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Strokes and traumatic spinal cord and brain injury

## **FACING THE CHALLENGES OF ACUTE CARE OF PEOPLE WITH STROKE IN THE 21ST CENTURY: ACHIEVING THE HIGHEST RATES OF REPERFUSION TREATMENTS, ELIMINATING INEQUALITIES IN ACCESS AND HANDLING BIG DATA**

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## 1. Summary

As a collaborative project it was carried out in three subprojects, led by three institutions: the Ictus Foundation (subproject 1), the Bellvitge Biomedical Research Institute - IDIBELL (subproject 2) and the Barcelona Supercomputing Center (subproject 3). The main researchers were Miquel Gallofre, Antoni Martínez Yélamos and Alfonso Valencia respectively

### **Project formulation**

Thrombolysis, stroke care, the development of stroke code systems (SCS), and mechanical thrombectomy have changed the natural history of stroke. The spectrum of candidates for reperfusion therapy (RT) is widening. Partly addicted patients and wake-up strokes are increasingly gaining access to RTs as their benefits are demonstrated. However, SCSs do not yet guarantee equity. In Catalonia, RT rates are among the highest in Europe and the number of SCS activations is constantly increasing. However, we do not know how many activatable patients escape the SCS circuit and lose the opportunity to receive RT. Exploring how our SCS works involves creating manually fed records that represent a workload for physicians.

### **Study hypotheses**

1. The Stroke Code System and reperfusion therapies have not achieved a ceiling effect in Catalonia and, therefore, both can be improved.
2. Problems related to time, comorbidity, previous disability, and diagnostic errors are probably the most relevant reasons for not activating the code.
3. The application of the rules for the exclusion of stroke activation is likely to be heterogeneous among health care levels, and therefore territorial inequality exists.
4. At present, any initiative aimed at measuring or quantifying errors in the stroke code system should be based on the manual entry of data into the appropriate records. The

development of data and text mining will help automate the process of feeding these records.

## 2. Results

### Results of the study of subproject 1

The scope of this subproject was the whole of Catalonia and the main objective was to evaluate the operation of the Stroke Code System throughout the territory. The final sample of valid cases for the analysis was 3,850 cases corresponding to consecutive patients admitted for stroke, data being collected from 40 hospitals. The population of Catalonia in 2020 was 7,722,203

Of the total cases with SC activation (SCP), 23.2% (521) did not strictly meet all activation criteria (erroneous SCP): 46% for previous Rankin  $\geq 3$ , 12% for time  $> 8h$ , 29% for symptoms with complete recovery before arrival at the hospital and 13% for more than one reason.

Of the cases without SC activation (SCN), it was confirmed that 60.66% of this group did not meet the criteria, but it was detected that 25.13% ( $n = 396$ ) should have been activated, while 14% did not have enough data to confirm the activation criteria).

Compared to the analysis carried out in 2008 the percentage of patients without activation of a stroke code in those who should have been activated was 19.1% (in 2019 it was 25%), although it should be noted that the activation criteria at that time were different. For non-activating SCN cases, the reasons for non-activation were previous Rankin  $\geq 3$  in 17.25%, time  $> 8h$  in 24%, and more than one reason 39.6%.

## **2.1 Quantifying the ceiling effect of stroke activation and reperfusion treatment (RT)**

The stroke code was activated in 58.34% of the patients with stroke who were admitted. Ideally, if all SCN-activators were identified as SCs, this percentage could increase to 69.12%, or 11% more, according to the SCs activation criteria in effect in 2019. Considering changing the SC activation criterion that refers to functional status by extending it to patients with previous Rankin 0-3 (instead of 0-2), 174 more cases could have been activated (SCN with Rankin = 3), which would mean an activation ceiling of up to 73% of the total strokes admitted.

For reperfusion treatments neglected due to non-activation of SC, estimates were made of the number of potential treatment candidates based on a hospital start-arrival time < 4h and an NIHSS >3 and considering two scale options. Rankin, the first between 0 and 2 and the second between 0 and 3. A total of 646 patients (444 IVT and 202 IVT + EVT) received intravenous thrombolytic therapy (IVT), which represents 22.2% of all cases of ischemic stroke.

Following the first definition, a total of 100 cases was estimated without SC activation that could have been possible candidates for IVT, so that the percentage of IVT could increase by 3.4%, from 22.2% to 25.6%.

Following the same criteria but including cases with a previous rank between 0 and 3, up to 154 more cases could have benefited. The ceiling in this case would increase by 5.3%, from 22.2% to 27.5% of ischemic strokes

Compared to the analysis conducted in 2008, where the percentage of potentially omitted IVT treatments was 7%, we observed a reduction in the number of neglected treatments. Regarding endovascular treatment (EVT), the potential candidate cases were considered, neglected for non-activation of SC, with a previous mRS 0-2, a hospital start-arrival time <8h or wake / unknown and an NIHSS >5, 468 patients received endovascular treatment, representing 16.1% of patients with ischemic stroke.

Applying the criteria defined as possible candidates, it is estimated that 214 patients with favorable neuroimaging and without SC activation could have been possible candidates for EVT, so that the percentage of EVT could increase from 16.1% to 23.4% of ischemic strokes.

This estimate is likely to be magnified as a cut-off point of NIHSS > 5 was established, but many of these cases may not have large vessel artery occlusion and therefore may not actually be candidates for EVT. Also, some cases were strokes of uncertain chronology, so they may have a pre-established stroke and really could not have benefited from treatment with mechanical thrombectomy.

## **2.2 Evaluating the reasons for neglecting the activation of the stroke code and reperfusion therapies, emphasizing delay and prior status**

The profile of patients most likely not to have an SCP is those who are alone at the time of the stroke, or who have mild or atypical symptoms. It is also influenced by a low level of education, a history of cognitive impairment and less severe symptoms related to balance and coordination.

With regard to reperfusion therapies, there is room for improvement in SC activation of up to 11%, but reperfusion therapies would only potentially increase from 22% to 25%. With this small room for improvement it was not considered appropriate to conduct a more detailed study to characterize patients neglected by reperfusion therapies. Comparisons have been made to find out what this group was like and in most cases they are mild strokes, with low scores on the NIHSS scale.

## **2.3 Estimating the percentage of error in the activation of the stroke code; knowing the number of candidates lost by activation and how many have lost the opportunity to be treated, determining the responsible health level**

Analysis of the quality of SC activations by territorial stroke code area shows slight differences between regions. As for the SCN-activables, the percentage varies between 7% and 16% of the total strokes admitted by region

## **Results of the study of subproject 2**

The scope was limited to a specific area of Catalonia, the Southern Metropolitan Health Region, and the main objective was to assess the equity of access of RTs to this area and specifically analyze the incidence of stroke and administration of RT in this territory, identifying individual characteristics, of environment and of hospital level that would make access to RT difficult.

The population of the Southern Metropolitan Region in 2020 was 1,247,729. The final number of hospitalized patients included in these sub-studies was 1,476 hospitalized patients, of whom 1,232 corresponded to Basic Health Areas in this region.

In this sub-study, the rate of access to reperfusion treatments was 17.11% of ischemic strokes for thrombolytic treatment and 14.02% for revascularization, with 4.86% of patients receiving both treatments. The percentage of patients in this area who had access to reperfusion treatment (26.3%) is one of the highest described in the literature.

Data from this sub-study showed that, in this area, access to reperfusion treatment was lower among men with a longer time between onset of symptoms and arrival at the emergency department, and that it increased with severity of the stroke and especially if the Stroke Code had been activated. Sociodemographic variables such as a more disadvantaged social class were associated with a lower likelihood of receiving thrombolytic treatment but not of any reperfusion treatment or with an impact on mortality.

The same assessment was applicable to accessibility for endovascular treatment among patients living alone, but this effect was not maintained when assessing access to any reperfusion treatment, although there was a trend that was not significant.

Factors such as the level of previous disability, taking anticoagulant medication or an unknown start time conditioned accessibility, as the indication of treatment or not depended on these variables. In terms of mortality, only the severity of the stroke and the age of the patient were variables independently associated with higher mortality.

No differences were found in the accessibility of reperfusion treatment in this health area depending on the patient's Basic Health Area of residence or socioeconomic factors that may condition this accessibility, although there may be some individual social variables (such as living alone or disadvantaged social class) that could negatively influence and affect accessibility to any reperfusion treatment when assessed in isolation, but this effect was not significant when analyzing the overall accessibility of any reperfusion treatment.

No differences were detected in living in a rural or urban area, either in the activation of the stroke code or in the rate of reperfusion treatments. Of the factors associated with accessibility (male gender, previous Rankin, episode of unknown start time, time between onset of episode and arrival at emergency room, severity of stroke measured with NIHSS and activation of Stroke Code) only the time between the onset of the stroke and the arrival at the emergency room and the activation of the Stroke Code would be modifiable factors.

### **Results of the study of subproject 3**

The exhaustive analysis of the characteristics of the discharge reports made it possible to assess the quality of the discharge reports in terms of their degree of completion, to detect the main challenges for the application of text mining techniques, and to propose easily implemented measures that improve the quality of reports and encourage the application of these techniques.

There is a collection of recommendations for improving the quality of discharge reports for stroke patients that are easy to implement, aim to encourage the application of text mining tools and are applicable to other clinical texts and other scenarios.

A registration report normalization tool can be developed that identifies and normalizes section headers, generating a standardized version of the report. A prototype identification of variables is available to be extracted from discharge reports.

## **CONCLUSIONS**

This study must be contextualized, comparing its data with the similar analysis of 10 years ago on the stroke code in Catalonia, also funded by La Marató, and which helped formulate the hypotheses of the current study.

With regard to the first two hypotheses of the current work, referring to the ceiling effect on stroke code activations and the most relevant elements of code non-activation, it should be noted that the population rate of stroke code activations in patients admitted to 2019 was 59 / 100,000 inhabitants, a rate 3 times higher than in 2008 when it was conducted in the same study, showing a clear improvement.

The system has a high sensitivity to identify patients with activation criteria, and only 10% of total stroke admissions are not activated, a similar percentage compared to 2008. The care times achieved are short (2.25 hours from the onset of symptoms to hospital care) and the volume of reperfusion treatments is very high (22% IVT and 16% EVT, from ischemic strokes). Intravenous reperfusion treatments potentially lost by inactivated codes stood at around 3%, and no more detailed study was considered necessary.

The natural evolution of the items of the stroke code over these ten years has meant that in practice and until today, the activation criteria have changed. There is currently no age activation limit, and time criteria have changed.

The conclusions of this study indicate the profile of patients in whom the stroke code is more likely not to be activated and in whom actions need to be focused: people who are alone at the time of the stroke or who have milder or atypical symptoms. It is also influenced by a low level of education, a history of cognitive impairment and less severe symptoms related to balance and coordination.

The sub-study of the Southern Metropolitan Region, together with the global data, is related to the third hypothesis, and shows that the territorial differences are very modest, which allows us to point out that there is no territorial inequity or that it is very limited.



Regarding the fourth hypothesis, on the development of data and text mining, the emphasis is on the need to automate the data entry process, but new work is needed to help develop these procedures.

## **RECOMMENDATIONS**

The activation of a stroke code has been fully integrated into the Catalan healthcare system since 2006 and its main actors are professionals, hospitals and Medical Emergency Systems, guaranteeing equity in accessibility and a probability of access. to these treatments equal or superior to those described in the literature. In order to ensure that all candidate patients can be activated, the time is shortened and all patients in whom it is indicated can be treated, the following recommendations are proposed:

- Strengthening the training of SEM professionals to detect atypical clinical strokes that may not be detected with the RAPID tool
- Continuing public awareness-raising campaigns on the need for urgent care for people who have just suffered a stroke, emphasizing the recommendation to call 112 urgently instead of taking the patient by their own means to any other level of health care
- In the current formulation of the stroke code, evaluating the extension of the time criterion from 8 hours to 24 hours or to stroke on the day of the alert
- In the current formulation of the stroke code, assessing the inclusion of patients with Rankin scale up to 3 points.

As an additional suggestion, the high impact of unhealthy lifestyle habits in the study group (e.g. more than 47% had a history of smoking) and the significant weight of risk factors (notably hypertension with 71.8%) is recommends insisting on widespread public health policies to reduce the impact of stroke.