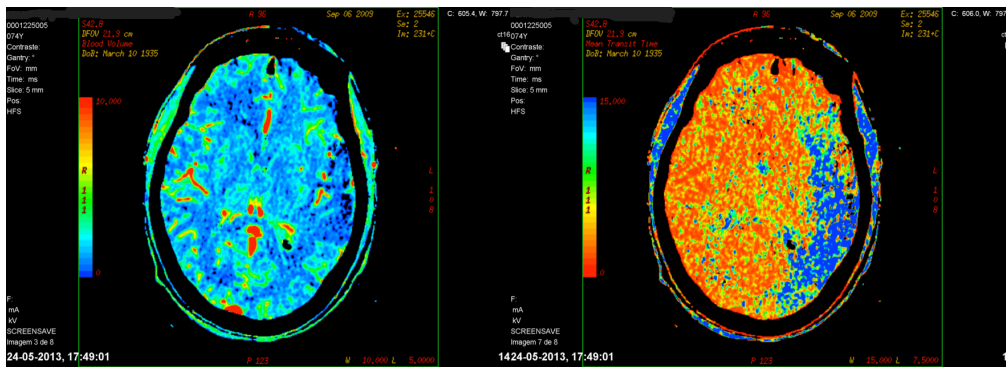


Dissertação – Artigo de Investigação
Mestrado Integrado em Medicina
2013/2014

Prognostic value of cerebral perfusion CT on stroke

Correlation between the size of stroke within the territory of the middle cerebral artery and the area of hypoperfusion on patients with acute stage stroke without intra-arterial thrombectomy



Name of Author: João Pedro Mendes Monteiro

Tutor: João Xavier, MD

Co-Tutor: José Eduardo Alves, MSc

Instituto de Ciências Biomédicas Abel Salazar – Universidade do Porto

E-mail address: jpmm_3@hotmail.com

Abstract

Introduction: In recent years the management of acute ischemic stroke has changed from a time-guided to a more physiologic-based approach. CT perfusion (CTP) is part of the initial evaluation of stroke patients, allowing differentiation between infarcted tissue and ischemic penumbra and helping in the selection of patients for endovascular treatment. In this study we assessed the reliability of qualitative mean transit time maps (MTT) evaluation in the definition of ischemic penumbra, its prognostic value to determine future area of infarction and identified potential pitfalls associated with this technique.

Material and Methods: Review of CTP scans of 18 consecutive patients admitted to our institution with anterior circulation acute ischemic stroke whom were not submitted to recanalization. The author and a neuroradiologist performed quantitative comparison between the areas of perfusion abnormality in the initial mean transit time (MTT) maps and the areas of hypodensity in the 24h follow-up non-contrast CT, used as surrogate marker for the area of definitive infarct. For each slice analyzed, the areas of qualitative alteration in MTT maps and follow-up CTs were measured (mm²) through manual placement of a ROI (Region of Interest)

Results: 16/18 (88,88%) patients presented initial MTT abnormalities larger than follow-up lesions; Mean total area of infarct (10,650mm²) was smaller than mean MTT prolongation (18,894mm²); The greater the initial MTT prolongation the larger the area of infarct.

Discussion: Even though MTT maps relate proportionally to final infarction outcome, in a majority of patients, MTT overestimated final infarct areas, probably because it does not differentiate true “at risk” penumbra from benign oligemia.

Conclusion: Qualitative evaluation of MTT maps is a useful tool to anticipate final infarction area, but it may overestimate real ischemic penumbra in patients with acute anterior circulation ischemic stroke.

Key Words

CT perfusion (CTP); acute stroke; brain infarction; Mean Transit Time (MTT),
endovascular treatment, intra-arterial treatment (IAT)

Word Count: 2445

Introduction

The cerebrovascular diseases, in particular stroke, leads the causes of mortality and morbidity in Portugal as demonstrated by the DGS in 2010 [1].

Ischemic stroke is defined as the sudden loss of blood circulation to an area of the brain, resulting in a corresponding brain lesion and consequent loss of neurologic function [2]. This process can occur secondary to one of the following mechanisms: thrombotic infarction, embolic infarction, haemorrhagic infarction and transient ischemic attack (TIA).

Focal ischemia that results from occlusion of an artery in the brain (ischemic stroke) accounts for more than 80% of all strokes [3]. Unless rapidly reversed, the occlusion of a major artery usually produces tissue infarction, in which affected parts of the brain exhibit a non-selective loss of all cells [4]. The size and location of these infarcts are important determinants of the long-term functional deficits [4].

When the blood flow falls to less than 20% of normal values, the resultant disruption to deliver glucose and oxygen leads to a greatly reduced ATP generation of this area with modification of the ionic gradients resulting on the formation of irreversible cerebral lesion called the ischemic core [5]. However, because of contributions to perfusion from adjacent vessels, a lesser ischemic region (typically exhibiting reductions to approximately 20–40% of normal flow) [5] develops in the tissue surrounding the core – the penumbral tissue [4]. This area reflects cerebral tissue severely hypoperfused that will swiftly transform into an irreversible lesion if early

reperfusion does not occur.

CT perfusion techniques have been used to assess both ischemic core and the “penumbral” tissue. In fact, it has been proven that a decrease in the *cerebral blood volume* (CBV) is well correlated with irreversible ischemic lesion (the ischemic core) and that the total area of brain at risk of infarction could be represented by the area of MTT prolongation. From these studies, it has emerged the concept that penumbral area could be assessed by the CBV-MTT mismatch – a *mismatch area* is a segment of the brain with a prolonged MTT, reduced/normal CBF and a preserved CBV. Hence this region represents tissue at risk of infarction but still viable, with potential to be saved if reperfusion is achieved. CT cerebral perfusion techniques are accessible and quick to obtain, making them predictably useful when selecting patients for reperfusion techniques [6,7].

The criteria used to select acute stroke patients for reperfusion techniques are still greatly discussed in the scientific community. Unfortunately we are still far from consensus because even though the use of CT perfusion sounds promising, as there is not yet sufficient scientific evidence to correlate the CT perfusion outcomes with the volume of final infarction, practitioners are forced to accept time-based criteria as the more reliable [8,9]. This lack of evidence to support the use of CT perfusion is mainly due to the absence of a universal standardisation of the values obtained through CT perfusion as result of the great variability between observers, of the computing systems and methods of acquisition. Thus, the current knowledge (centred primarily on animal models) that demonstrates that we can reduce infarct volume particularly in the penumbra during the initial few hours following the onset of stroke [5] seems

enough to support the use of time-based criteria.

However, for the time-based criteria to work, it must assume that the progress of ischemia is similar in all patients. This is not the case, as reports such as Martini SR *et al* have suggested that the adequacy of collateral blood flow and metabolic milieu of the individual are only some of the elements which will contribute to the existence of individual variability on the velocity of progression of ischemia and development of irreversible lesion. [10] In addition, neuroradiologists sometimes find themselves surprised with the fact that not always the quickest reperfusion is enough. For example, in *benign oligemia*, the tissue with delay in contrast arrival will not evolve to clinically relevant ischemia, thus recovering even though no reperfusion technique is applied [11].

Taking these facts into consideration, this study tries to assess the reliability of qualitative evaluation of CT perfusion in the definition of ischemic penumbra, to determine the prognostic value of initial MTT abnormality in the estimation of future infarction and to identify potential pitfalls associated with this technique.

Methods and Materials

Sample

This is a retrospective review of all consecutive patients admitted to our institution (CHP-HSA) with the diagnosis of acute ischemic stroke from May 2009 to August 2013. It consists of 18 patients whom fulfilled the following inclusion criteria:

- 1) Admission CTP scanning within 8 hours of clinical onset,
- 2) CTA confirmation of large vessel occlusion in the anterior circulation (top of internal carotid artery, M1 and M2 segments of the middle cerebral artery),
- 3) Not submitted to intra-arterial thrombectomy during the episode. The reason behind the privation of the intra-arterial procedure can be any of the following: absence of team/materials necessary for the practice, nonexistence of a proximal thrombus, absolute contraindication to the procedure or medical decision.
- 4) Follow-up CT imaging performed between 24h to 48h after clinical onset.

Method

Image Acquisition:

The CTP Protocol was performed on multidetector helical scanners (either GE BrightSpeed® 16 row or GE LightSpeed VCT® 64 row) as a 45-second cine series,

beginning 5 seconds after power injection of 50mL of non-ionic contrast media (Ultravist 370 or Xenetix 350) at 4 mL/s. Image acquisition was obtained at a rate of 2 images/second (80 kVp, 120 mA) with a spatial coverage of 20 mm slab (4x5 mm slices) for the 16 row equipment and a 40 mm slab (8x5 mm slices) for the 64 row one. The most caudal imaging was acquired at the level of the basal ganglia and the most cranial immediately above them, at the level of lateral ventricles.

Imaging Analysis:

Firstly, CTP maps were postprocessed by using standard deconvolution software package (CTP3 “Std,” GE Healthcare). Then, the author carried on qualitative visual evaluations of MTT maps, using 24h follow-up non-contrast CT hypodensity area as a surrogate marker for the area of definitive infarct. For each slice analysed, the area of qualitative alteration in MTT map and follow-up CT was measured (mm²) through manual placement of a ROI (Region of Interest). A neuroradiologist verified these values in order to reach a final consensus.

Statistical analysis

Descriptive statistics are presented for the baseline demographic data, occlusion location and results. Test of Normality (Kolmogorov-Smirnov/ Shapiro-Wilk), Coeficiente of Spearman and ANOVA were used to assess correlation between variables and statistical significance of results.

Results:

We identified 18 patients eligible for analysis; 11 (61%) were men and the mean age was 61 years (range 44-81 years). The majority of patients were more than 50 years old (39% 50-69 years old and 39% more than 70 years old). Location of occlusions were as follows: ICA terminus (4 patients), M1 (10), M2 (6), being the left M1 segment of the middle cerebral artery the most commonly affected, 38,9% (Figure I). From all 18 patients analysed, one (patient 10) had poor quality CT acquisition due to motion artefacts, rendering the area of qualitative alteration in MTT slice 4 non-measurable (Table I).

By using the Coeficient of Spearman it can be assumed that there is a statistically significant correlation between final infarct area and admission MTT abnormality ($RS[18]=0,554$, $p=0,017$), showing that the greater the initial MTT prolongation the larger the area of infarct (Figure II).

When comparing initial MTT abnormality to the final infarct area, 16 out of 18 patients presented final infarct areas smaller than the initial MTT abnormality, while 2 patients had final infarct areas larger than the initial MTT defect. The mean total area of infarct was $10,650\text{mm}^2$ and MTT prolongation $18,894\text{mm}^2$. Thus infarct areas are usually smaller than initial MTT (Figure III) being this statistically significant using ANOVA ($p<0,0001$).

Discussion

Perfusion studies, such as MTT color maps, have been successfully used to assess infarct core and ischemic penumbra and in some studies have even replaced time-window as major selection criteria for intra-arterial treatment [5, 6, 12, 13, 14].

However, this qualitative technique is dependent on user interpretation, so recognition of potential pitfalls and diagnostic challenges is essential [15].

MTT prolongation is generally accepted as the parameter that best correlates with tissue at risk of infarction [16, 17]. Our results corroborate this by demonstrating that the greater the initial MTT prolongation the larger the area of infarct.

However, even though it was expected that with no recanalization the final infarct would approximately match the initial MTT lesion, our results revealed that in a majority of patients (88,88%) the final area of infarct was significantly smaller than the admission MTT abnormality, hence showing that MTT overestimated final infarct lesion (figure III).

This overestimation results from the fact that areas of MTT prolongation include not only true critical ischemic regions (“at risk” penumbra) but also hypoperfused tissue with delay in contrast arrival that is clinically silent and not destined for infarction, the so-called benign oligemia. The concept of benign oligemia is very recent and not taken into account by much of previous literature regarding perfusion studies in acute stroke [11], and is vaguely explained by an inherent delay and dispersion of the collateral perfusion which may cause errors, such as, underestimating cerebral blood

flow and overestimating or exaggerating time-domain parameters such as MTT. [18]

Kamalian *et al* have shown that appropriately threshold MTT maps could differentiate true “at risk” penumbra destined to infarct from noncritical benign oligemia, nevertheless this is still insufficient as they reveal other studies using various perfusion parameters to estimate penumbra, including CBF and MTT, which have reached different conclusions depending, in part, on variables such as scan acquisition time, patient cohort, and type of post-processing software. [11]

Potential limitations of our study include the relatively small number of patients identified with large vessel occlusion that did not undergo recanalization, which limits the statistical power of the results. Even though this study quantitatively compares areas of infarct and MTT abnormalities, the assessment of these alterations was done through visual inspection, which is always subjective and dependent of operator. In this matter, one may argue that follow-up CT is not a perfect marker for final infarct area due to the effect of vasogenic edema. By limiting the follow-up CT to a 24h-window after the ischemic event we tried to diminish the impact of vasogenic edema contribution to the CT hypodensity area. However, it is impossible to completely eliminate the edema effect, which may act as a confounding variable leading to an overestimation of final infarct areas. The possibility that final infarct areas might be overestimated means that discrepancies between initial MTT abnormalities and final infarcts are, in fact, still underestimated, even in our conclusions.

Additionally, the limited spatial coverage (2cm and 4cm slabs) may have decreased our power to detect more differences between MTT maps and the follow-up CTs.

Furthermore, a limitation inherent to all stroke imaging studies is that they represent a “snapshot” in time and we did not perform any follow-up angiographic study to assess vascular recanalization, which could potentially explain the differences between the MTT and follow-up CT lesions. However it has been shown that the probability of acute spontaneous recanalization after large vessels occlusion is very low [19, 20].

Conclusions

Our study has shown that in patients with acute anterior circulation vessel occlusion and no recanalization CPT- MTT abnormality relates to the area of irreversible ischemic lesion, emphasizing the benefits of using CT perfusion data as one of the criteria in a multi-parameter approach to select patients that undergo recanalization and to estimate their prognosis.

However qualitative definition of CTP-MTT lesion seems to overestimate the final infarct area. Thus, even though MTT maps relate proportionally to final infarction outcome, visual qualitative interpretation of MTT maps may not be a suitable method to optimally identify true “*at risk*” penumbra and to differentiate it from benign oligemia.

In order to validate the use of CTP techniques as a prognostic and “decision making” tool for patients with acute stroke it is essential to achieve quantitative, standardized universally accepted CT perfusion technique and parameters; furthermore, additional investigation is warranted to determine more precisely the volume and location of “true” ischemic penumbra in CTP studies. In the future, the employment of effective, appropriate, standardized perfusion imaging methods will probably be essential to a proper selection of patients for IAT and to the successful management of acute ischemic stroke.

References

- 1) Elementos estatísticos: Informação Geral: Saúde 2008 / Direcção-Geral da Saúde – Lisboa: Direcção-Geral da Saúde, 2008
- 2) Imaging of Stroke: Part 1, Perfusion CT—Overview of Imaging Technique, Interpretation Pearls, and Common Pitfalls: Andrew Mark Allmendinger¹, Elizabeth R. Tang², Yvonne W. Lui² and Vadim Spektor (Janeiro 2010)
- 3) R.W.V. Flynn, R.S.M. MacWalter, A.S.F. Doney: The cost of cerebral ischaemia *Neuropharmacology*, 55 (2008), pp. 250–256
- 4) Neil R. Sims, Hakan Muyderman: Mitochondria, oxidative metabolism and cell death in stroke: Janeiro 2010
- 5) T. Back, T. Hemmen, O.G. Schuler: Lesion evolution in cerebral ischemia *J. Neurol.*, 251 (2004), pp. 388–397
- 6) Jovin et al. Imaging-based endovascular therapy for acute ischemic stroke due to proximal intracranial anterior circulation occlusion treated beyond 8 hours from time last seen well: retrospective multicenter analysis of 237 consecutive patients. *Stroke* 2011; 42:2206-11
- 7) Turk et al. CT perfusion-guided patient selection for endovascular recanalization in acute ischemic stroke: a multicenter study. *J Neurointerv Surg.* 2013; 5(6): 523-7.
- 8) González RG et al. (*JNIS* 2013)
- 9) Dani KA, Thomas RG, Chappell FM, et al. Computed tomography and magnetic resonance perfusion imaging in ischemic stroke: definitions and thresholds. *Ann Neurol.* 2011; 70(3): 384-401.
- 10) Martini SR et al (*J Cereb Blood Flow Metab* 2007)
- 11) Kamalian S et al. CT perfusion mean transit time maps optimally distinguish ischemic benign oligemia from true “at risk” ischemic penumbra, but thresholds vary by postprocessing technique. *Am J Neuroradiol.* 2012; 33(3):545-9

- 12) Natarajan et al. Safety and Effectiveness of Endovascular Therapy After 8 Hours of Acute Ischemic Stroke Onset and Wake-Up Strokes. *Stroke*. 2009; 40(10):3269-74
- 13) Hellier KD, Hampton JL, Guadagno JV, et al. Perfusion CT helps decision making for thrombolysis when there is no clear time of onset. *J Neurol Neurosurg Psychiatry*. 2006; 77: 417-19.
- 14) Lui YW et al. Evaluation of CT Perfusion in the setting of cerebral ischemia: patterns and pitfalls. *Am J Neuroradiol*.2010; 31(9): 1552-63
- 15) Best AC et al. Recognizing False Ischemic Penumbra in CT Brain Perfusion Studies. *Radiographics*. 2012; 32(4): 1179-63
- 16) Wintermark M, Flanders A, Velthuis B, et al. Perfusion-CT Assessment of Infarct Core and Penumbra - Receiver Operating Characteristic Curve Analysis in 130 Patients Suspected of Acute Hemispheric Stroke. *Stroke*. 2006; 37: 979-985.
- 17) Wintermark M, Fischbein NJ, Smith WS, et al. Accuracy of dynamic perfusion CT with deconvolution in detecting acute hemispheric stroke. *Am J Neuroradiol*. 2005; 26: 104-112.
- 18) Bang OY et al. Benign oligemia despite a malignant MRI profile in acute ischemic stroke. *J Clin Neuro*. 2010; 6(1): 41-5
- 19) Ribo M, Molina CA, Rovira A, et al. Safety and efficacy of intravenous tissue plasminogen activator stroke treatment in the 3- to 6-hour window using multimodal transcranial Doppler/MRI selection protocol. *Stroke*. 2005;36:602-606
- 20) Silva D, Fink J, Christensen S, et al. Assessing reperfusion and recanalization as markers of clinical outcomes after intravenous thrombolysis in the echoplanar imaging thrombolytic evaluation trial (EPITHET). *Stroke*. 2009; 40: 2872-2874
- 21) Emedecine: Ischemic Stroke Author: Edward C Jauch, MD, MS, FAHA, FACEP;

Acknowledgments and Funding

We acknowledge Vera Araújo for assistance with statistical analysis.

Figure/Table/Image Legends

Table I – Patients area of infarction and MTT.

Patient	Area of infarction 1(mm2)	Area of infarction 2(mm2)	Area of infarction 3(mm2)	Area of infarction 4(mm2)	Area of infarction 5(mm2)	Area of infarction 6(mm2)	Area of infarction 7(mm2)	Area of infarction 8(mm2)	Total area(mm2)
1	1962.2	4717.5	4215.2	3069.9					13964.8
2	388.5	123.4	0	0					511.9
3	464	1002.7	1766.8	2026.8					5260.3
4	3745.7	4096.1	4300.3	3782.5	3401.6	3216.3	2676.9	2320	27539.4
5	3454.4	4323.8	4146.7	4781.8					16706.7
6	152.9	835.2	1033.1	1167.2					3188.4
7	4257.4	3089.6	1791.5	801.5					9940
8	566.8	1078.7	1129.8	1248.9					4024.2
9	2044.3	2486.4	2829.3	2800.8					10160.8
10	278	123.1	86	152.6					639.7
11	644	1617.2	2058.3	2089	2446.9	2813.2	2642.8	2730.5	17041.9
12	2498.3	2981.2	2920.4	3268.2					11668.1
13	1810.6	3550.2	3300.2	4310.9	4822.9	4000.6	3660.3	2989	28444.7
14	638.7	824.1	810	777.8					3050.6
15	1410.6	1570	1813	1586.9					6380.5
16	0	595.8	731,5	691					1286.8
17	3615.2	3669.7	3260.2	2410.7					12955.8
18	4268	4568	4658	4711					18205
Patient	MTT1 (mm2)	MTT2 (mm2)	MTT3 (mm2)	MTT4 (mm2)	MTT5 (mm2)	MTT6 (mm2)	MTT7 (mm2)	MTT8 (mm2)	Total area(mm2)
1	6265	5601	5600	5058					22524
2	4805	4493	4581	3734					17613
3	4098	3996	3798	3091					14983
4	5227	5335	3940	3551	4019	4435	4794	5114	36415
5	5568	5825	5567	5431					22391
6	4232	4049	723	0					9004
7	1513	2740	2448	3024					9725
8	4457	5006	5253	5027					19743
9	4743	4524	3937	3525					16729
10	3070	4686	3753	No reading due to motion artifacts					11509
11	4552	4753	4455	4293	5142	5070	4216	4689	37170
12	4307	4163	3462	3383					15315
13	3557	5254	5451	4779	5073	4031	3811	3429	35385
14	3853	4409	4245	4218					16725
15	4020	5084	4668	4403					18175
16	2613	2398	2388	2488					9887
17	2964	3178	3109	3592					12843
18	3998	3719	3871	3134					14722

Figure I – Location of occlusions by number of patients.

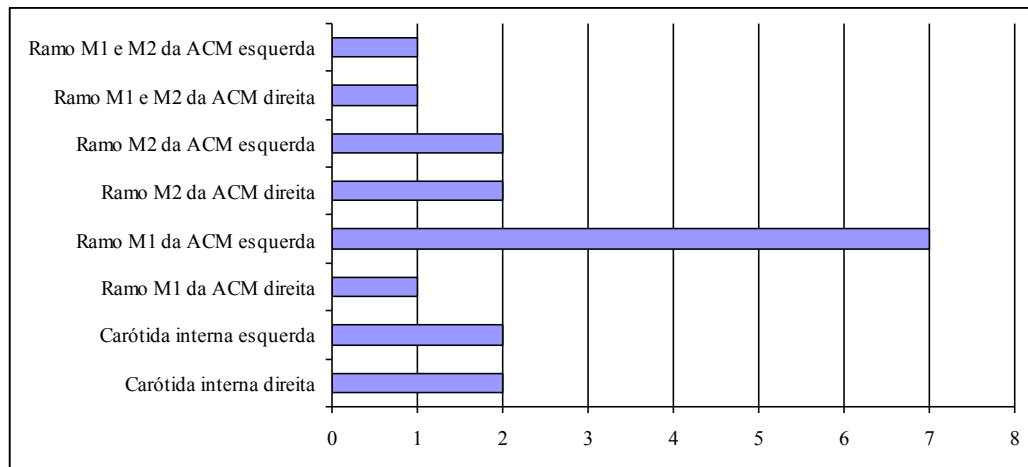


Figure II – Line of regression between total area of infarct and MTT abnormality:

Shows that the greater the admission MTT prolongation the larger the final outcome (area of infarct in mm²).

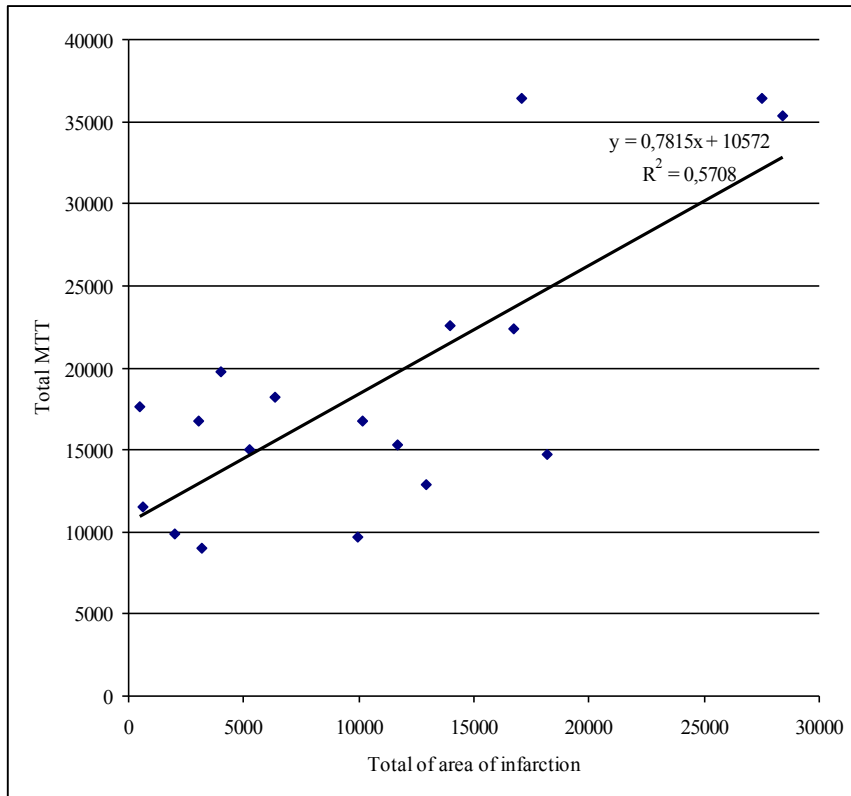


Figure III – Line graph showing per patient the relationship between final area (in mm²) of infarct and initial MTT prolongation.

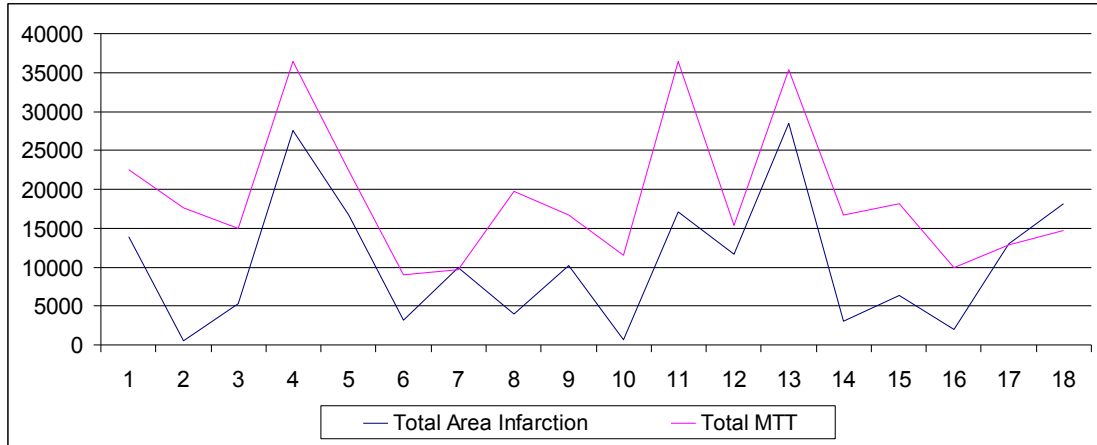


Image I – Perfusion CT showing Blood Volume Map of patient 3.

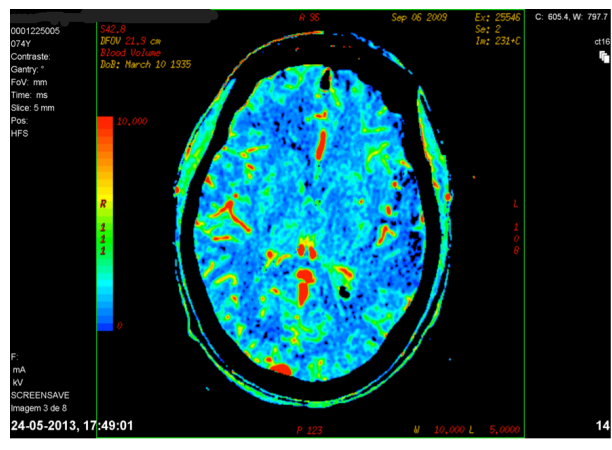


Image II – Perfusion CT showing MTT Map of patient 3.

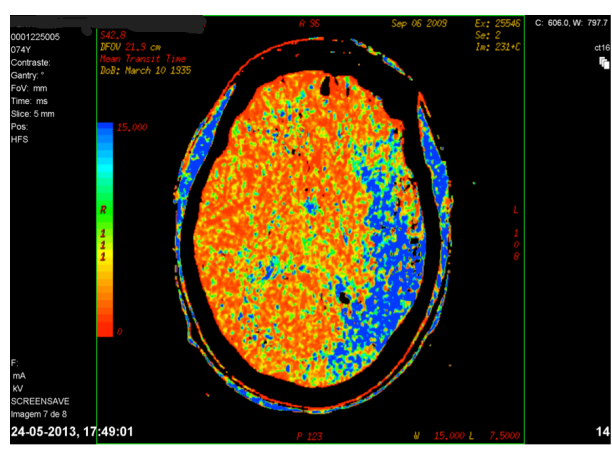


Image III- Follow-up CT showing final infarct area of patient 3.



Image IV - Perfusion CT showing Blood Volume Map of patient 9.

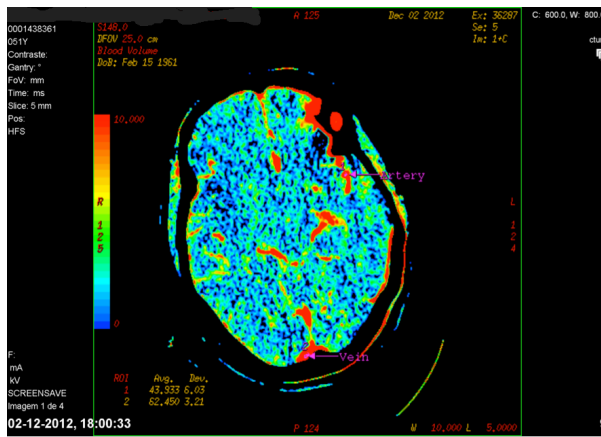


Image V – Perfusion CT showing MTT Map of patient 9.

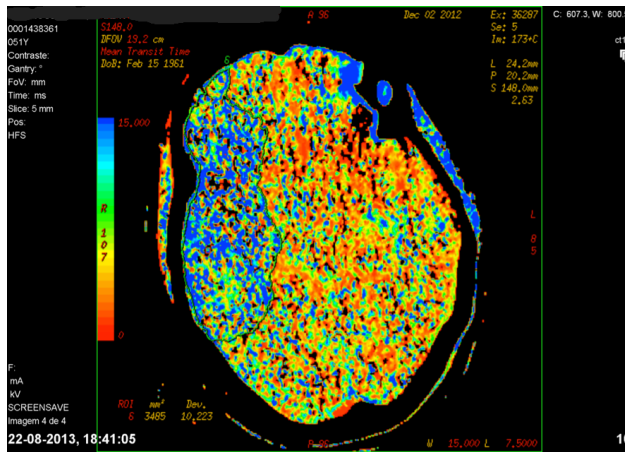


Image VI - Follow-up CT showing final infarct area of patient 9.



Image VII – Perfusion CT showing Blood Volume Map of patient 2.

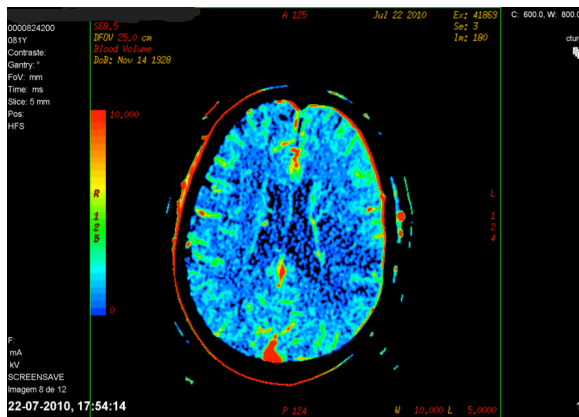


Image VIII – Perfusion CT showing MTT Map of patient 2.

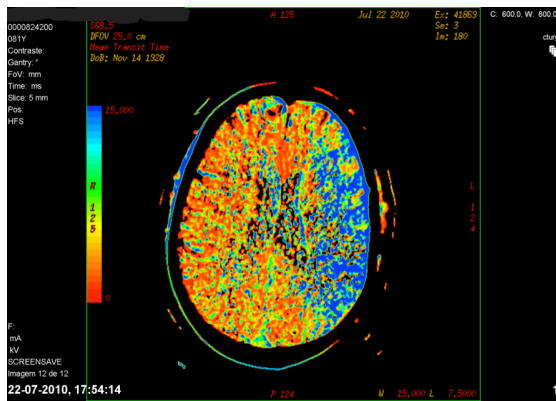


Image IX - Follow-up CT showing final infarct area of patient 2.



Resumo Circunstanciado em Língua Portuguesa

Introdução

As doenças cérebro-vasculares lideram as causas de mortalidade e morbidade hospitalar em Portugal sendo este facto visivelmente demonstrado pela direção geral de Saúde em 2010 [1]. Destas doenças dá-se especial relevo ao enfarte cerebral agudo.

Quando o fluxo sanguíneo diminui, atingindo valores de menos de 20% do normal, a diminuição drástica no aporte de glicose e oxigénio causa uma redução na geração de ATP nesta zona com alterações nos gradientes iónicos levando à formação do core isquémico. Este representa o parênquima cerebral enfartado, zona em que a lesão cerebral é irreversível [5]. Contudo, a existência de perfusão por vasos adjacentes, permite que se forme uma zona com menor isquemia no tecido que circunda o core, a penumbra isquémica [4]. Esta área, que, classicamente reflete uma redução para aproximadamente 20-40% do fluxo sanguíneo normal, traduz tecido cerebral gravemente hipoperfundido que irá progredir para lesão irreversível (enfarte) se não houver reperfusão precoce [5].

A área de penumbra isquémica pode ser medida por estudos de perfusão por TC apresentando-se como uma mismatched area. Uma mismatched area é uma área que apresenta um mean transit time (MTT) prolongado, cerebral blood flow (CBF) diminuído/normal e cerebral blood volume (CBV) preservado. Assim, esta área representa tecido possivelmente viável mas em risco, que pode ser salvo através de

uma adequada reperfusão.

Os atuais critérios de seleção para o uso de técnicas de reperfusão baseiam-se em grande parte na janela temporal. Para elaborar estes critérios e uniformizar a seleção de doentes assume-se que o ritmo de evolução de isquemia é semelhante em todos os doentes. No entanto, diversos estudos demonstraram existência de grande variabilidade individual na velocidade de progressão do evento isquémico agudo e no desenvolvimento de lesão irreversível. Martini SR et al determinaram alguns dos fatores que contribuem para esta variabilidade: existência de circulação colateral, reserva funcional e metabolismo individual [10]. Devido à acessibilidade e segurança, os estudos de perfusão por TC parecem alternativas ideais ao critério tempo, se provarem sensibilidade e especificidade satisfatórias [6,7]. No entanto, a ausência de consenso científico em volta da utilidade deste promissor meio complementar de diagnóstico, obriga a que o estado da arte atual dê preferência ao uso do critério tempo na seleção dos doentes para reperfusão [8,9]. Este debate na comunidade científica deve-se principalmente à existência de diferentes métodos de aquisição, diferentes softwares de pós-processamento e variabilidade interobservador na interpretação dos mapas resultando numa heterogeneidade dos mapas gerados, não permitindo, até à data, determinar valores padrão para os diferentes parâmetros avaliados. Em contrapartida, neurorradiologistas deparam-se, por vezes, com evidências de que nem sempre reperfusão rápida é o melhor, pois fenómenos como oligemia benigna, surgem na literatura, sugerindo que tanto critérios baseados no tempo como critérios de perfusão por TC podem sobrestimar a área de core isquémico, insinuando que, sem qualquer intervenção, o doente recuperaria tecido inicialmente dado como inviável [18].

Objetivos

Com este estudo retrospectivo pretende-se obter resultados que sejam uma mais-valia para o futuro método de seleção de doentes para reperfusão. Para tal, pretende-se esclarecer o papel e as limitações dos estudos de perfusão por TC, especialmente o MTT, no prognóstico de doentes que não foram submetidos a trombectomia através das respostas às seguintes questões:

- 1- Existe alguma relação estatisticamente significativa entre alterações no mapa MTT à entrada no serviço de urgência e a área de enfarte no TC de controlo (passado 24h)?
- 2- O MTT inicial é previsor da área de enfarte final (ou seja, área semelhante) ou frequentemente sobrestima a área de core isquémico, por exemplo através de fenómenos como oligemia benigna, tornando este meio de diagnóstico demasiado impreciso?

Metodologia

Amostra

Análise retrospectiva de uma amostra de todos os doentes que deram entrada na nossa instituição (CHP-HSA) com o diagnóstico de enfarte cerebral hiperagudo da circulação cerebral anterior desde Maio 2009 a Agosto 2013 em que não foi efetuado reperfusão e apresentam estudo de perfusão por TC durante as primeiras 8 horas do

quadro clínico e TC de controlo entre as 24-48 horas após quadro agudo.

Aquisição de imagem:

O protocolo de imagem envolveu dois equipamentos TC (GE BrightSpeed 16 row® or GE LightSpeed VCT 64 row®) com aquisição de imagem a ser obtida a 2 imagens/segundo em cortes de 20mm (4x5 mm) para o equipamento “16 row” e cortes de 40 mm (8x5 mm) para o “64 row”.

Análise de Imagem:

Primeiramente os mapas de perfusão por TC foram processados usando, “standard deconvolution software package (CTP3 “Std,” GE Healthcare)”. Em seguida, o autor com a colaboração de um neurorradiologista, avaliou qualitativamente os mapas MTT usando as áreas de hipodensidade do TC de controlo de 24h como marcador da área definitiva de enfarte. Para cada corte analisado a área qualitativamente alterada no mapa MTT e TC de controlo foi medida (mm²) através da colocação de um “ROI (Region of Interest)”.

Análise estatística

Estatística descritiva é apresentada para espelhar os dados demográficos, o local de oclusão e resultados finais. O Teste de Normalidade (Kolmogorov-Smirnov/ Shapiro-Wilk), Coeficiente de Spearman e ANOVA foram utilizados para avaliar a correlação entre as variáveis e a significância estatística dos resultados.

Resultados

18 doentes foram avaliados; 11 (61%) são homens e a média de idades foi 61 anos (variando entre os 44-81 anos). A localização da oclusão foi a seguinte: Artéria carótida (4), M1 (10), M2 (6) (Figure I).

O Coeficiente de Spearman demonstra relação estatisticamente significativa entre a área final de enfarte e a anormalidade de MTT (RS[18]=0,554, p=0,017), inferindo que quanto maior a região com prolongamento de MTT inicial, maior será o enfarte (figure II).

Quando comparamos o prolongamento de MTT inicial e a área de enfarte, 16 dos 18 doentes apresentaram áreas de enfarte final menores que a anormalidade no MTT, enquanto 2 doentes revelavam o oposto. A média da área total de enfarte final foi $10,650\text{mm}^2$ e de prolongamento de MTT $18,894\text{mm}^2$. Logo as áreas totais de enfarte foram maioritariamente menores que a área inicial de MTT (figure III) sendo que estes dados são estatisticamente significativos como demonstrado por ANOVA (p<0,0001).

Discussão/Conclusão

O nosso estudo revela que em doentes sem reperfusão, os mapas MTT são marcadores confiáveis de lesão isquémica na circulação cerebral anterior, havendo possível benefício, no futuro, de tais marcadores se revelarem como um dos critérios na abordagem multifacetada de seleção de doentes para reperfusão por trombectomia

e seu prognóstico.

No entanto, a avaliação quantitativa do MTT demonstrou sobrestimar a área final de enfarte. Assim deduzimos, que, apesar dos mapas MTT terem uma relação proporcional com o resultado final de enfarte, a interpretação visual quantitativa de alterações no MTT pode não ser um método perfeito para identificar a verdadeira área de penumbra “em risco” e a diferenciar de forma fiável da oligémia benigna. Este fenómeno surgiu apenas recentemente na literatura, sugerindo que um atraso e dispersão da circulação colateral seja responsável por possíveis leituras subvalorizadas do *cerebral blood flow* (CBV) e sobrestimadas do MTT [18].

Para no futuro validar os estudos de perfusão por TC como meios de imagem úteis para o prognóstico e critério de decisão “major” de orientação de doentes com enfarte cerebral agudo, é essencial desenvolver estudos com maiores amostras, menos dependentes do operador e com mais especialistas (neurorradiologistas) que elaborem critérios específicos, quantitativos e universalmente padronizados demonstrando nitidamente a relação entre a hipoperfusão nos estudos de perfusão e a consequente área de enfarte. Entretanto, fica claro o potencial de um estudo de perfusão por TC sensível, específico e apropriado em se tornar uma ferramenta essencial para a orientação adequada do doente com enfarte cerebral agudo.