MESTRADO INTEGRADO EM MEDICINA

Hospital Emergency Admissions for Acute Cerebrovascular Disease During COVID-19 Pandemic: the impact on a central hospital

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2021

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Dissertação de candidatura ao grau de Mestre em Medicina, submetida ao Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto

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Porto, 2 de junho de 2021

Resumo

Contexto: Vários artigos têm sido publicados, em todo o mundo, que demonstram que os doentes evitam recorrer aos serviços de saúde, especificamente ao Serviço de Urgência (SU), durante a pandemia de COVID-19. O objetivo do nosso estudo é avaliar o impacto desta pandemia nas admissões hospitalares no SU por eventos cerebrovasculares agudos num hospital central com um centro de referência em neurorradiologia de intervenção.

Métodos: Foram revistos os registos clínicos eletrónicos dos doentes admitidos no SU do Hospital de Santo António, de 1 de março de 2019 a 28 de fevereiro de 2021, com o diagnóstico de Acidente Vascular Cerebral (AVC), Ataque Isquémico Transitório (AIT) e Hemorragia Subaracnoideia (HSA). Numa base de dados foi registada a informação sobre os dados demográficos dos doentes, fatores de risco cardiovascular, a pontuação, à admissão, na Escala do *National Institutes of Health Stroke* (NIHSS) para os AVC, tratamento de reperfusão, pontuação $ABCD^2$ no caso dos AIT e mortalidade.

Resultados: Foram elegíveis para o estudo 1270 processos no período pré-pandemia (idade média 71 ± 13,9 anos; 50,5% homens) e 1129 no primeiro ano da pandemia (72 ± 13,8 anos; 52,8% homens). Observou-se uma diminuição no número de admissões por doença cerebrovascular aguda, particularmente durante os primeiros três meses da pandemia (345 vs. 280). O número de trombectomias sofreu um pequeno declínio (224 vs. 260), ao passo que, o número de trombólises permaneceu estável (86 vs. 89); as taxas de mortalidade foram semelhantes (1,6% vs. 1,2%).

Conclusões: O número de admissões no SU, por AVC, AIT e HSA diminuiu durante o primeiro ano da pandemia de COVID-19, no entanto, os tratamentos de reperfusão não foram significativamente afetados, e a taxa de mortalidade também foi semelhante ao ano anterior. Não obstante, é imprescindível consciencializar a população sobre a importância de continuar a recorrer aos serviços médicos, mesmo durante momentos críticos como este.

Palavras-chave

AVC, Ataque Isquémico Transitório, Hemorragia Subaracnoideia, Admissões no Serviço de Urgência, SARS-CoV-2, COVID-19

Abstract

Background: There have been reports around the globe that patients are avoiding the hospitals, mainly emergency services, during the SARS-CoV-2 pandemic. The aim of our study is to evaluate the effect of the COVID-19 pandemic on emergency hospital admissions for acute cerebrovascular events in a central hospital with a reference centre for interventional neuroradiology.

Methods: We retrospectively reviewed the electronic medical records of patients admitted to the emergency department (ED) of Hospital de Santo António from March 1^{st} 2019 to February 28^{th} 2021 with a code diagnosis of stroke, transient ischemic attack (TIA) and subarachnoid haemorrhage (SAH). We collected data on patients' demographics, cardiovascular risk factors, stroke admission National Institutes of Health Stroke Scale (NIHSS) score, reperfusion treatment, TIA $ABCD^2$ score and mortality.

Results: From ED registries, 1270 reports of patients were eligible for the study in the pre-pandemic period (mean age 71 ± 13.9 years; 50.5% men) and 1129 in the first year of the pandemic (72 ± 13.8 years; 52.8% men). A decline in the number of acute cerebrovascular disease admissions was observed, particularly during the first three months of the pandemic (345 versus 280). The number of thrombectomies procedures have had a small decline (224 versus 260) while the number of thrombolysis remained stable (86 versus 89); mortality rates remained similar (1.6% versus 1.2%).

Conclusions: The overall number of emergency admissions due to stroke, TIA and SAH decreased during the first year of the COVID-19 pandemic, however, reperfusion treatments were not significantly affected, and the mortality rate was also similar to the year before. Nonetheless, it is imperative to educate the population about the importance of continuing to seek emergency medical care during critical times.

Keywords

Stroke, Transient Ischemic Attack, Subarachnoid Haemorrhage, Emergency Admissions, SARS-CoV-2, COVID-19

Acronyms and Abbreviations

AF – Atrial Fibrillation

AHT – Arterial Hypertension

AIT – Ataque Isquémico Transitório

AVC – Acidente Vascular Cerebral

CHUPorto - Centro Hospitalar Universitário do Porto

CMIN – Centro Materno Infantil do Norte Albino Aroso

COVID-19 - Coronavirus Disease 2019

CT – Computed Tomography

DM – Diabetes mellitus

ECG – Electrocardiogram

ED – Emergency Department

HSA – Hemorragia Subaracnodeia

ICD-10 – International Classification of Diseases 10

ICD-9 – International Classification of Diseases 9

ICU – Intensive Care Unit

IMCU – Intermediate Care Unit

MRI – Magnetic Resonance Imaging

NIHSS – National Institutes of Health Stroke Scale

rt-PA – recombinant tissue Plasminogen Activator

SAH – Subarachnoid Haemorrhage

SARS-CoV-2 - Severe Acute Respiratory Syndrome Coronavirus 2

SNS24 – National Health Service Contact Centre

SU – Serviço de Urgência

TIA – Transient Ischaemic Attack

WHO - World Health Organization

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Introduction

The outbreak of the new coronavirus began in December of 2019, in Wuhan, China[1]. On March 2nd, the first patient with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in Portugal was admitted to Hospital de Santo António and, on March 11th, World Health Organization (WHO) declared coronavirus disease 2019 (COVID-19) a global pandemic[2]. To reduce the spread of the virus and avoid an overflow of patients on the National Health Service, a state of emergency was declared on March 18th with the closure of schools and non-essential business and the civic obligation to stay home. So far, more than 849 000 cases have been confirmed and more than 17 000 people have died from the infection in our country, being the northern region of Portugal the most affected one[3].

However, the impact of this disease goes far beyond a lower respiratory tract infection. Soon after the beginning of this pandemic, a phenomenon was observed throughout the world: as the number of infections from the new coronavirus raised, the number of patients admitted to hospital for other causes decreased[4]. This is particularly dangerous when it comes to medical or surgical acute conditions. The pressure on health services by a continuously increasing number of patients infected by the new coronavirus coupled with the consequent shortage of human and material resources may have negatively affected the services' response to emergencies[5] such as acute cerebrovascular events, by compromising rapid triage of patients and treatment delivery[6], particularly when treatment effectiveness is time-dependent and has a direct impact on prognosis.

We hypothesised that patients with acute vascular cerebral events are among those for whom there was a decrease in admissions to the ED in Hospital de Santo António, Porto, as seen in other European countries[7], China[8] and United States of America (U.S.A)[9,10]. Interestingly, the opposite could be occurred, due to a possible increase in the number of cases, given the sedentary lifestyle inherent to the confinement and the resulting venous stasis, an important component of the Virchow triad, that also includes endothelial injury and hypercoagulability, factors that favour the thrombosis phenomenon[11], in addition to subsequent vascular lesions associated with COVID-19[12]. This infection may be responsible for an increased risk of cerebrovascular events and thrombotic complications due to the development of a multisystem inflammatory response and hypercoagulable state[13,14]. Stroke, especially ischaemic, and cerebral venous sinus thrombosis have been associated with COVID-19 triggered by either direct viral injury of the brain tissue or through the immune system's inflammatory response[15].

Both, stroke and TIA, are neurological (and medical) emergencies, in need of investigation and immediate treatment after the onset of symptoms, with serious consequences for patients if left untreated, as stroke is the first cause of death and the leading cause of disability[13]. Acute reperfusion treatments are very time-sensitive, for this reason, an underutilization of medical services may have a direct impact on the prognosis of ischaemic stroke patients and lead to increased morbidity and mortality.

The purpose of this study was to evaluate the differences in the pattern of admissions for acute cerebrovascular events in Hospital de Santo António, Porto, during the first year of the COVID-19 pandemic compared to the year before.

Methods

All registries of Emergency Admissions to Centro Hospitalar Universitário do Porto between March 1st 2019 and February 28th 2021 were retrieved through electronic data. Clinical registries with a diagnosis of acute cerebrovascular disease (ICD-9 codes 430 to 438 from March 1st 2019 to September 30th 2020 and ICD-10 codes I60 to I69, G45 and G46 from October 1st 2020 to February 28th 2021) were reviewed, covering the year pre-pandemic COVID-19 and the first year of the pandemic. Admissions to ED of CMIN from CHUPorto were not included. Patients with a diagnosis of vertigo and subdural hematoma were excluded in the first step. We then proceeded to review the clinical registries and excluded: 1) patients with other diagnosis and no evidence of acute cerebrovascular disease, 2) scheduled admission (for clinical reassessment, surgery and repeat brain imaging or other exams), 3) readmissions after performing thrombectomy in another hospital, 4) died before brain imaging. The selected patients were classified according to the diagnosis in ischaemic stroke, SAH, TIA, intraparenchymal haemorrhage and other diagnosis which included nonpyogenic thrombosis of intracranial venous sinus. We collected data on the following variables: sex, age, date of arrival, patient's origin and destination, stroke code activation, service of hospitalization, vascular risk factors, brain imaging, electrocardiogram (ECG) and echo-doppler performed at ED and mortality.

A stroke is defined according to the WHO as rapidly developing clinical symptoms and/or signs of focal, and at times global (applied to patients in deep coma and to those with SAH), loss of cerebral function, with symptoms lasting more than 24 hours or leading to death, with no apparent cause other than of vascular origin[16] and can have different expressions of severity of the deficit. Pathological types of stroke (cerebral infarction, intracerebral haemorrhage, subarachnoid haemorrhage) were classified according to Sudlow and Warlow standard definitions[17]. TIA is defined as a clinical syndrome characterized by acute loss of focal cerebral or monocular function (amaurosis fugax) lasting less than 24 hours whose etiology is attributed to inadequate cerebral or ocular blood supply as a result of arterial thrombosis or embolism associated with arterial, cardiac, or haematological disease[18]. Stroke code activations were defined as a stroke team notification of patients who presented to the ED with stroke-like symptoms with less than 24 hours from symptom onset. For ischemic stroke we considered initial NIHSS score to access stroke severity, intravenous thrombolysis (IVT), and endovascular thrombectomy (EVT) treatment. To be eligible to receive IVT with recombinant-tissue Plasminogen Activator (rt-PA) a patient must receive medical help in the first 4.5 hours from symptom onset and have no contraindications. For EVT treatment, patients must present to the ED within the first 6 hours after the neurological deficit onset. In specific cases, a patient can undergo EVT withing the 24h of last seen without deficits[19]. For TIA we considered the $ABCD^2$ Score to access the risk of following stroke[20].

The patients admitted during the first year of the pandemic (from March 1st 2020 to February 28th 2021) were compared to the ones admitted during the same period of the prior year (from March 1st 2019 to February 29th 2020).

Normally distributed continuous variables were summarized using mean ± standard deviation and a t test was used for comparing the two periods (pre-COVID-19 and COVID-19). Non-normally distributed continuous data are presented as median and interquartile range and a Mann-Whiney test was used for comparison. Categorical variables were analysed by means of Pearson's Chi-square and summarized using frequency and percentages. Results were considered statistically significant for p values < 0.05. The data was analysed with Statistical Package for Social Science, SPSS® version 27.

The study was approved by CHUPorto Ethics Committee. The requirement for informed consent was waived due to the anonymization of the data and its retrospective design.

Results

There were 3317 clinical registries with a diagnosis of acute cerebrovascular disease during the year pre-pandemic COVID-19 and the first year of the pandemic (March 1st 2019 and February 28th 2021). We first excluded 304 patients with a diagnosis of vertigo and 270 with subdural hematoma. We then reviewed 2743 clinical registries and excluded 200 patients with other diagnosis and no evidence of acute cerebrovascular disease, 121 patients with scheduled hospitalization for clinical reassessment, repeat brain imaging and screening with doppler ultrasound of the cervical vessels or surgery, 20 patients that came back after being transferred to another hospital to perform thrombectomy and 3 patients who died before brain imaging. We included 2399 emergency records: 1270 during the pre-pandemic year and 1129 during the first year of COVID-19 pandemic (Figure 1).

The overall number of emergency admissions to Centro Hospitalar Universitário do Porto for all causes was persistently lower during the first year of COVID-19, when comparing to the year before. This was particularly noticeable during the first and fourth trimesters of the pandemic. As for acute cerebrovascular disease code admissions, the number was also lower, although not consistently throughout the year. The major difference was observed during the first three months of the pandemic (Figure 2).

During the previous year of the pandemic, 50.5% of patients admitted to the ED with acute cerebrovascular disease were men (mean age: 71 ± 13.9 years) while during the first year of COVID-19 there were 52.8% (mean age: 72 ± 13.8 years) (Table I).

Four trimesters in each year were considered for further analysis. No significant differences in the overall admissions for acute cerebrovascular disease were observed considering all the trimesters. There was a decline in admissions during the first three months of the COVID-19 pandemic, from 345 to 280. During the summer months: June, July, and August, the number of admissions practically did not change, with 308 patients in 2020 and 309 patients in 2019. In September, October, and November, there was again a decrease in admissions from 297 in 2019 to 261 in 2020, and during the months of December, January, and February, from 318 to 280. For all trimesters, there does not seem to be a noteworthy difference in the mean age of the patients. (Table I)

As for patients' gender, during the first trimester of the pandemic, men accounted for 55% of admissions compared to 49%, in 2019. During the second and third trimesters of COVID-19, most admissions were men, 54.9 % and 51.7 %, respectively, similarly to the corresponding months of the year prior, 52.4% and 51.9%. On the contrary, during the fourth trimester of the first year of the pandemic, men comprised the minority of patients admitted (49.3%), with no marked differences to the corresponding months of the year prior (48.9%) (Table I).

We observed a significant decline in the proportion of patients with arterial hypertension (60.8% versus 66.7%, p=0.003) and hypercholesterolemia (38.8% versus 42.8%, p=0.045) during the pandemic. The percentage of patients with atrial fibrillation or flutter was slightly lower (22.2% versus 24.1%, p=0.281) while the percentage of patients with diabetes mellitus increased (28.7% versus 26.6%, p=0.254), although these differences were not significant. The proportion of smokers remained the same (14.0%). Arterial hypertension and hypercholesterolemia were the most common risk factors in both groups (Table I).

During the months of March, April, and May 2020 we observed a significant decline in the percentage of patients who had hypercholesterolemia (36.4% versus 44.3%, p=0.045) and atrial fibrillation or flutter (20.0% versus 27.5%, p=0.029) when comparing to 2019. In the second trimester of COVID-19 the percentage of patients with arterial hypertension was 59.7% compared to 68.6% in 2019 (p=0.022). The percentage of active smokers was significantly lower during the months of September, October, and November of 2020 (8.8% versus 14.5%, p=0.039). Conversely, in the trimester composed by December 2020 and January and February 2021 the proportion of patients who were smokers was significantly higher comparing to the homologous months of the previous year (18.6% versus 11.9%, p=0.023) (Table I).

Regarding patients' access to the ED, we observed a significant difference (p<0.001) between the two periods: the number of walk-in patients decreased from 267 before the pandemic to 159 during it (21.0% versus 14.1%). The number of patients who went to a Health Centre or called the National Health Service Contact Centre number (SNS 24) before going to hospital also declined from 66 to 42 during COVID-19 period (5.2% versus 3.7%). On the other hand, the percentage of patients who arrived at the hospital by means of the National Institute of Medical Emergency (INEM) increased slightly from 41.3% to 45.1% during the pandemic. As for transfers from other public hospitals, this percentage was also slightly higher during the pandemic (34.6% versus 30.2%). The percentage of patients transferred from a private hospital remained similar (2.0% versus 1.8%). The number of patients who were already in hospital when the neurological deficits began was also similar in both periods (5 versus 7).

During the first three months of the pandemic the proportion of walk-in patients decreased markedly from 21.7% to 12.5%. The percentage of patients who resorted to a Health Centre or called SNS24 before arriving to hospital was also lower (4.6% versus 7.8%). As for patients who resorted to INEM means, the proportion increased in 2020 from 39.1% to 50.7%. For interhospital transfers, the proportion of patients transferred from other public hospitals remained similar (28.6% versus 29.0%) as the proportion of patients transferred from private ones increased (2.0% versus 3.6%); these differences appear to be significant (p=0.010) (Table I).

As for June, July, and August, it was observed significant differences in patients' access to hospital (p=0.001). There was a decrease in the percentage of walk-in patients in 2020 (16.6% versus 21.7%) whilst the number of patients who went to a Health Centre or called SNS24 number before resorting to the ED remained similar (3.9% versus 4.2%). As opposed to the previous months, we noticed a decline in the proportion of patients arriving by emergency services transportation in 2020 (38.0% versus 46.0%), whilst the number of patients transferred from other public hospitals suffered a notable increase, comprising 41.2% of the admissions compared to 26.2% in 2019 (Table I).

During the months of September, October and November, the differences in patient's access did not appear significant (p=0.334). In December, January, and February we observed, again, a significant change in patients' access to hospital (p=0.009) between the two periods. The proportion of patients accessing the hospital through INEM transportation increased to 50.0% in the COVID-19 period comparing to 41.7% the previous year. During the pandemic, only 10.0% of admissions were walk-in patients in comparison to 17.2% the year prior. There was also a decline in patients admitted to the hospital referred by a Health Centre physician or by SNS24 (2.5% versus 5.3%). The proportion of patients transferred from another hospital, either public (35.4% versus 33.2%) or private (2.1% versus 1.3%) remained similar (Table I).

During COVID-19 period, 44.1% of admissions were stroke code activations, in contrast to 39.7% the year before. This increase appeared to be significant (p=0.028). During the summer months, the percentage of stroke code activations went from 38.5% to 46.8% (p=0.038). During winter, this difference was even more significant, with more than half (52.5%) of the admissions being stroke code activations, in comparison to 40.4% the same period, the year before (Table I).

In what concerns diagnosis, during the pre-COVID-19 year there were 165 patients with TIA compared to 124 during the pandemic (13.0% versus 11.0%). The number of ischaemic strokes also decreased from 899 to 831 (70.8% versus 73.6%). The number of intracerebral haemorrhages suffered a slight decrease as well, from 138 to 113 during the pandemic (10.9% versus 10.0%); for SAH, the percentage remained practically stable (4.8% versus 4.6%). These differences did not appear to be significant (p=0.497).

There were no significant differences during the first three months of COVID-19 comparing to the homologous months of 2019: the percentage of ischaemic stroke was practically the same (71.1% versus 71.6%) whilst the proportion of TIA declined from 13.3% to 9.6% and the percentage of haemorrhagic stroke suffered a small increase from 11.0% to 13.6%. The percentage of SAH increased slightly from 3.8% to 5.0% as did the number of patients admitted for nonpyogenic thrombosis of intracranial venous sinus from 0.3% to 0.7% (Table I).

However, during the months of June, July, and August 2020 we noted a significant difference (p=0.017), particularly regarding TIA, comprising only 9.1% of the admissions compared to 16.8% in 2019. During these months, the number of patients with ischaemic stroke increased from 211 to 239, though the percentage remained similar when comparing to 2019 (67.6% versus 68,3%). Contrarily to the prior three months, the percentage of intracerebral haemorrhages decreased from 10.4% to 7.1% (Table I).

During the third trimester, the only noteworthy difference, although not significant, was in the percentage of intracerebral haemorrhages: 8.0% in 2020 compared to 12.5% in 2019 (p=0.490) (Table I).

In the fourth trimester of the pandemic, the percentage of TIA and haemorrhagic strokes increased slightly from 9.4% to 12.1% and 9.7% to 11.4%, respectively, while the proportion of SAH declined from 6.0% to 3.2%. These changes are not significant (Table I).

The number of men with ischaemic strokes did not differ (438 versus 438) whilst the number of women decreased (393 versus 461) during the pandemic. On the contrary, regarding TIA, the greatest reduction was observed in men (65 versus 100) whereas the number of women remained similar (59 versus 65). As for intracerebral haemorrhage we observed a decline in both men (68 versus 75) and women (45 versus 63) during COVID-19. In respect of SAH, the number of men did not differ (24 versus 24) and the number of women only suffered a modest declined (30 versus 34).

When it comes to stroke severity, the median NIHSS score at presentation was 12 before the pandemic, and 11 during it. During the first three months of COVID-19, median NIHSS score at admission was 10, the same as the year before. During the second trimester of COVID-19, the median NIHSS at presentation was 12 as opposed to 9.5 the year prior, although this difference did not reach significance levels. Both in the third and fourth trimesters of the first year of COVID-19 the median NIHSS was 11, while the year before it was 12. It should be noted, however, that the information about the NIHSS scores was accessed for only 1070 (54%) stroke patients (Table I).

Regarding TIA ABCD^2 score, we noticed a decrease in the percentage of patients admitted with a score of 0-3 during COVID-19 (21.6% versus 28.6%) as the percentage of patients with a score of 6-7 increased (26.9% versus 19.0%). These differences were not significant (p=0.284). Breaking it down into trimesters, during the first three months of the pandemic, the percentage of patients with a low stroke risk after TIA was 4.2% compared to 13.5% in 2019, whereas the percentage of patients scoring 6-7 was 37.5% compared to 27.0% the year prior. During the second trimester there was a decrease in the percentage of patients presenting with a 0-3 score as well as the ones presenting with a 6-7 score (23.8% versus 35.9% and 9.5% versus 15.4%, respectively), while the percentage of patients with a moderate risk of stroke increased (66.7% versus 48.7%). In the third trimester, there was a decline in the percentage of patients with a low and moderate risk of developing a stroke (30.8% versus 37.9% and 38.5 versus 51.7%, respectively) whilst the percentage of patients at high risk for stroke almost tripled (30.8% versus 10.3%). In the fourth trimester the were no noteworthy changes between the two periods. None of the differences encountered reached significance levels. The ABCD^2 score was accessed for 219 (76%) TIA patients (Table I).

For laboratory investigations and patient management, the proportion of patients performing brain imaging in the ED did not vary much between the two periods (89.1% versus 90.9%). There were no significant differences in the proportion of diagnostic imaging preformed in the ED in any of the trimesters (Table II).

It was observed an increase in the proportion of patients who performed an ECG in the ED in the pandemic period (29.5% versus 24.6%, p=0.002). During the summer months of the pandemic, only 24.7% of patients did an ECG in the ED in comparison to 41.7% in 2019 (p<0.001). On the other hand, during the winter months, this percentage reached 30.5% compared to 19.8% the year before (p<0.001) (Table II).

As for doppler sonography, only 13.8% of patients admitted during the pandemic performed a doppler ultrasound of the cervical vessels in the ED compared to 19.8% the year before (p<0.001). In regard to the results, there does not seem to be a significant difference between the group of patients in the two periods (p=0.413): most patients did not have haemodynamically significant intraluminal stenosis of the carotids in either group (51.3% versus 55.7%). In the COVID-19 period, 17.9% of patients had >70% intraluminal stenosis, while the year before there were 13.8%. The percentage of patients with no atherosclerotic disease of the carotids was also similar (20.5% versus 18.2%).

The percentage of patients who underwent a doppler sonography of the cervical vessels in the ED was significantly lower in the first (11.4% versus 19.7%, p=0.005), second (15.3% versus 21.7%, p=0.040) and fourth (11.4% versus 18.2%, p=0,021) trimesters of the COVID-19 pandemic period. During the third trimester, although there was not a noteworthy difference in the number of patients preforming a doppler ultrasonography of the cervical vessels, there was a significant difference (p=0.015) in the results of these exams: the percentage of patients who had no sign of atherosclerotic disease in the carotids, more than doubled in 2020 (31.1% versus 15.0%) and the percentage of patients with <50% intraluminal stenosis decreased from 58.3% to 42.2%. The greatest declined was observed in the percentage of patients with 50-70% atherosclerotic stenosis (2.2% versus 13.3%) (Table II).

With respect to reperfusion therapy there was a slight reduction, although not significant (p=0.363), in the number of ischaemic stroke patients who underwent endovascular thrombectomy (224 versus 260) while the number of intravenous thrombolysis performed remained similar before and during COVID-19 pandemic, 86 and 89, respectively (p=0.431). There were no significant differences in any of the trimesters. During the first trimester of COVID-19 the percentage of endovascular thrombectomies decrease slightly from 27.5% to 24.6% (p=0,488), the same happened during the third and fourth trimesters (25.0% versus 27.1% and 30.2% versus 33.3%, respectively). As for the percentage of thrombolysis, it was higher in all four trimesters during the pandemic, although more noticeable during the fourth one with 13.7% of ischaemic stroke patients undergoing thrombolysis treatment compared to 9.4% the year prior (p=0.161) (Table II).

As for the destination of patients, it was not observed any significant differences between the two periods. More than half of the patients were hospitalized, before and during COVID-19 pandemic (53.9% versus 56.6%). The proportion of patients referred for out-patient clinic appears to be similar as well (18.7% versus 17.3%). During the pandemic, 13.8% of patients were referred to their attending physician, compared to 15.0% the year prior. The percentage of ED deaths was also similar between the two time periods (1.2% versus 1.6%) (Table II).

Although not significant, we observed a decrease in patient mortality in the ED, particularly during the summer months of 2020, with 0.3% of deaths compared to 1.3% in the same period of 2019. However, the differences in the fourth trimester appear to be significant ($p<0.040$): there was an increase in the percentage of hospitalized patients (62,1% versus 54,5%). Conversely, there were less patients referred to the outpatient clinic and to their primary care physician (15.0% and 8.2% compared to 19.7% and 14.4%, respectively) and the percentage of ED deaths doubled from 0.9% to 1.8% during COVID-19 (Table II).

When comparing the two periods in terms of the inpatient admission service, there were again significant differences. We noted a reduction in the number of patients in the Intermediate Care Unit (IMCU), with 50 patients hospitalized in this service during the first year of COVID-19, compared to 80 in the non-pandemic period (7.8% versus 11.7%), whilst the proportion of patients hospitalized in the Neurology Service increased to 69.3% from 61.0% the year before. There seemed to be no difference in the number of patients in the Intensive Care Unit (ICU) (35 versus 39) and in the Neurosurgery Service (54 versus 52) between these two years. As for patients in the Internal Medicine Services and in other services not discriminated in Table 2, there was a decline from 2.8% to 1.4% and from 11.2% to 7.5%, respectively, during the pandemic when comparing to the year prior.

Furthermore, we found significant differences in the first and fourth trimesters of COVID-19 pandemic. During the months of March, April, and May, 59.9% of the patients were in the Neurology Service, compared to 64.7% the year before. There was also a slight increase in the percentage of patients in the IMCU (12.9% versus 9.8%). As for patients in the ICU, this number dropped from 8 in 2019 to 2 in 2020 (4.3% versus 1.4%). The greatest difference, though, was in the number of patients hospitalized in the Neurosurgery service, as it doubles from 11 to 22 during the pandemic (6.0% versus 15.0%, p=0.047). In the fourth trimester, the number of patients in the IMCU dropped significantly from 32 before the pandemic, to 1 during it (18.4% versus 0.6%, $p<0.001$). On the other hand, the percentage of patients in the Neurology Service increased from 59.8% to 83.3%. Additionally, the percentage of patients hospitalized in the Neurosurgery ward was lower during the pandemic (4.6% versus 8.0%) (Table II).

Discussion and Conclusion

A decline in the number of acute cerebrovascular disease admissions was observed (1129 versus 1270), particularly during the first three months of the pandemic (280 versus 345). The number of walk-in patients decreased from 267 before the pandemic to 159 during it (21.0% versus 14.1%). During this period, 44.1% of admissions were stroke code activations, in contrast to 39.7% the year before. There were 124 patients with TIA compared to 165 before the pandemic and we noticed a decrease in the percentage of patients admitted with a score of 0-3 (21.6% versus 28.6%) as the percentage of patients with a score of 6-7 increased (26.9% versus 19.0%). The number of thrombectomies suffered a small decline (224 versus 260) while the number of thrombolysis remained stable (89 versus 86). ED mortality rates remained similar (1,2% versus 1,6%). We noted a reduction in the number of patients in the Intermediate Care Unit (IMCU), with 50 patients hospitalized in this service during the first year of COVID-19, compared to 80 in the non-pandemic period.

During the first twelve months of the COVID-19 pandemic there were fewer overall admissions for acute cerebrovascular disease, particularly for TIA and ischaemic stroke. These results corroborate what was already observed in other countries stating that admissions for acute cerebrovascular disease have decreased during the COVID-19 pandemic[21], even though our hospital capacity for acute stroke management remained unchanged.

Adherence to lockdown measures and fear of getting infected with the new coronavirus in hospital environment are pointed out as the primary reasons for this phenomenon[22]. Additionally, people may have been discouraged to present to the ED with the fear of disrupting the functioning of already under stressed hospitals, as the media would often showcase overworked healthcare professionals, ambulance flooded emergency entries, nurseries filled with COVID-19 patients alongside the health authorities plead to only refer to hospitals if necessary. This might have been particularly true for TIA patients: these patients may have deterred themselves from resorting to the ED with mild neurological deficits or did not feel the need to seek medical help after the resolution of symptoms, not knowing that, even though temporary, a TIA is still a medical emergency who demands proper treatment and secondary prevention, as these patients are at risk for recurrent TIA, ischaemic strokes and increased disability[10]. This reduction in TIA admissions was observed all throughout Europe[13].

Furthermore, it is possible that the isolation of the population and the social distancing might have been responsible for an under recognition of symptoms, since in a significant proportion of cases, family members or friends are the ones who alert the emergency services. The first decline in admissions coincided with the beginning of the emergency state on the country and the stay-at-home recommendations in the middle of March. Quarantine and social isolation may have contributed for the lack of acknowledgment or a delay in recognition of neurological deficits as patients with strokes with altered mental status, severe motor deficits or aphasia might have been unable to call for help and were left without assistance for a significant amount of time before being found. Consequently, the increased volume of patients during the month of May can be the result of the loosening of the initial confinement measures around this time.

Moreover, this isolation may have reduced the number of stroke admissions for another reason, as we limited coronavirus transmission, we also limited exposure to influenza virus that is associated with increased stroke risk[23]. On the other hand, it is possible that stroke symptoms in patients with respiratory tract infections might be overlooked at first when arriving to the hospital[24].

The increased number of admissions during the months of June, July, and August particularly for ischaemic stroke can be explained by the larger number of patients transferred from other hospitals during this time. Hence, the overall decline of patients cannot be explained by a reduction in interhospital transfers. Additionally, we can hypothesise that the fear of in-hospital infection was not as glaring in the periphery[22], as the absolute number and percentage of patients transferred to our hospital increased during the pandemic, and a great proportion of these transfers come from inland hospitals, where the number of COVID-19 infections was also lower. On the other hand, the increased number of strokes during these months may be the consequence of the reduction in the number of TIA admissions during the first three months of the pandemic: patients with TIA who did not seek medical help were not treated and did not receive the appropriate secondary prevention being, therefore, at higher risk for developing a stroke in the months that followed.

Another reason contributing to this decrease in admissions, particularly for ischaemic events, has to do with the cancelling of some elective procedures including surgeries that would require patients to temporarily discontinue their anticoagulation medication and consequently increase their risk of developing an ischaemic stroke[22].

Underlying conditions like Diabetes mellitus or arterial hypertension are associated with a higher risk of stroke[25]. The differences in the proportion of patients with these and other vascular risk factors might be the result of a registration bias: in the records of patients admitted in the year prior to the pandemic, information that was not always disclosed during the acute episode, was sometimes registered in the following consultation, either because the physician forgot to register it or because the patient completed the etiologic study in an outpatient setting and was diagnosed with arterial hypertension, diabetes mellitus, atrial fibrillation or flutter or hypercholesterolemia only after the acute episode and so this information would only appear in the follow-up consultation. During the COVID-19 pandemic, neurology consultations were done via telephone and consultation information was not always registered during this period. Additionally, patients would sometimes miss these calls or would not complete the etiologic study of the acute episode. For this reason, vascular risk factors of patients admitted during this time might be underestimated when comparing to patients admitted the year prior.

Normally patients with milder or temporary deficits who were still able to drive themselves to the hospital or had someone to do so for them, and the reduced number of walk-in patients observed during the pandemic could be attributed to the option of a wait-and-see approach. Furthermore, there were also less patients referred from health centres and SNS24. The reasons for this can be varied: patients may also be avoiding primary care facilities, there may have been fewer referrals by primary care providers[24] to avoid overcrowding emergency rooms with patients without severe deficits or patients may have been referred or advised to go to the hospital but chose not to go. A saturation of the emergency transportation system capacity during the pandemic does not explain the reduced number of admissions since the absolute number of patients who resorted to these means of transport suffered only a slight decrease.

In conflict with other authors[5], we observed an increase in the percentage of stroke code activations. Nonetheless, the overall percentage of acute reperfusion treatment remained similar. Contradictory results were observed in different countries as some studies showed a decrease in recanalization treatment performed[7,26], while others showed no change in stroke treatment[27] numbers. These findings corroborate the thought that patients with more severe strokes continue to timely present to hospital whilst patients with milder symptoms are the ones avoiding the healthcare facilities, supported by the similar number of thrombolysis performed during the pandemic, especially when this procedure has a 4.5 hour window of opportunity to be performed from symptom onset. Interestingly, a declined in absolute number was observed in thrombectomies when one would have expected the opposite: a decrease in thrombolysis associated with an increase in the volume of thrombectomies, as patients might have presented too late to the ED to be eligible for thrombolysis but still in time for thrombectomy, as in some cases this procedure can be performed until up to 24 hour of symptom onset. Additionally, the increase in stroke code activations may have been due to non-large-vessel occlusions and therefore these patients were not candidates to recanalization treatment.

As we already expected, the volume of admissions for subarachnoid haemorrhage and brain bleeds remained similar during the pandemic. These conditions usually present with sudden marked deficits and are frequently associated with altered mental status and therefore, patients and their family members rarely dismiss such symptoms and tend to resort to hospital shortly after onset.

An increase in stroke severity was reported in tertiary hospitals in the USA[28].On the contrary, in our hospital, median NIHSS score at presentation was even lower during COVID-19 and mortality rates remained similar. These results do not corroborate the hypothesis that only the more severe patients resorted to the ED or that patients waited longer to seek medical help and had, therefore, more deficits. On the other hand, the NIHSS score was only available for 1070 (54%) patients with the diagnosis of stroke, and therefore, these results might be biased.

Although not significant, TIA appear to be more severe as the there was an increase in the percentage of patients with higher $ABCD^2$ score.

The differences in the number of patients hospitalized in the IMCU, Internal Medicine Services and services other than the ones specified in Table II may have to do with the fact that a proportion of beds in these nurseries was allocated to COVID-19 patients, particularly in the IMCU. A marked decreased was noted especially during the months of December 2020 and January and February 2021, which coincides with the third, and greatest wave of coronavirus infection in Portugal, and the IMCU was most likely almost entirely dedicated to COVID-19 patients.

The limitation of this study is the fact that it is retrospective and only presents the experience of a single stroke centre. It may not be generalized to other hospitals' experience.

The decreased volume of admissions is one of the many collateral damages of the coronavirus outbreak. People may be hesitant to resort to healthcare facilities for fear of being infected by the new coronavirus in hospital environment. Additionally, the media as well as health authorities and even physicians' advice to stay home and only resort to hospitals when strictly necessary, may have been misinterpreted and contributed to patients with mild or temporary neurological deficits to refrain themselves from hospitals with the fear of overcrowding, unnecessarily, the emergency rooms.

Ischemic strokes have narrow therapeutic windows. The prognosis for patients presenting with this condition depends directly on the interval between the onset of symptoms and the institution of an appropriate treatment. Procedures such as mechanical thrombectomy for large vessel occlusion have a very low number needed to treat to get a benefit being, therefore, one of the most valuable time-dependent interventions there is[29]. Even though we have not noted a significant decrease in the number of acute recanalization treatments during COVID-19 pandemic, it is still important to educate the population on how to identify a stroke and emphasize that a delay in seeking healthcare may deem patients' ineligible for treatment and, consequently, lead to more disabling sequelae and mortal strokes that might be, at least in part, preventable.

Although there has been a flattening of the spreading curve of infection since February 2021, raising the populations' awareness for the consequences of the delay in seeking medical health care in acute conditions such as cerebrovascular acute events and encouraging them to an early presentation to the hospital, continues to be vital and should be a priority for public health officials, in order to mitigate some of the unplanned consequences of this present crisis, as well as future ones.

Figures and Tables

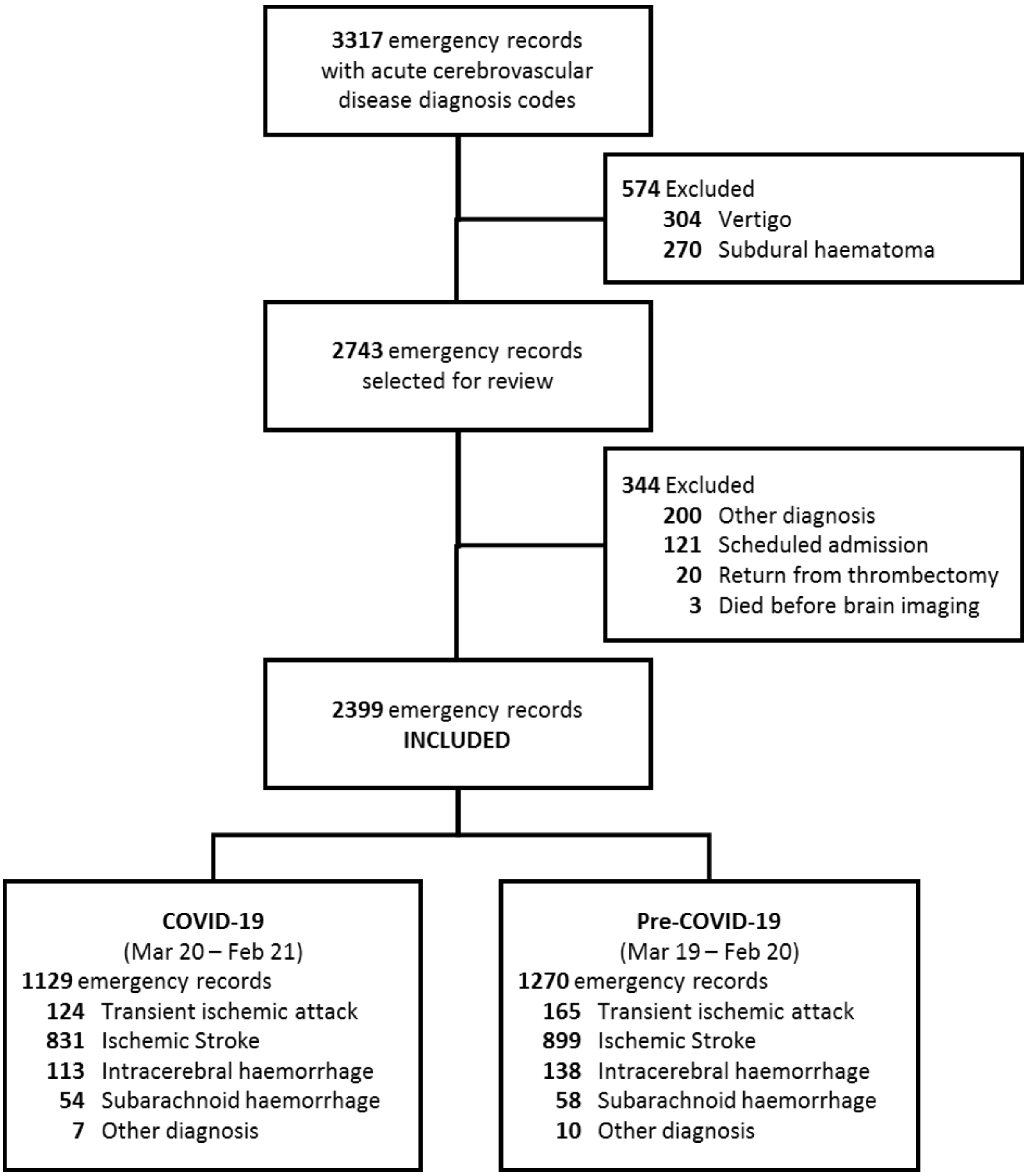

Figure 1 – Records' selection process.

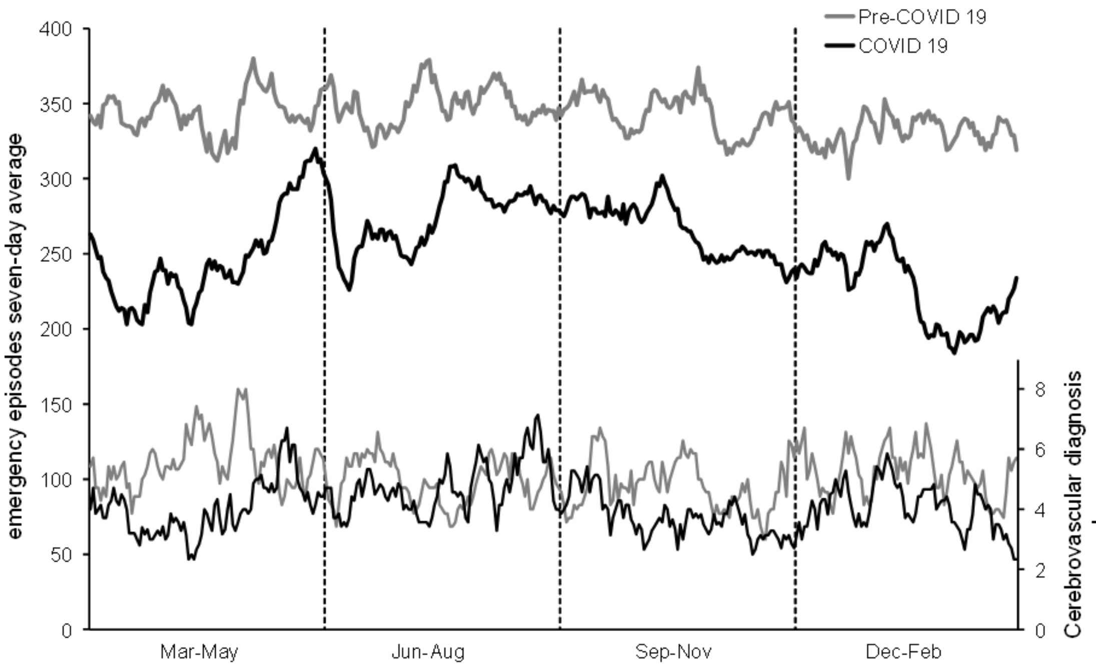

Figure 2 – Comparison of emergency department admissions: March 1st 2019 to February 29th 2020 (before COVID-19 pandemic) and March 1st 2010 to February 28th 2021 (first year of COVID-19 pandemic).

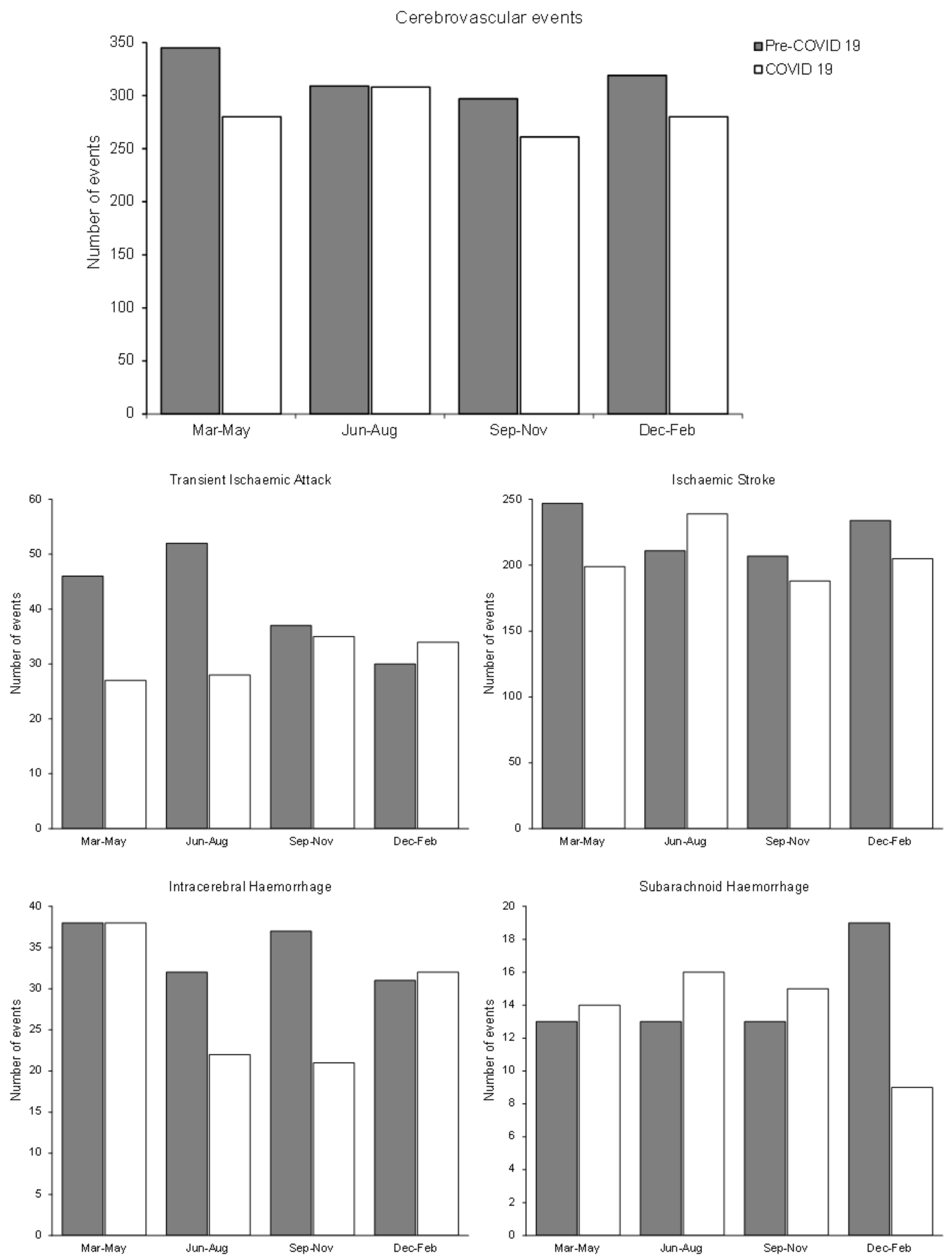

Figure 3 – Overall acute cerebrovascular disease, transient ischaemic attack, ischaemic stroke, intracerebral haemorrhage, and subarachnoid haemorrhage admissions: March 1st 2019 to February 29th 2020 (before COVID-19 pandemic) and March 1st 2010 to February 28th 2021 (first year of COVID-19 pandemic), by trimesters.

Table I – Comparison of acute cerebrovascular emergency admissions to Hospital de Santo António**,** March 1st 2019 to February 29th 2020 (before COVID-19 pandemic) and March 1st 2010 to February 28th 2021 (first year of COVID-19 pandemic):

	All				***P Value***	***Mar-May***				***P Value***	***Jun-Aug***				***P Value***	***Sep-Nov***				***P Value***	***Dec-Feb***				***P Value***
	Pre-COVID-19		**COVID-19**			***Pre-COVID-19***		**COVID-19**			***Pre-COVID-19***		**COVID-19**			***Pre-COVID-19***		**COVID-19**			***Pre-COVID-19***		**COVID-19**		
No. of patients	1270		1129			345		280			309		308			297		261			318		280		
Mean age (SD), years	71	(13.9)	72	(13.8)	0.644	72.2	(13.9)	71.6	(13.9)	0.801	71.5	(13.8)	71.9	(13.3)	0.576	71	(13.6)	72.5	(14.4)	0.728	72	(14.3)	73	(13.8)	0.760
Men	641	50.5	596	52.8	0.257	169	49.0	154	55.0	0.135	162	52.4	169	54.9	0.543	154	51.9	135	51.7	0.976	156	48.9	138	49.3	0.925
Cardiovascular Risk Factors																									
Arterial hypertension	847	66.7	686	60.8	**0.003**	243	70.4	182	65.0	0.147	212	68.6	184	59.7	**0.022**	187	63.0	146	55.9	0.091	205	64.3	174	62.1	0.591
Hypercholesterolemia	544	42.8	438	38.8	**0.045**	153	44.3	102	36.4	**0.045**	129	41.7	117	38.0	0.340	129	43.4	104	39.8	0.391	133	41.7	115	41.1	0.878
Diabetes mellitus	338	26.6	324	28.7	0.254	99	28.7	85	30.4	0.650	69	22.3	78	24.7	0.492	85	28.6	78	29.9	0.743	85	26.6	85	30.4	0.315
Atrial fibrillation/flutter	306	24.1	251	22.2	0.281	95	27.5	56	20.0	**0.029**	64	20.7	73	18.2	0.427	70	23.6	73	28.0	0.235	77	24.1	66	23.6	0.871
Smoking	178	14.0	158	14.0	0.988	42	12.2	38	13.6	0.603	55	17.8	23	14.6	0.282	43	14.5	23	8.8	**0.039**	38	11.9	52	18.6	**0.023**
Access to Emergency department					**<0.001**					**0.005**					**0.001**					0.334					**0.009**
INEM	524	41.3	509	45.1		135	39.1	142	50.7		142	46.0	117	38.0		114	38.4	110	42.1		133	41.7	140	50.0	
Public Hospital	383	30.2	391	34.6		100	29.0	80	28.6		81	26.2	127	41.2		96	32.3	85	32.6		106	33.2	99	35.4	
Walk in	267	21.0	159	14.1		75	21.7	35	12.5		67	21.7	51	16.6		70	23.6	45	17.2		55	17.2	28	10.0	
Health Centre/ SNS24	66	5.2	42	3.7		27	7.8	13	4.6		13	4.2	12	3.9		9	3.0	10	3.8		17	5.3	7	2.5	
Private Hospital	23	1.8	23	2.0		7	2.0	10	3.6		5	1.6	0	0.0		7	2.4	7	2.7		4	1.3	6	2.1	
Hospital Santo António	7	0.6	5	0.4		1	0.3	0	0.0		1	0.3	1	0.3		1	0.3	4	1.5		4	1.3	0	0.0	
Stroke Code Activation	504	39.7	498	44.1	**0.028**	136	39.4	101	36.1	0.391	119	38.5	144	46.8	**0.038**	120	40.4	106	40.6	0.960	129	40.4	147	52.5	**0.003**
Diagnosis					0.497					0.439					**0.017**					0.490					0.083
Transient ischemic attack	165	13.0	124	11.0		46	13.3	27	9.6		52	16.8	28	9.1		37	12.5	35	13.4		30	9.4	34	12.1	
Ischemic Stroke	899	70.8	831	73.6		247	71.6	199	71.1		211	68.3	239	67.6		207	69.7	188	72.0		234	73.4	205	73.2	
Intracerebral haemorrhage	138	10.9	113	10.0		38	11.0	38	13.6		32	10.4	22	7.1		37	12.5	21	8.0		31	9.7	32	11.4	
Subarachnoid haemorrhage	58	4.6	54	4.8		13	3.8	14	5.0		13	4.2	16	5.2		13	4.4	15	5.7		19	6.0	9	3.2	
Other diagnosis	10	0.8	7	0.6		1	0.3	2	0.7		1	0.3	3	1.0		3	1.0	2	0.8		5	1.6	0	0.0	
Median NIHSS at presentation (IQR)*	12	(5-18)	11	(5-18)		10	(5-17)	10	(4-18)		9.5	(5-18.75)	12	(5-19)		12	(6-18)	11	(5-18)	0.507	12	(6-19)	11	(5-17)	0.586
TIA ABCD² Score†					0.284					0.405					0.410					0.166					0.967
0 – 3	36	28.6	20	21.6		5	13.5	1	4.2		14	35.9	5	23.8		11	37.9	8	30.8		6	28.6	6	27.3	
4 – 5	66	52.4	48	51.6		22	59.5	14	58.3		19	48.7	14	66.7		15	51.7	10	38.5		10	47.6	10	45.5	
6 – 7	24	19.0	25	26.9		10	27.0	9	37.5		6	15.4	2	9.5		3	10.3	8	30.8		5	23.8	6	27.3	

Data are reported as No. and percentage unless otherwise specified.

*Excluding TIA and SAH, 1070 reports (54%): 551 pre-COVID-19 (148, 132, 124 and 147 in 1st, 2nd, 3rd and 4th quarter, respectively) and 519 during COVID-19 (115, 155, 111 and 138 in the 1st, 2nd, 3rd and 4th quarter, respectively.

† 219 reports (76%): 126 pre-COVID-19 (37, 39, 29 and 21 in the 1st, 2nd, 3rd and 4th quarter, respectively) and 93 during COVID-19 (24, 21, 26 and 22 in the 1st, 2nd, 3rd and 4th quarter, respectively).

Table II – Laboratory investigation and patient management

	All				***P Value***	***Mar-May***				***P Value***	***Jun-Aug***				***P Value***	***Sep-Nov***				***P Value***	***Dec-Feb***				***P Value***
	Pre-COVID-19		**COVID-19**			***Pre-COVID-19***		**COVID-19**			***Pre-COVID-19***		**COVID-19**			***Pre-COVID-19***		**COVID-19**			***Pre-COVID-19***		**COVID-19**		
Brain Imaging	1155	90.9	1006	89.1	0.132	317	91.9	254	90.7	0.605	281	90.9	269	87.3	0.151	267	89.9	231	88.5	0.596	290	90.9	252	90.0	0.705
Electrocardiogram	460	24.6	427	29.5	**0.002**	133	37.9	123	34.6	0.355	134	41.7	106	24.7	**<0.001**	98	24.8	95	29.2	0.183	95	19.8	103	30.5	**<0.001**
Ecodoppler‡	253	19.8	156	13.8	**<0.001**	68	19.7	32	11.4	**0.005**	67	21.7	47	15.3	**0.040**	60	20.2	45	17.2	0.375	58	18.2	32	11.4	**0.021**
Atherosclerotic Disease‡					0.413					0.517					0.220					**0.015**					0.378
Normal	46	18.2	32	20.5		15	22.1	5	15.6		17	25.4	8	17.0		9	15.0	14	31.1		5	8.6	5	15.6	
<50%	141	55.7	80	51.3		34	50.0	21	65.6		34	50.7	25	53.2		35	58.3	19	42.2		38	65.5	15	46.9	
50-70%	31	12.3	13	8.3		8	11.8	2	6.3		8	11.9	4	8.5		8	13.3	1	2.2		7	12.1	6	18.8	
>70%	35	13.8	28	17.9		11	16.2	4	12.5		8	11.9	10	21.3		8	13.3	8	17.8		8	13.8	60	18.8	
Other	0	0	3	1.9		0	0.0	0	0.0		0	0.0	0	0.0		0	0.0	3	6.7		0	0.0	0	0.0	
Acute recanalization treatment§																									
Thrombolysis	86	9.6	89	10.7	0.431	22	8.9	15	7.5	0.602	25	11.8	29	12.1	0.926	17	8.2	17	9.0	0.769	22	9.4	28	13.7	0.161
Thrombectomy	260	28.9	224	27.0	0.363	68	27.5	49	24.6	0.488	58	27.5	66	27.6	0.978	56	27.1	47	25.0	0.643	78	33.3	62	30.2	0.488
Patients' destination					0.619					0.963					0.656					0.986					**0.040**
Inpatient	685	53.9	639	56.6		184	53.3	147	52.5		165	53.4	173	56.2		162	54.5	145	55.6		174	54.5	174	62.1	
Service					**0.005**					**0.047**					0.630					0.105					**<0.001**
Neurology	418	61.0	443	69.3		119	64.7	88	59.9		107	64.8	109	63.0		88	54.3	101	69.7		104	59.8	145	83.3	
IMCU	80	11.7	50	7.8		18	9.8	19	12.9		12	7.3	16	9.2		18	11.1	14	9.7		32	18.4	1	0.6	
ICU	39	5.7	35	5.5		8	4.3	2	1.4		10	6.1	16	9.2		14	8.6	8	5.5		7	4.0	9	5.2	
Neurosurgery	52	7.6	54	8.5		11	6.0	22	15.0		14	8.5	15	8.7		13	8.0	9	6.2		14	8.0	8	4.6	
Internal Medicine	19	2.8	9	1.4		3	1.6	2	1.4		7	4.2	3	1.7		5	3.1	3	2.1		4	2.3	1	0.6	
Other	77	11.2	48	7.5		25	13.6	14	9.5		15	9.1	15	8.1		24	14.8	10	6.9		13	7.5	10	5.7	
Outpatient clinic	238	18.7	195	17.3		62	18.0	54	19.3		60	19.7	53	17.2		53	17.8	46	17.6		63	19.7	42	15.0	
Family doctor	191	15.0	156	13.8		57	16.5	49	17.5		48	15.5	48	15.6		40	13.5	36	13.8		46	14.4	23	8.2	
Deaths	20	1.6	14	1.2		8	2.3	5	1.8		4	1.3	1	0.3		5	1.7	3	1.1		3	0.9	5	1.8	
Other	136	10.7	125	11.1		25	7.4	18	6.5		32	10.4	33	10.7		37	12.5	31	11.9		33	10.3	36	12.9	

Data are reported as No. and percentage unless otherwise specified.

‡ Only for ischaemic event.

§ Excluding 6 intravenous thrombolysis and 1 mechanical thrombectomy performed in patients with a diagnosis of TIA.

References

1. Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *New England journal of medicine.* 2020.
2. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. *Acta Bio Medica: Atenei Parmensis.* 2020;91(1):157.
3. COVID-19 Relatório de Situação 31-05-2021. covid19.min-saude.pt. Accessed May 31, 2021.
4. Lange PW, Gazzard M, Walker S, et al. Where are our patients? Retrospective cohort study of acute medical unit admissions during and prior to the COVID-19 pandemic. *Internal medicine journal.* 2020;50(9):1132-1134.
5. Paliwal PR, Tan BY, Leow AS, et al. Impact of the COVID-19 pandemic on hyperacute stroke treatment: experience from a comprehensive stroke centre in Singapore. *Journal of thrombosis and thrombolysis.* 2020;50(3):596-603.
6. Derraz I. Stroke health care use and COVID-19. *American Journal of Neuroradiology.* 2020.
7. Hoyer C, Ebert A, Huttner HB, et al. Acute Stroke in Times of the COVID-19 Pandemic: A Multicenter Study. *Stroke.* 2020;51(7):2224-2227.
8. Zhao J, Li H, Kung D, Fisher M, Shen Y, Liu R. Impact of the COVID-19 epidemic on stroke care and potential solutions. *Stroke.* 2020;51(7):1996-2001.
9. Altschul D, Haranhalli N, Esenwa C, et al. The Impact of COVID-19 on Emergent Large-Vessel Occlusion: Delayed Presentation Confirmed by ASPECTS. *American Journal of Neuroradiology.* 2020;41(12):2271-2273.
10. Nagamine M, Chow DS, Chang PD, Boden-Albala B, Yu W, Soun JE. Impact of COVID-19 on acute stroke presentation at a comprehensive stroke Center. *Frontiers in Neurology.* 2020;11.
11. Kushner A, West WP, Pillarisetty LS. Virchow Triad. *StatPearls*. Treasure Island FL: © 2020, StatPearls Publishing LLC.; 2020.
12. Evans PC, Rainger GE, Mason JC, et al. Endothelial dysfunction in COVID-19: a position paper of the ESC Working Group for Atherosclerosis and Vascular Biology, and the ESC Council of Basic Cardiovascular Science. *Cardiovascular Research.* 2020.
13. Bersano A, Kraemer M, Touzé E, et al. Stroke care during the COVID-19 pandemic: experience from three large European countries. *European journal of neurology.* 2020;27(9):1794-1800.
14. Katsanos AH, Palaiodimou L, Zand R, et al. The Impact of SARS-CoV-2 on Stroke Epidemiology and Care: A Meta-Analysis. *Annals of neurology.* 2021;89(2):380-388.
15. Fraiman P, Junior CG, Moro E, Cavallieri F, Zedde M. COVID-19 and Cerebrovascular Diseases: A Systematic Review and Perspectives for Stroke Management. *Frontiers in neurology.* 2020;11.
16. Hatano S. Experience from a multicentre stroke register: a preliminary report. *Bulletin of the World Health Organization.* 1976;54(5):541.
17. Sudlow C, Warlow C. Comparable studies of the incidence of stroke and its pathological types: results from an international collaboration. *Stroke.* 1997;28(3):491-499.
18. Hankey GJ, Warlow C. *Transient ischaemic attacks of the brain and eye.* WB Saunders London; 1994.
19. Powers WJ, Rabinstein AA, Ackerson T, et al. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke.* 2018;49(3):e46-e99.

20. Giles MF, Rothwell PM. Systematic review and pooled analysis of published and unpublished validations of the ABCD and ABCD2 transient ischemic attack risk scores. *Stroke.* 2010;41(4):667-673.
21. Nogueira RG, Abdalkader M, Qureshi MM, et al. Global impact of COVID-19 on stroke care. *International Journal of Stroke.* 2021:1747493021991652.
22. Amukotuwa SA, Bammer R, Maingard J. Where have our patients gone? The impact of COVID-19 on stroke imaging and intervention at an Australian stroke center. *Journal of medical imaging and radiation oncology.* 2020;64(5):607-614.
23. Morelli N, Rota E, Terracciano C, et al. The baffling case of ischemic stroke disappearance from the casualty department in the COVID-19 era. *European neurology.* 2020:1.
24. Dowlatshahi D, Stotts G, Bourgoin A, et al. Decreased stroke presentation rates at a comprehensive stroke center during COVID-19. *Canadian Journal of Neurological Sciences.* 2021;48(1):118-121.
25. Yang H, Chen Z, Fan Y, et al. Difficulties and Countermeasures in Hospital Emergency Management for Fast-Lane Treatment of Acute Stroke During the COVID-19 Epidemic Prevention and Control. *Frontiers in Neurology.* 2020;11:1476.
26. Hsiao J, Sayles E, Antzoulatos E, et al. Effect of COVID-19 on emergent stroke care: a regional experience. *Stroke.* 2020;51(9):e2111-e2114.
27. Rinkel L, Prick J, Slot R, et al. Impact of the COVID-19 outbreak on acute stroke care. *Journal of neurology.* 2021;268(2):403-408.
28. Sharma M, Lioutas V-A, Madsen T, et al. Decline in stroke alerts and hospitalisations during the COVID-19 pandemic. *Stroke and vascular neurology.* 2020;5(4).
29. Martinez-Gutierrez JC, Leslie-Mazwi T, Chandra RV, et al. Number needed to treat: a primer for neurointerventionalists. *Interventional Neuroradiology.* 2019;25(6):613-618.