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Pre-thrombectomy imagiologic revaluation in ischemic stroke in transferred patients from a primary stroke centre

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Pre-thrombectomy imagiologic revaluation in ischemic stroke in transferred patients from a primary stroke center

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Abstract

Background and Purpose

Stroke is one of the leading causes of death and disability worldwide, so obtaining the best functional outcome possible is crucial. Currently, the most effective treatment involves mechanical thrombectomy. When patients are diagnosed in a primary stroke hospital (PSC), without the means to perform endovascular treatment, they need to be transferred to a comprehensive stroke center (CSC). That transfer takes time and might alter clinical and imagiological findings that could turn the predicted treatment futile or dangerous due to reperfusion lesion. The purpose of our study is to determine the effect of repeating computed tomography (CT) assessment before thrombectomy in transferred patients.

Methods

We did a retrospective, unicenter analysis of data from patients transferred to our hospital between 1/1/2016 untill 31/12/2018. Patients' demographic features, clinical data, timings of events, imagiological assessments (Alberta stroke program early CT score), treatments performed and complications were studied. Patient outcome was defined by modified Rankin Scale (mRS) at 3 months. Group differences were assessed by $\chi 2$ or Fisher exact test for categorical variables, Student t test and Mann-Whitney U test for continuous variables as appropriate. To estimate the probability of mRS 0-2 according to CT revaluation a logistic regression was performed.

Results

We included 363 patients. Mean age was 70.85 (standard deviation of 12.66) and 182 were female (50.14%, standard deviation of 0.501). 243 (66.8%) were revaluated by CT. In univariate analysis, the only statistically significant difference was a higher frequency of hypertension in the group that repeated CT (48.8% vs. 20.11%, p=0.025). The repetition of CT led to an increased median time of femoral puncture from 41 to 106 minutes ($p<0.001$). There were no significant differences between groups related to mRS at 3 months and hemorrhagic transformation.

Conclusions

In patients that underwent thrombectomy transferred from a PSC to a CSC, CT revaluation delayed treatment and was not associated with clinical outcomes.

Resumo

Introdução

O acidente vascular cerebral (AVC) é uma das principais causas de morte e incapacidade a nível mundial, sendo crucial minimizar as suas sequelas. À luz do conhecimento atual, o melhor tratamento para esta patologia envolve trombectomia mecânica. No entanto, apenas um restrito número de hospitais tem este recurso disponível, sendo necessária a transferência destes doentes quando não houver acesso a este. Essa transferência, pelo tempo que o processo exige, pode levar a uma evolução da patologia que exija uma abordagem diferente da prevista. O objetivo do nosso estudo passa por determinar o benefício de repetir a tomografia computorizada (TC) quando estes doentes chegam ao hospital terciário, antes de realizarem trombectomia.

Métodos

Foi realizada uma análise retrospetiva dos dados dos doentes que foram transferidos com diagnóstico de AVC para o nosso hospital no período entre 1/1/2016 a 31/12/2018. Foram analisadas características demográficas dos utentes, informação clínica, temporalização do evento ocorrido, consequentes ações e resultados imagiológicos, assim como aos tratamentos a que foram submetidos e suas complicações. O prognóstico do doente foi definido segundo a escala modificada de Rankin (mRS) aos 3 meses. As diferenças entre grupos foram avaliadas pelo teste $\chi 2$ ou teste exato de Fisher para variáveis categóricas e para variáveis continuas foi aplicado o teste t Student ou Mann- Whitney U de acordo com as suas características. Para estimar a probabilidade de mRS 0-2 de acordo com a reavaliação imagiológica por TC foi realizada uma regressão logística.

Resultados

Foram incluídos 363 doentes no estudo e em 243 (66.8%) foi feita a reavaliação por TC. Tinham uma idade média de 70.85 anos (desvio padrão de 12.66) e 182 eram mulheres (50.4%, com desvio padrão de 0.501). Numa analise univariavel, a única diferença estatisticamente relevante foi uma maior incidência de hipertensão no grupo que repetiu a TC (48.8% vs. 20.11%, p=0.025). Essa repetição também originou um aumento do valor da mediana relativa ao tempo que demorou para ocorrer a punção femoral de 41

para 103 minutos (p<0.001). Não houve alterações significativas entre os dois grupos relacionado com complicações do tratamento, scores de sucesso do tratamento ou prognóstico.

Conclusão

A reavaliação imagiológica por Tomografia Computorizada prévia à trombectomia em doentes transferidos para um hospital terciário atrasou o início da terapêutica e não esteve associada ao resultado clínico.

Key words: Ischemic Stroke; Mechanical Thrombolysis; Diagnostic Imaging; Tomography, Spiral Computed;

Subject Terms: Ischemic Stroke, Cerebrovascular Procedures, Imaging, Computerized Tomography (CT)

Word Count: 4320

Introduction

Stroke is one of the main causes of death and long-term impairment in our society, so it is fundamental that we learn the best way to mitigate its impact.[1] It has been proven that the best approach for acute ischemic stroke with large vessel occlusion (LVO-AIS) relays on endovascular treatment (EVT),[2–5] whose success is significantly dependent on the time of reperfusion. [3,6] However, not all patients when diagnosed with ischemic stroke are initially at hospitals with resources to perform EVT, so there is a need to transfer to other more specialized hospitals with that capacity. Such process takes time and that can change the initial diagnosis findings and its eligibility EVT particularly regarding Alberta stroke program early CT score (ASPECTS). An inadequate patient selection for EVT can lead to complications, worse prognostic and unsuccessful procedures. In a disease that each minute untreated is associated with a significant and irretrievably neuron loss, it is crucial that any postponement of the treatment serves a valid objective and its pros and cons must be rigorously accounted.[7]

Currently, there is no evidence regarding the need and indications for CT revaluation in transferred patients from PSC to CSC before EVT. The main goal of this study was to determine if CT scan revaluation prior to EVT changes the outcome of AIS-LVO patients transferred from PSC and submitted to EVT.

Methods

Study Population

We analysed data from consecutive patients admitted to our CSC transferred from PSC between 1/1/2016 until 31/12/2018 with the diagnosis of AIS-LVO. We included patients transferred from 7 different PSC eligible to EVT due to LVO-AIS confirmed by Computed tomography angiography (CTA). We excluded all patients that did not undergo endovascular treatment due to spontaneous recanalization or infarct growth contraindication. The study was approved by the hospital medical ethics committee that waived the requirement to obtain of the informed consent due to the large number of patients and the significant scientific international value associated with this investigation.

Data Collection

We designed a unicenter, retrospective and observational cohort study. Data was collected from a standardized local clinical registry that included Emergency Room reports, clinical reports obtained telephonically from PSC physicians before transfer and information from consecutive follow-up appointments. We compared several variables regarding patients characteristics such as: age, sex, hypertension (Systolic Blood Pressure (SBP) ≥140 or Diastolic Blood Pressure ≥90 mmHg before stroke or use of antihypertensive medication), dyslipidaemia (abnormally high values of LDL cholesterol, HDL cholesterol and/or triglycerides) atrial fibrillation, diabetes (previously diagnosed or with fasting values greater than 126 mg/dL or ≥ 200mg nonfasting evaluations), smoking habits, use of oral anticoagulant, glucose and SBP values measure at admission, if they were transferred from other hospitals and the time of admission at our hospital.

The authors had complete control over the data and information submitted and attest to its integrity, the fidelity to the study design, and the exhaustiveness and accuracy of the reported data.

Imagiological Evaluation, Neurologic and Hemodynamic Assessment

We also analysed the specific characteristics of the stroke itself (anterior and posterior circulations) and symptoms onset (recurring to information of when the patient was last seen normal or when the symptoms were recognized).

For the imagiological evaluation we sought to assess if it was done a conventional CT after transfer or if the patient went directly to the angiography suite.

In the treatment itself, we focused on the occurrence or not of intravenous tissue plasminogen activator (IV tPA) administration and its timing, the time of arrival at angiography suite and the groin puncture. Regarding the response/efficacy of the procedure we used the Thrombolysis in Cerebral Infarction (TICI) scale, assessing the value before and after EVT and considered that scores ≥ 2B corresponded to successful reperfusion. In terms of consequences of the process it was studied the existence of a follow-up parenchymatous hematoma (PH) according to ECASS II classification[8].

The National Institute of Health Stroke Scale (NIHSS) was used to determine the impact of the event. We compared the values at baseline and at discharge or at the seventh day after the stroke. For the assessment of the impact of repeated imagiological exams the Alberta Stroke Program Early Computed Tomography Score (ASPECTS) was applied and we compared the value in PSC and CSC, when applicable. In terms of functional

outcomes, we resorted to the modified Rankin Scale (mRS), relating values before the stroke, when the patient was discharged from the hospital and 3 months after the event, allowing us to subcategorize the patients with 90-Day Good Outcome (if mRS 0-2) or 90-Day Mortality (= mRS of 6).

Statistics

In the statistics analysis, we used different methods adjusted to the variables at cause. To compare categorical variables the chosen method was the qui^2 or Fisher exact test. For the continuous variables we applied the Student t test and Mann-Whitney U test after normality exclusion. To ascertain the probability of a Good Outcome after treatment (mRS 0 to 2) regarding the computed tomography revaluation or lack of thereof we made a logistic regression. The statistical analyses were made recurring to IBM SPSS Statistics software, version 25.

Anonymised patient data will be made available by the corresponding author upon reasonable request.

Results

In the time period we selected, a total of 417 patients were transferred to our hospital with ischemic stroke diagnosis. Of those, 363 patients were included in our study. They had a mean age of 70,85 and mean NIHSS of 17,1. Of all the transferred patients, 243 (66.8%) were revaluated by CT (Figure 1). In an univariate analysis, the only difference was a higher incidence of hypertension in the group that repeated CT (48.48% versus 20.11%, p=0.025) (Figure 2). In that group, the CT revaluation increased the median time of femoral puncture from 41 to 103 minutes (p<0.001) (Figure 3). The comparative analysis of the demographic characteristics of the patients of those two groups are presented in Table 1. There were no significant differences between groups regarding the recanalization (TICI 2b/3), haemorrhagic transformation and mRS at 3 months with an Odds Ratio (OR) of 0,881, with a confidence interval (IC) of 95% (0,557-1,393) and p=0,588 (Table 1 and Figure 4). A logistic regression model adjusting for all matching variables (hypertension and posterior circulation stroked) showed no statistically significant difference in the probability of obtaining mRS 0-2 with or without a CT scan revaluation (odds ratio 0.891; 95% CI, 0.559–1.421; *P*=0.629)

Discussion

Our study showed no evidence of significant benefit in CT scan revaluation in stroke patients after transfer to a tertiary hospital and before EVT. It delays the start of the treatment without any change in terms of efficacy or safety. We hypothesize that this delay in time to reperfusion is counterbalanced by a better selection of patients to EVT substantial value in terms of efficacy or safety.

Related to the topic of imagiologic evaluation in stroke, there are many studies published about the benefits and limitations of the different available exams but not a lot can be found regarding our specific conundrum and what is published does not applied to our specific study population (transferred patients). A study was done before analysing the direct to angiosuite approach after initial CT in comparison with CT plus CTA and MRI that concluded no superiority of any specific strategy but they did not study transferred patients.[9] A recent study with data from United States of America concluded that inter hospital transfers caused worse prognostics due to the postponement of the therapy, proposing that the same would occur in countries where the transfer distance would be smaller, although it anticipated the prospective of better outcome with direct transfer to intervention centers.[10] And even though in certain studies EVT did not show superiority over IV-tPA, it has been proved that there were several limitations such as late initiation of therapy, ineffective and antique devices, failure to confirm occlusion and so on.[11,12] So, it is clearly shown in a multitude of different studies the importance of mechanical thrombectomy in opposition to therapy with medical therapy only.[13–16] Consequently, if the patients show the appropriate clinical, laboratorial and imagiological criteria they should undergo thrombectomy according to the latest guidelines.[2] However, not all hospitals have the resources necessary to perform such procedures and if the patients were diagnosed in a primary hospital, they need to be transferred to a health unit with the necessary capacities. Strategies have been studied and developed in order to reduce workflow time, such is the case of a recent study on the use of flat-detector computed tomography (FDCT) in the angiography suite that allows intravenous thrombolysis and thrombectomy all in the same room as a mean to reduce door-to-groin and door-to-reperfusion times.[23] Other study evaluated the strategy of direct referral to angio-suite (with cone-beam CT technology) of patients with pre-hospital suspected LVO-AIS. A reduction of the door-to-groin time, the door-to-reperfusion time, and a significant increase odds of good clinical outcome was found.[24] Another study concluded that thrombi suffers change in terms of location, area and density that are dependent on time within the first 5 hours after symptom onset in ischemic stroke.[25] All of this support the

evidence that the outcome of EVT has a close dependence with time.[26] But apart from time, patient selection has also proven enormous importance regarding the benefit of EVT, particularly related to the exclusion of patients where the treatment would be futile, meaning poor functional outcome even with appropriate recanalization.[17–22] Just as "Time is Brain", "Imaging is Brain" meaning that individual vascular and physiologic information shown by different imaging techniques can be as relevant as time in terms of EVT effectiveness.[27] This duality between time and patient selection may explain the neutrality of our findings, where the increase of time to reperfusion is counterbalanced by a better patient selection warranted by CT scan revaluation.

The higher percentage of posterior circulation strokes in the population without CT scan revaluation may be explained by the fact that this technique, particularly non-contrast head CT, has a poor sensitivity to assess infarction in this territory and EVT can be a life-saving procedure when vertebrobasilar circulation is compromised.

To our knowledge, our study is the first evaluating the specific subject of transferred patients from PSC and evaluating a simple and widespread technology of neuroimaging which is CT imaging, in order to answer a common and relevant clinical day-to-day question in CSC.

We had some limitations. One of them was that it was a single-centred study. Also, the patients studied were transferred from a limited number of hospitals because only a restricted number of primary hospitals are in protocol with ours. Despite analysing a moderately large stroke population, studying a greater number of patients in a multicentre approach would increase confidence and generalisability in the results obtained. Moreover, by excluding patients that did not undergo a cerebral angiogram due to severe infarct growth or haemorrhage, we were unable to understand which patients could specifically benefit from a CT scan evaluation. It should also be noted that the decision of repeating CT was taken by the vascular neurologist, with inherent bias to those patients that the physician decided would probably require a second assessment, however, we adjusted for possible confounders to minimize any possible effect.

In the future, including these patients, collecting outcome variables for a longer period of time, involving a larger sample and a multicentre design would give us more insight into the question of who should be neuroimagiologically revaluated prior to EVT.

Conclusion

Knowing that the prognosis of stroke depends on a time sensitive approach, any procedure done that interferes in time with has to have proved benefit. Our findings suggest that in patients that underwent thrombectomy for LVO-AIS transferred from a PSC repeating a CT study delays time to reperfusion without significant impact on safety or efficacy outcomes.

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Conflict(s)-of-Interest/Disclosure(s)

The authors deny any conflict of interest and have nothing to disclose.

References

1. Apirakkan M, Vuthiwong W, Kobkitsuksakul C, Keandoungchun J, Chanthanaphak E. Value of brain computed tomographic angiography to predict post thrombectomy final infarct size and clinical outcome in acute ischemic stroke. *Asian J Neurosurg*. 2019;14(4):1126. doi:10.4103/ajns.AJNS_242_19

2. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke . *Stroke*. 2019;50(12). doi:10.1161/STR.0000000000000211

3. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387(10029):1723-1731. doi:10.1016/S0140-6736(16)00163-X

4. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med*. 2015;372(24):2285-2295. doi:10.1056/NEJMoa1415061

5. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med*. 2015;372(24):2296-2306. doi:10.1056/NEJMoa1503780

6. Mulder MJHL, Jansen IGH, Goldhoorn R-JB, et al. Time to Endovascular Treatment and Outcome in Acute Ischemic Stroke. *Circulation*. 2018;138(3):232-240. doi:10.1161/CIRCULATIONAHA.117.032600

7. Saver JL. Time is brain - Quantified. *Stroke*. 2006;37(1):263-266. doi:10.1161/01.STR.0000196957.55928.ab

8. Hacke W, Kaste M, Fieschi C, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). Second European-Australasian Acute Stroke Study Investigators. *Lancet (London, England)*. 1998;352(9136):1245-1251. http://www.ncbi.nlm.nih.gov/pubmed/9788453. Accessed March 16, 2020.

9. Tong E, Hou Q, Fiebach JB, Wintermark M. The role of imaging in acute ischemic stroke. *Neurosurg Focus*. 2014;36(1):E3. doi:10.3171/2013.10.FOCUS13396

10. Venema E, Groot AE, Lingsma HF, et al. Effect of Interhospital Transfer on Endovascular Treatment for Acute Ischemic Stroke. *Stroke*. 2019;50(4):923-930. doi:10.1161/STROKEAHA.118.024091

11. Broderick JP, Palesch YY, Demchuk AM, et al. Endovascular therapy after intravenous t-PA versus t-PA alone for stroke.[Erratum appears in N Engl J Med. 2013 Mar 28;368(13):1265]. *N Engl J Med*. 2013;368(10):893-903. doi:https://dx.doi.org/10.1056/NEJMoa1214300

12. Ciccone A, Valvassori L, Nichelatti M, et al. Endovascular treatment for acute ischemic stroke. *N Engl J Med*. 2013;368(10):904-913. doi:10.1056/NEJMoa1213701

13. Campbell BCV, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015;372(11):1009-1018. doi:10.1056/NEJMoa1414792

14. Berkhemer OA, Fransen PSS, Beumer D, et al. A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke. *N Engl J Med*. 2015;372(1):11-20. doi:10.1056/NEJMoa1411587

15. Goyal M, Demchuk AM, Menon BK, et al. Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke. *N Engl J Med*. 2015;372(11):1019-1030. doi:10.1056/NEJMoa1414905

16. Saver JL, Goyal M, Bonafe A, et al. Stent-Retriever Thrombectomy after Intravenous t-PA vs. t-PA Alone in Stroke. *N Engl J Med*. 2015;372(24):2285-2295. doi:10.1056/NEJMoa1415061

17. Berkhemer OA, Fransen PSS, Beumer D, et al. A Randomized Trial of Intraarterial Treatment for Acute Ischemic Stroke. *N Engl J Med*. 2015;372(1):11-20. doi:10.1056/NEJMoa1411587

18. Krajíčková D, Krajina A, Herzig R, et al. Mechanical recanalization in ischemic anterior circulation stroke within an 8-hour time window: A real-world experience. *Diagnostic Interv Radiol*. 2017;23(6):465-471. doi:10.5152/dir.2017.17049

19. Campbell BCV, Mitchell PJ, Kleinig TJ, et al. Endovascular Therapy for Ischemic Stroke with Perfusion-Imaging Selection. *N Engl J Med*. 2015;372(11):1009-1018. doi:10.1056/NEJMoa1414792

20. Rudkin S, Cerejo R, Tayal A, Goldberg MF. Imaging of acute ischemic stroke. *Emerg Radiol*. 2018;25(6):659-672. doi:10.1007/s10140-018-1623-x

21. Albers GW, Marks MP, Kemp S, et al. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med*. 2018;378(8):708-718. doi:10.1056/NEJMoa1713973

22. Nogueira RG, Jadhav AP, Haussen DC, et al. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Engl J Med*. 2018;378(1):11-21. doi:10.1056/NEJMoa1706442

23. Psychogios M-N, Maier IL, Tsogkas I, et al. One-Stop Management of 230 Consecutive Acute Stroke Patients: Report of Procedural Times and Clinical Outcome. *J Clin Med*. 2019;8(12):2185. doi:10.3390/jcm8122185

24. Mendez B, Requena M, Aires A, et al. Direct Transfer to Angio-Suite to Reduce Workflow Times and Increase Favorable Clinical Outcome. *Stroke*. 2018;49(11):2723-2727. doi:10.1161/STROKEAHA.118.021989

25. Pikija S, Magdic J, Trkulja V, et al. Intracranial thrombus morphology and composition undergoes time-dependent changes in acute ischemic stroke: A CT densitometry study. *Int J Mol Sci*. 2016;17(11). doi:10.3390/ijms17111959

26. Bourcier R, Goyal M, Liebeskind DS, et al. Association of Time from Stroke Onset to Groin Puncture with Quality of Reperfusion after Mechanical Thrombectomy: A Meta-analysis of Individual Patient Data from 7 Randomized Clinical Trials. *JAMA Neurol*. 2019;76(4):405-411. doi:10.1001/jamaneurol.2018.4510

27. Puig J, Shankar J, Liebeskind D, et al. From “Time is Brain” to “Imaging is Brain”: A Paradigm Shift in the Management of Acute Ischemic Stroke. *J Neuroimaging*. February 2020:jon.12693. doi:10.1111/jon.12693

Figure Legends

Figure 1 -Algorithm for patient inclusion. CT indicates Computed Tomography.

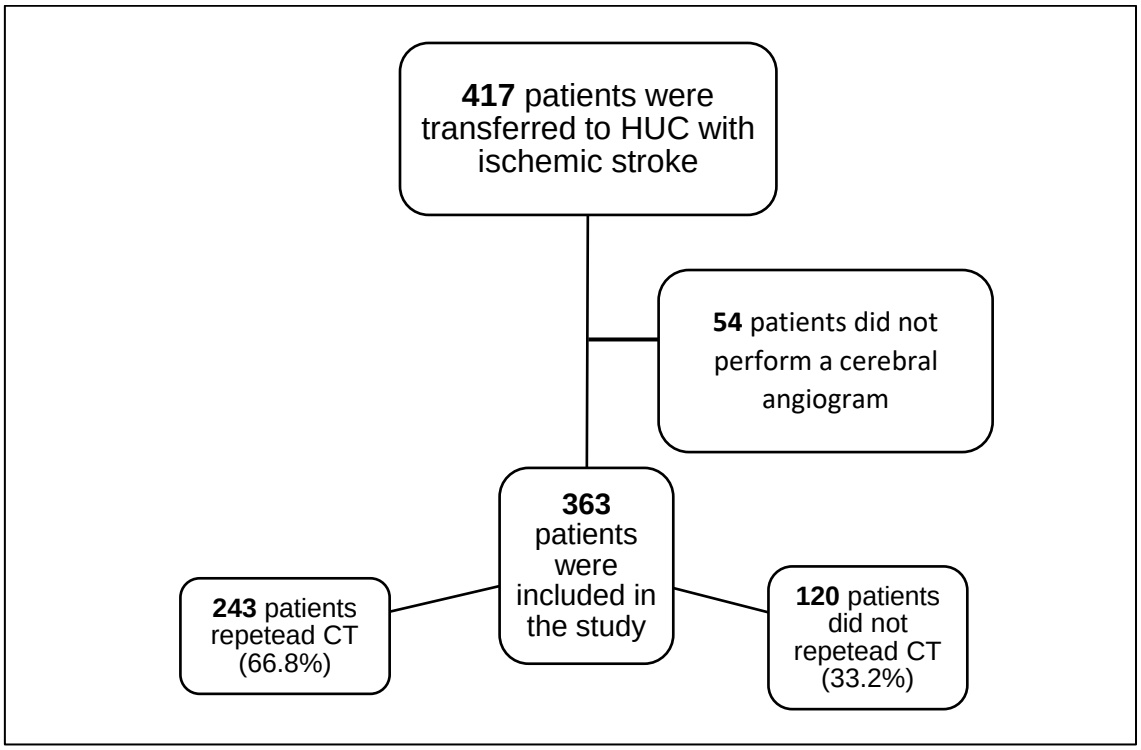
Figure 2 – Association between Hemorrhagic Transformation and the repetition of the computed tomography (CT) scan after transfer to our hospital in patients with ischemic stroke.

Figure 3 – Connection of the median time between arrival at hospital and groin puncture (measured in minutes and second - mm:ss) and the repetition or not of CT scan.

Figure 4 - Relation between repeated conventional computed Tomography (CT) post ischemic stroke and functional outcome at 90 days (through modified Rankin Scale [mRS]), represented in percentage for each category.

Table 1 – Dichotomous variables are presented as frequency (%). BP indicates blood pressure and NIHSS, National Institute of Health Stroke Scale.

Figures:



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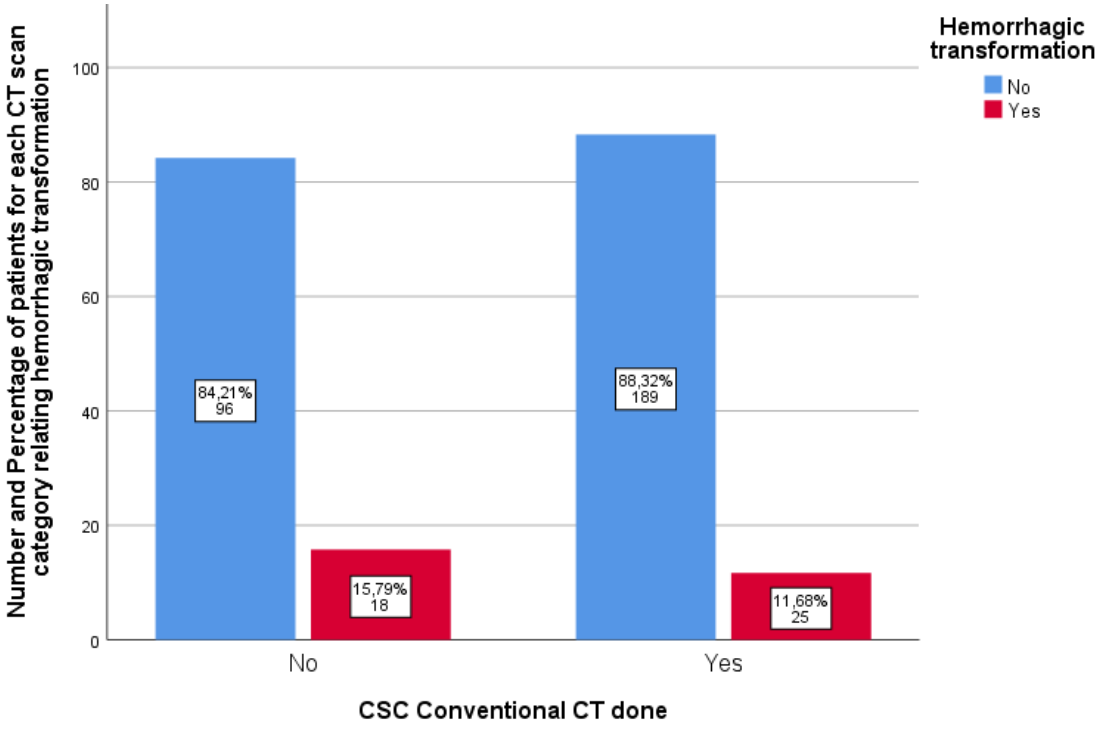

Figure 2 – Association between Haemorrhagic Transformation and the repetition of the computed tomography (CT) scan after transfer to our hospital in patients with ischemic stroke.

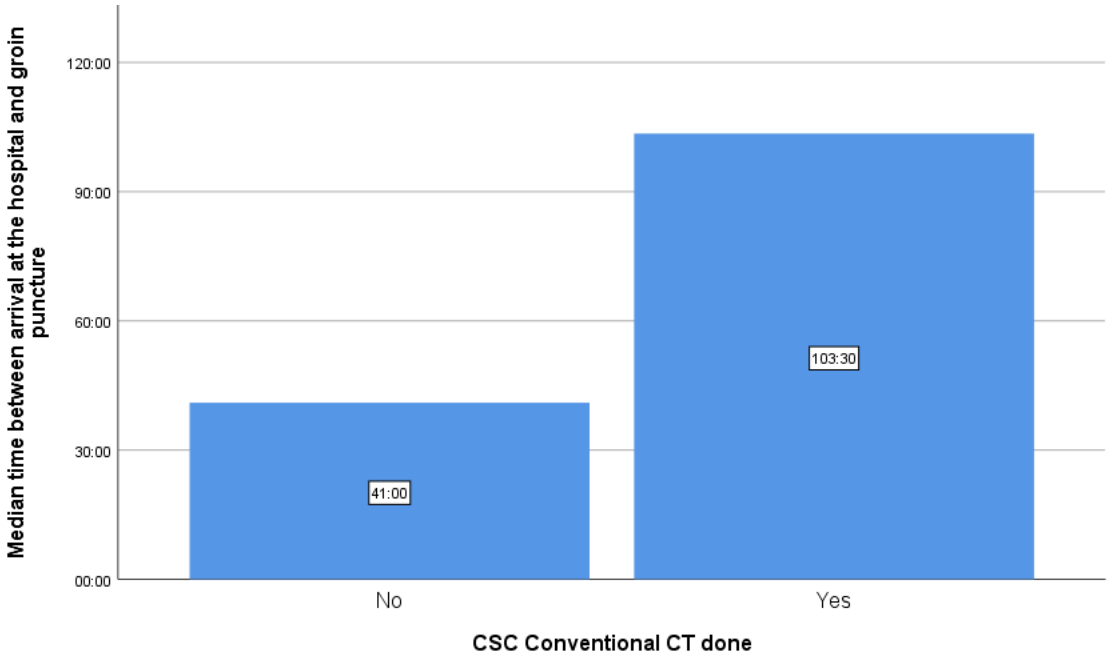

Figure 3- Connection of the median time between arrival at hospital and groin puncture (measured in minutes and second - mm:ss) and the repetition or not of CT scan.

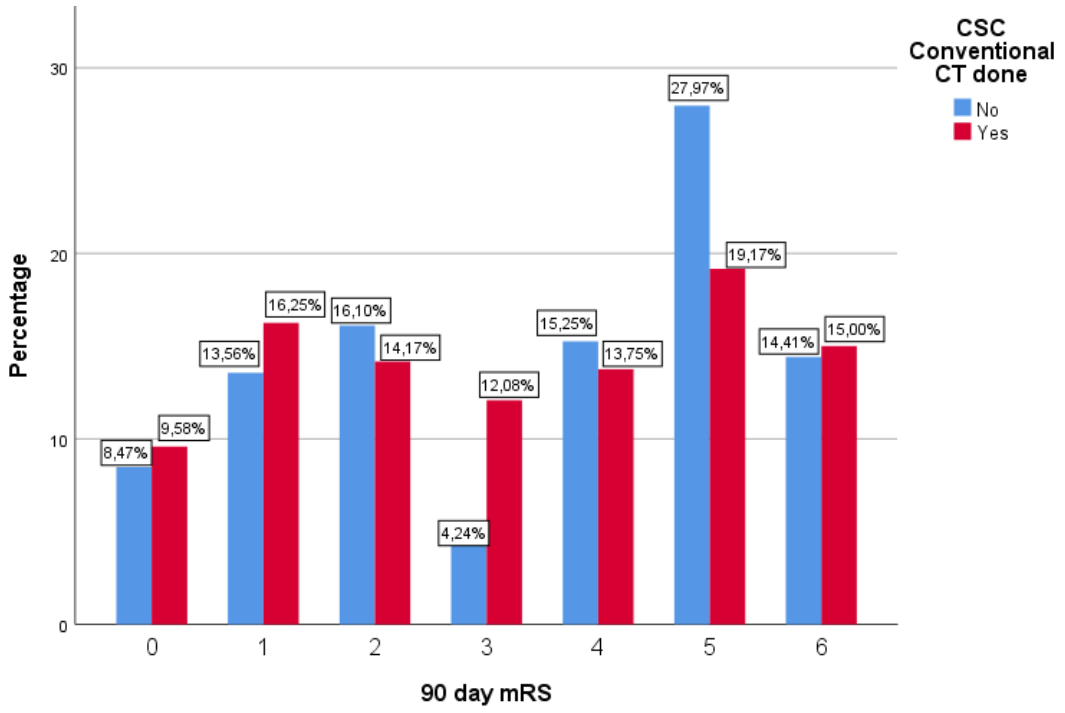

Figure 4 - Relation between repeated conventional computed Tomography (CT) post ischemic stroke and functional outcome at 3 months days (through modified Rankin Scale [mRS]), represented in percentage for each category.

Table:

Variable	Total (n=363)	Repeat CT	Did not repeat CT	*p value*
Age (years,mean ± SD)	70.85 (12.65)	71.06 (12.99)	70.42 (12.00)	0.540
Female Gender	182 (50.14%)	125(51.4%)	57 (47.5%)	0.481
Lipid Disorder	246 (68.0%)	167 (68.7%)	79(65.8%)	0.543
Atrial Fibrillation	192 (53.0%)	133 (54.73%)	59 (49.17%)	0.231
Diabetes	71 (19.6%)	48 (19.75%)	23 (19.17%)	0.880
Oral Anticoagulant	73 (20.33%)	50 (20.58%)	23 (19.17%)	0.782
Smoking Habits	34 (9.4%)	23 (9.46%)	11 (9.2%)	0.99
Glucose at admission (median ± IQR)	122.0 (41)	122.0	122.5	0.716
SBP at admission (median ± IQR)	150 (36)	153	145	0.071
NIHSS baseline (median ± IQR)	18.0 (11)	17.0	19.0	0.169
NIHSS discharge or 7 day after (median ± IQR)	6.0 (16)	5.0	9.0	0.123
ASPECTS in PSC (median ± IQR)	9.0 (4)	9.0	10.0	0.906

ASPECTS in CSC (median ± IQR)	10.0 (5)	10.0	10.0	0.180
Pre mRS (median ± IQR)	0.0 (1)	0.0	0.0	0.993
Discharge mRS (median ± IQR)	4.0 (2)	4.0	5.0	0.153
IV tPA given	199 (54.8%)	127 (52.26%)	72 (60%)	0.722
Recanalization (TICI 2b/3)	268 (76.1%)	170 (69.96%)	98 (81.67%)	0.416
Haemorrhagic Transformation	43 (13.11%)	25 (10.3%)	18 (15.0%)	0.295
Posterior Circulation	35 (9.62%)	17 (7.2 %)	18 (15.2%)	0.02

Table 1 – Dichotomous variables are presented as frequency (%). SBP indicates sistolic blood pressure, NIHSS National Institute of Health Stroke Scale, PSC Primary stroke centre, CSC comprehensive stroke centre and IQR Interquartile Range.