that of the 3,684 individuals with other traumas (Table 1) indicated that those admitted to the ICU for TBI were significantly younger and had worse prognostic scores on admission (APACHE II, SOFA and GCS scores); they remained hospitalized longer, and there was a higher proportion of deaths in this group.

The 1114 individuals with TBI accounted for 23.2% of trauma patients admitted to the ICU from 2012 to August 2019. The annual incidence of ICU admission by TBI ranged from 32.9 to 17.9%, with the lowest incidence recorded in 2017 (Fig. 2A). The overall mortality rate for the individuals with TBI was 27.6%, with no significant difference between the rates in the years evaluated (Fig. 2B).

Table 1 Characteristics of patients admitted for trauma and a comparison between those with and without TBI

Variables	Total (n = 4798)	Without TBI (n = 3684)	With TBI (n = 1114)	P -value
Male sex, n (%)	3180 (66.3)	2232 (60.6)	948 (85.1)	< 0.001[b]
Age (years), mean ± SD	54.4 ± 23.5	57.1 ± 24.1	45.3 ± 19.1	< 0.001[c]
Apache II score, mean; med. (min-max)	17.2; 16 (0–59)	16.4; 15 20; 19 (0–59)	(0–49)	< 0.001[d]
Worst Glasgow Coma Scale score in the 1st 24 h, mean; med. (min-max)	12; 14 (3–15)	13.1; 15 9; 10 (3–15)	(3–15)	< 0.001[d]
SOFA score in the 1st 24 h[a], mean; med. (min -max)	4.9; 4 (0–21)	4.4; 3 6.5; 6 (0–21)	(0–18)	< 0.001[d]
Length of ICU stay, mean; med. (min-max)	9; 5 (0-141)	8.5; 4 10.8; 7 (0-141)	(1–90)	< 0.001[d]
ICU outcome, n (%)				< 0.001[d]
Discharge	4001 (83.4)	3194 (86.7)	807 (72.4)	
Death	797 (16.6)	490 (13.3)	307 (27.6)	

[a] Valid n of 4221 for the total, 3247 for the group without TBI and 974 for the group with TBI [b] Significant, Fisher's exact test [c] Significant, Student's t test for independent samples [d] Significant, nonparametric Mann–Whitney test

Abbreviations: ICU, intensive care unit; TBI, traumatic brain injury; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential organ failure assessment $p < 0.05$ indicates statistical significance

Of the 1,114 patients admitted to the ICU due to TBI, 27.6% died. Among them, the mean age was 47.6 ± 19.7 years, higher than those who progressed to discharge. Among those with TBI, there was a predominance of males, with no difference in the proportion of deaths between the sexes (Table 2).

The most common trauma mechanisms were falls from the same level followed by motorcycle accidents, corresponding to 39.6% of all TBIs. However, the TBI mechanism with the highest mortality rate was GSW/SW, followed by bicycle accidents and being run over. There was a significant difference in the proportion of deaths between the trauma mechanisms (Table 2).

More than 60% of patients had only one injury on cranial CT, and the increase in the number of associated injuries was directly related to mortality. The most frequent injuries evidenced on tomography were SDH and SAH. Patients with ischaemia, cerebral oedema and intraventricular haemorrhage had the highest mortality rates. In addition, compared toother injuries, a significantly higher proportion of patients with brain contusions, skull fractures, SAH, SDH, IPH, intraventricular haemorrhage, cerebral oedema and ischaemia died ($p < 0.05$) (Table 2).

The majority, 46.6%, were characterized as severe TBI (GCS 3 to 8), 18.4% as moderate (GCS 9 to 12) and 35% as mild (GCS 13 to 15). The presence of severe TBI was significantly associated with mortality. Furthermore, patients who died had significantly lower GCS scores and higher APACHE II and SOFA scores in the first 24 h in ICU. The presence of trauma in other areas, except chest trauma was not significantly related to death. (Table 2).

Most TBIs were treated surgically, with no difference in the mortality rate between surgical and conservative treatment. Among the surgical procedures, the most frequent was ICPm, and the approach associated with higher mortality was decompressive craniectomy. The median length of stay in the ICU was 7 days, which was significantly longer among those who died. At the time of ICU outcome, the majority (74.1%) of the patients were classified as life-sustaining treatments (LST) level A i.e., all necessary, possible, and available LST measures to save life and restore health, including cardiopulmonary resuscitation if cardiopulmonary arrest. (Table 2).

Of the 807 survivors, 781 (96.8%) had the Glasgow Coma Scale recorded at ICU discharge. The mean score was 13.2, and the median was 14, ranging from 3 to 15. Among the 307 patients who died, the direct cause of death was noted in the discharge summary of 262 (85.3%) patients. Brain death was the most frequent, accounting for 42.7% of deaths, followed by infection (40.8%), hemorrhagic shock (4.6%), unidentified cause (3.4%), pulmonary thromboembolism (PTE) (1.9%), sepsis plus acute respiratory distress syndrome (ARDS) (1.5%), ARDS alone (1.1%), acute myocardial infarction (AMI) (1.1%), cardiac arrest (CA) duo toventricular fibrillation (VF) (1.1%), and others (1.5%).

Variables that were significantly different between discharge and death were analysed as prognostic factors for mortality using univariate logistic regression analysis (Table 3). Older age, higher APACHE II and SOFA scores and lower GCS scores at admission were associated with higher mortality. Regarding TBI mechanisms, less lethal trauma (physical aggression), GSW/SW, being run over and bicycle accidents were associated with a higher risk of mortality (Table 3).

The greater the number of injuries on cranial CT, the greater the risk of mortality when compared with the absence of brain lesion; patients with 3 injuries on cranial CT were 10 times more likely to die. The presentation of ischaemia, intraventricular haemorrhage, cerebral oedema, cerebral contusions, skull fractures, SAH, SDH and/or IPH increased the odds of death of patients with TBI. Cerebral ischaemia and oedema increased the odds by 29 and 21 times, respectively (Table 3). Polytrauma was not associated with a worse outcome; however, the presence of associated chest injury increased the odds of death (Table 3).

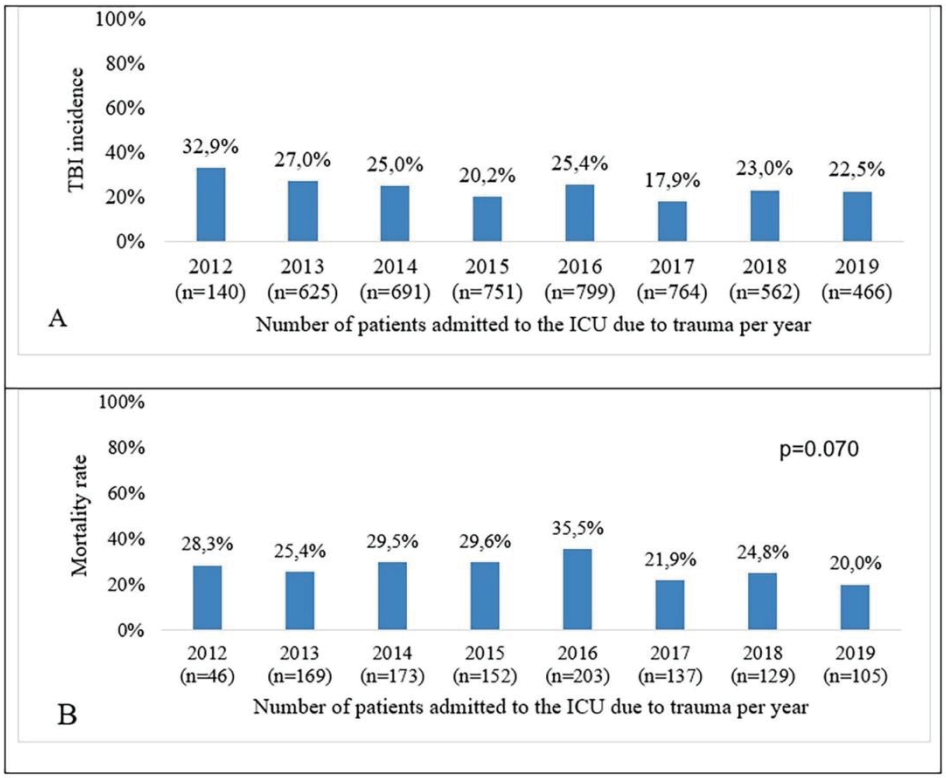

Fig. 2 Annual incidence and mortality rate for TBI in ICU. **A**: Annual incidence of ICU admissions due to TBI among traumatic reasons. **B**: Mortality rate for TBI victims admitted to the ICU per year. Abbreviations: ICU, intensive care unit; TBI, traumatic brain injury

Finally, older age, a higher APACHE II score, a lower GCS score in the first 24 h, a greater number of brain injuries identified on CT, and the presence of associated chest trauma remained risk factors for mortality in patients with TBI after adjusting for each in a multiple regression model (Table 4).

Discussion

Compared with other severe traumas, TBI is the most prevalent and, among traumas, has the highest morbidity and mortality [13, 14]. In trauma, injuries to the central nervous system are the main causes of death, followed by hemorrhagic shock and sepsis [14–16]. Individuals with TBI are younger and mostly men [17–19] and have worse prognostic score values at admission and longer ICU stays. As observed in Europe, patients with neurological injuries admitted to the ICU had higher SOFA scores, lower GCS scores on admission, longer ICU stays and higher mortality rates [20].

In this study, the mortality rate for patients with TBI was 27.6%. Older age, a higher APACHE II score, a lower Glasgow score in the first 24 h, a higher number of brain injuries identified on CT, and the presence of associated chest trauma were independent predictors of mortality.

The findings corroborate previous studies that identified older age and lower GCS scores as predictors of mortality in patients with severe TBI [7, 17, 21–25]. A population based study conducted in Rwanda, Africa, showed that age over 50 years and GCS score lower than 13 were significantly associated with death [23]. In previous studies, younger patients had higher GCS scores at ICU admission and discharge [26], and mortality increased with increasing age [14, 27]. One explanation for the increased mortality in patients with advanced age is the increased use of anticoagulant and antiplatelet drugs, leading to greater bleeding complications in patients with severe trauma [13].

Falls from the same level and traffic accidents were the main trauma mechanisms identified, similar to those reported in European studies [18, 28]. Falls from the same level are more common in the elderly population, while traffic accidents are more common in the young population [17, 18, 29]. The higher incidence of falls in the elderly population can be explained by their increased in life expectancy accompanied by the increase in comorbidities [13]. For TBIs caused by traffic accidents, the most common mechanism among our cohort was motorcycle accidents, a finding that is different from

Table 2 Description of the characteristics of individuals with TBI and their association with ICU outcome

VARIABLES	Total (n = 1114)	Discharge	Death	p value
ICU ADMISSION				
Age (years), mean ± SD	45.3 ± 19.1	44.5 ± 18.9	47.6 ± 19.7	0.016[b]
Male, n (%)*	948 (85.1)	689 (72.7)	259 (27.3)	0.707[c]
Trauma mechanism, n (%) *				< 0.001[a]
GSW/SW	77 (7.4)	47 (56.6)	36 (43.4)	
Physical Aggression	142 (12.7)	113 (79.6)	29 (20.4)	
Run over	158 (14.2)	104 (65.8)	54 (34.2)	
Cyclist	50 (4.5)	29 (58)	21 (42)	
Collision	93 (8.3)	73 (78.5)	20 (21.5)	
Motorbike	203 (18.2)	159 (78.3)	44 (21.7)	
SLF	238 (21.4)	172 (72.3)	66 (27.7)	
OLF	147 (13.2)	110 (74.8)	37 (25.2)	
Passage to the operating room before ICU addition, n(%)				0,033[c]
Yes	789 (70.8)	557 (70.6)	232 (29.4)	
No	325 (29.2)	250 (76.9)	75 (23.1)	
Apache II score, mean; med. (min-max)	20; 19 (0–49)	16.5; 15 (0–41)	29.1; 30 (6–49)	0.000[d]
Worst Glasgow Coma Scale (GCS) in the first 24 h, mean; med. (min-max)	9; 10 (3–15)	10.5; 12 (3–15)	5.3; 3 (3–15)	0.000[d]
Classification of Severity of TBI by the worst GCS in the first 24 h, n(%)				< 0,001[a]
Severe (GCS 3 to 8)	519 (46.6)	264 (50.9)	255 (49.1)	
Moderate (GCS 9 to 12)	205 (18.4)	176 (85.9)	29 (14.1)	
Mild (GCS 13 to 15)	390 (35.0)	367 (94.1)	23 (5.9)	
SOFA score in the first 24 h, mean; med. (min-max) [#]	6.5; 6 (0–18)	5.4; 5 (0–16)	9.5; 9 (2–18)	0.000[d]
Number of injuries on cranial CT, n (%) *				< 0.001[a]
None	43 (3.9)	39 (90.7)	4 (9.3)	
One	736 (66.1)	552 (75)	184 (25)	
Two	250 (22.4)	176 (70.4)	74 (29.6)	
Three	85 (7.6)	40 (47.1)	45 (52.9)	
Injuries evidenced on CT, n (%) *				
Cerebral contusion	167 (15.0)	122 (73.1)	45 (26.9)	0.015[e]
DAI	47 (4.2)	40 (85.1)	7 (14.9)	0.527[e]
Fracture and/or depression	99 (8.9)	70 (70.7)	29 (29.3)	0.009[e]
SAH	379 (34.0)	244 (64.4)	135 (35.6)	< 0.001[e]
SDH	401 (36.0)	268 (66.8)	133 (33.2)	< 0.001[e]
EDH	151 (13.6)	127 (84.1)	24 (15.9)	0.335[e]
IPH	149 (13.4)	112 (75.2)	37 (24.8)	0.034[e]
Haemoventriculum	19 (1.7)	8 (42.1)	11 (57.9)	< 0.001[e]
Cerebral edema	55 (4.9)	17 (30.9)	38 (69.1)	< 0.001[e]
Ischaemia	8 (0.7)	2 (25)	6 (75)	< 0.001[e]
Pneumocephalus	13 (1.2)	11 (84.6)	2 (15.4)	0.615[e]
Presence of polytrauma, n (%) *	318 (28.5)	230 (72.3)	88 (27.7)	1c
Number of injury follow-ups in addition to TBI, n (%) *				0.260[a]
None	796 (71.5)	577 (72.5)	219 (27.5)	
One	190 (17.1)	142 (74.7)	48 (25.3)	
Two	94 (8.4)	61 (64.9)	33 (35.1)	
Three or more	34 (3.1)	27 (79.4)	7 (20.6)	
Injury follow-up in addition to TBI, n (%) *				
Thorax	140 (44)	87 (62.1)	53 (37.9)	0,015[f]
Abdomen	56 (17.6)	37 (66.1)	19 (33.9)	0,355[f]
Pelvis	14 (4.4)	11 (78.6)	3 (21.4)	0,768[f]
SCI	59 (18.6)	44 (74.6)	15 (25.4)	0,880[f]
ICU ADMISSION				
Limbs	129 (40.6)	93 (72.1)	36 (27.9)	0,916[f]
Face and/or neck (except spine)	84 (26.4)	75 (89.3)	9 (10.7)	< 0,001[f]
TREATMENT OF TBI				
Approach to TBI treatment, n (%) *				0,138[c]
Conservative	494 (44.3)	369 (74.7)	125 (25.3)	
Surgical	620 (55.7)	438 (70.6)	182 (29.4)	
Procedures performed to treat TBI, n (%) *				
ICPm	418 (67.4)	272 (65.1)	146 (34.9)	0,002[g]
Craniectomy	158 (25.5)	86 (54.4)	72 (45.6)	< 0.001[g]
Haematoma drainage	140 (22.6)	122 (87.1)	18 (12.9)	0.002[g]
EVD	94 (15.5)	71 (75.5)	23 (24.5)	1 g
Correction of fracture and/or depression	8 (1.3)	8 (100)	0 (0)	0.210[g]
ICU OUTCOME				
Length of stay, mean; med. (min-max)	10.8; 7 (1–90)	12; 8 (1–90)	7.4; 5 (1–74)	< 0.001[d]
Level of LST, n (%) [§]				< 0.001[a]
LST-A	803 (74.1)	742 (92.4)	61 (7.6)	

LST-B	74 (6.8)	24 (32.4)	50 (67.6)
LST-C	77 (7.1)	14 (18.2)	63 (81.8)
LST-D	17 (1.6)	1 (5.6)	17 (94.4)
LST-E	113 (10.4)	0 (0)	113 (100)

Abbreviations: TBI, traumatic brain injury; ICU, intensive care unit; OR, odds ratio; GSW, Gunshot wound; SW, Stab wound; SLF, Same-level fall; OLF, Fall from height; SCI, spinal cord injure; APACHE, Acute Physiology and Chronic Health Evaluation; CT, computed tomography; DAI, Diffuse axonal injury; SAH, Subarachnoid haemorrhage; SDH, subdural haematoma; EDH, epidural haematoma; IPH, Intraparenchymal haemorrhage; ICPm, intra cranial pressure monitoring; EVD, External ventricular derivation; LST: life-sustaining treatments; LST-A: All necessary, possible, and available LST measures to save life and restore health, including cardiopulmonary resuscitation if cardiopulmonary arrest; LST-B: All necessary, possible, and available LST measures to save life and restore health, but no cardiopulmonary resuscitation if cardiopulmonary arrest; LST-C: Maintenance of LST measures already in place, withholding new ones apart from those aimed at comforting the patient and his or her family; LST-D: Removal of LST measures when considered futile in the face of a terminal condition and beginning of palliative care; LSTT-E: All necessary, possible and available LST measures for patients with brain death until organ donation

[*] For the variables in the column "Total", the percentages calculated are presented considering the total number of cases in the column, while in the columns "Discharge" and "Death", the percentages calculated considering the total number of cases in the row are presented

[#] 140 missing data points in the total sample (88 among discharges and 52 among deaths) [§] 30 missing data points in the total sample (26 among discharges and 4 among deaths) [a] Significant, chi-square test [b] Significant, Student's t test for independent samples [c] Significant, Fisher's exact test [d] Significant, nonparametric Mann–Whitney test [e] Significant, Fisher's exact test, compared with the 43 patients who did not present any injury on cranial CT. [f] Significant, Fisher's exact test, compared with the 796 patients who had no record of injuries [g] Significant, Fisher's exact test, compared with the 494 patients who underwent conservative treatment

observations in Europe, where bicycle accidents were more frequent [28–30].

Subdural and subarachnoid haemorrhages were the most frequent findings on CT of the head of patients with TBI, a finding consistent with the results of a European study [6]. The increase in the occurrence of intracranial haemorrhages is associated with olderage and a decrease in GCS score [31]. The presence of SAH due to trauma is often accompanied by other intracranial haemorrhages [32]. When SAH is concomitant with 2 other intracranial haemorrhage, there is a 9-fold increase in mortality, and when associated with SDH, there is a 16-fold increase in the chance of death [25, 32]. Thus, a greater number of brain injuries, especially haemorrhagic ones, is associated with a greater chance of death.

The association of thoracic trauma with TBI significantly increased the mortality of patient in our study. These findings are corroborated by other studies, also demonstrating higher mortality among patients with pulmonary contusions [33], and that the presence of TBI and concomitant chest trauma significantly increased mortality and prolonged ICU stay and duration of mechanical ventilation [34].

Higher APACHE II scores are a risk factor for mortality in patients admitted to ICUs [35, 36]. In the present study, individuals with TBI admitted to the ICU had

Table 3 Univariate model of prognostic factors for mortality among TBI patients admitted to the ICU.

Prognostic factors	N of the model	OR (95% CI) for mortality[a]	p value[b]
Age (years)	1114	1.008 (1.002–1.015)	0.016
Trauma mechanism	1114		
Physical Aggression		Ref	
GSW/SW		2.985 (1.645–5.415)	0.000
Run over		2.023 (1.198–3.417)	0.008
Cyclist		2.822 (1.409–5.649)	0.003
Collision		1.068 (0.562–2.027)	0.842
Motorbike		1.078 (0.636–1.827)	0.779
SLF		1.495 (0.91–2.458)	0.113
OLF		1.311 (0.754–2.277)	0.337
Apache II score	1114	1.180 (1.155–1.204)	< 0.001
Worst Glasgow Coma Scale score in the first 24 h	1114	0.730 (0.700–0.760)	< 0.001
Classification of Severity of TBI by the worst GCS in the first 24 h	1114		
Severe (GCS 3 to 8)		Ref	
Moderate (GCS 9 to 12)		2.629 (1.478–4.677)	0,001
Mild (GCS 13 to 15)		15,413 (9,778–24,295)	< 0,001
SOFA score in the first 24 h	974	1.400 (1.330–1.473)	< 0.001
Number of injuries on cranial CT	1114		
None		Ref	
One		3.250 (1.146–9.218)	0.027
Two		4.099 (1.414–11.883)	0.009
Three		10.969 (3.602–33.406)	< 0.001
The presence of each of brain injury evidenced on cranial CT compared to having no injuries on CT	210	3.596 (1.216–10.636)	0.021

Cerebral contusion (ref: 43 patients without injury)			
DAI (ref: 43 patients without injury)	90	1.706 (0.463–6294)	0.422
Fracture and/or depression (ref: 43 patients without injury)	142	4.039 (1.323–12.335)	0.014
SAH (ref: 43 patients without injury)	422	5.394 (1.887–15.420)	0.002
SDH (ref: 43 patients without injury)	444	4.839 (1.694–13.824)	0.003
EDH (ref: 43 patients without injury)	194	1.842 (0.603–5.634)	0.284
IPH (ref: 43 patients without injury)	192	3.221 (1.079–9.619)	0.036
Haemoventriculum (ref: 43 patients without injury)	62	13.406 (3.393–5 2.977)	< 0.0001
Cerebral edema (ref: 43 patients without injury)	98	21.794 (6.715–70.732)	< 0.001
Ischaemia (ref: 43 patients without injury)	51	29.250 (4.364–196.069)	< 0.001
Pneumocephalus (ref: 43 patients without injury)	56	1.773 (2.86–10.990)	0.539
Presence of trauma in another segment in addition to the skull	1114	1.008 (0.754–1.348)	0.957
Number of injured segments in addition to TBI	1114		
None		Ref	
One		0.891 (0.620–1.280)	0.531
Two		1.425 (0.908–2.238)	0.124
Three or more		0.683 (0.293–1.591)	0.377
Injury follow-up in addition to TBI			
Associated thorax injury (ref: absence of thoracic injury)	1114	1.727 (1.192–2.501)	0.004
Associated abdominal injury (ref: absence of abdominal injury)	1114	1.373 (0.777–2.427)	0.275
Associated pelvis injury (ref: absence of pelvis injury)	1114	0.714 (0.198–2.577)	0.607
Associated MRT (ref: absence of MRT)	1114	0.891 (0.488–1.625)	0.706
Associated limb injury (ref: absence of limb injury)	1114	1.020 (0.677–1.536)	0.925
Associated face and/or neck injury (except spine) (ref: absence of face/neck injury)	1114	0.295 (0.146–0.596)	< 0.001

Abbreviations: TBI, traumatic brain injury; ICU, intensive care unit; OR, odds ratio; GSW, Gunshot wound; SW, Stab wound; SLF, Same-level fall; OLF, Fall from height; APACHE, Acute Physiology and Chronic Health Evaluation; CT, computed tomography; DAI, Diffuse axonal injury; SAH, Subarachnoid haemorrhage; SDH, subdural haematoma; EDH, epidural haematoma; IPH, Intraparenchymal haemorrhage [a] Odds ratio (OR) and 95% confidence interval of the OR (95% CI) of the univariate binary logistic regression model for mortality [b] Significant, Wald test of the logistic regression model

Table 4 Multiple logistic regression of prognostic factors for mortality among patients with TBI in ICU

Prognostic factors	N of the model	OR (95% CI) for mortality[a]	P value[b]
Age (years)	1114	1.008 (1.002–1.015)	0.016
Apache II		1.180 (1.155–1.204)	< 0.001
Worst Glasgow Coma Scale score in the first 24 h		0.730 (0.700–0.760)	< 0.001
Number of injuries on cranial CT			
None		Ref	
One		3.250 (1.146–9.218)	0.027
Two		4.099 (1.414–11.883)	0.009
Three		10.969 (3.602–33.406)	< 0.001
Associated thorax injury (ref: absence of thoracic injury)		1.727 (1.192–2.501)	< 0.001

[a] Odds ratio (OR) and 95% confidence interval of the OR (95% CI) of the multiple binary logistic regression model for mortality

[b] Significant, Wald test of the logistic regression model

Abbreviations: TBI, traumatic brain injury; ICU, intensive care unit; OR, odds ratio; APACHE, Acute Physiology and Chronic Health Evaluation; CT, computed tomography

a mean APACHE score of 20 points, and among the patients who died, the mean score was 29 points. These data are very similar to those reported in a study conducted in Turkey [37], in which the mean APACHE II score was 30 points for patients with TBI who died. This scale has shown good performance in terms of discrimination, calibration, accuracy and satisfactory results in the prediction of ICU mortality in patients with TBI [35, 38].

In the univariate analysis, the SOFA score was significantly related to mortality, with higher scores for patients who died [38]. Zygun D et al. [39] demonstrated that the increased mortality of patients with TBI is related to higher scores on the cardiovascular component of the SOFA.

Regarding therapeutic management, no differences were observed in mortality between conservative or surgical intervention. However, in 2020, Gao et al. [21] showed that decompressive craniotomy and craniectomy reduced mortality in patients with severe TBI and no pupillary light reflex.

At the time of ICU outcome, the majority (74.1%) of the patients were classified as life-sustaining treatments (LST) level A. In our institutional protocol, in view of the brain trauma foundation protocols and focus on rehabilitation, it is recommended to wait 6 months for support limitation. These data are in agreement with the results of other authors who suggest caution in considering the withdrawal of care in patients with TBI duo to the delay in the recovery of the level of consciousness [40].

Due to the retrospective nature of this study, not all data were available, such as: Injury Severity Score (ISS), regional AIS (Abbreviated injury score), Marshal Score, morbidity, incidence of ARDS and pneumonia. Since data were collected exclusively from electronic medical records, information on prehospital care, pupil assessment, functional outcome, and haemostasis disorders

was not available. Data collection was performed only at the time of hospitalization, it was not possible to control confounding factors regarding the evolution of each patient during hospitalization. However, the findings of our study, derived from the analysis of a large TBI patients in a trauma referral hospital, allow a broad understanding of the epidemiological profile of TBI patients.

In conclusion, individuals with TBI have higher chances of mortality and longer hospital stay, are younger, have higher APACHE II and SOFA scores and have lower GCS scores on ICU admission. Significantly associated predictors of ICU mortality include older age, higher APACHE II score, lower GCS score in the first 24 h, higher number of brain injuries, and concomitant chest trauma. TBI results in extensive consequences for patients' quality of life and represents a substantial burden on health services. Therefore, understanding the risk factors and predictors of mortality is necessary for the development of more effective preventive and therapeutic measures and for better planning of the management of patients with TBI, in order to reduce morbidity and mortality.

Abbreviations

TBI	T raumatic brain injury
ICUs	I ntensive care units
APACHE	A cute Physiology and Chronic Health Evaluation
SOFA	S equential organ failure assessment
GCS	Glasgow Coma Scale
OR	O dds ratio
CT	Computed tomography
GSW	G unshot wound
SW	S tab wound
SAH	S ubarachnoid haemorrhage
SDH	S ubdural haematoma
EDH	Epidural haematoma
DAI	Diffuse axonal injury
IPH	Intraparenchymal haemorrhage
ICPm	Intra cranial pressure monitoring
EVD	E xternal ventricular derivation
PTE	P ulmonary thromboembolism
ARDS	A cute respiratory distress syndrome
AMI	A cute myocardial infarction
CA	C ardiac arrest
VF	V entricular fibrillation
SLF	Same-level fall
OLF	F all from other level
SCI	Spinal cord injure

Acknowledgements

We thank all the participating centers and Verônica Barros for the support, interventions in our study and all the collaboration.

Authors' contributions

Conceptualization: ARN, EDSJ and GH; data curation, RSB and ARN; formal analysis, RSB, MMJ; investigation, VBS and MBC; methodology, ARN, EDSJ, GH, RSB, ACKN and MCO; project administration, ARN; supervision, ARN and MCO; visualization, ARN, HAGT, EDSJ, GH, VBS, RSB, ACKN, FBR, MBC and MCO; writing—original draft preparation, EDSJ, GH, RSB, ACKN, MCO; writing— review and editing, ARN, HAGT, EDSJ, GH, VBS, RSB, ACKN, MMJ, FBR, MBC and MCO.

All authors have approved the submitted version and agreed to be personally accountable its own contributions and ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

Funding

No funding was received.

Data availability

The dataset supporting the conclusions of this article is available in the Zenodo repository, DOI and hyperlink to dataset is https://doi.org/10.5281/zenodo.7054506.

Declarations

Ethics approval and consent to participate

The study was approved by the local ethics committee of the Instituto de Neurologia de Curitiba under protocol number 5.663.561 on September 17, 2018, and the need for informed consent was waived given the noninterventional study design and data collection was performed only in clinical records, without contact with the participants. All research procedures were conducted in accordance with the ethical standards of the institutional committee on human experimentation and with the Helsinki Declaration of 1975 and Resolution 466/12 of the National Health Council (Conselho Nacional de Saúde - CNS). The STROBE guidelines were used to ensure the reporting of this study.

The ethics committee of the Instituto de Neurologia de Curitiba approved the waiver of informed consent.

Consent for publication Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Received: 26 September 2022 / Accepted: 27 February 2023

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