Neuroimaging patterns of cerebral hyperperfusion

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Abstract. Cerebral hyperperfusion syndrome (CHS) after revascularization is a rare phenomenon associated with post-ischemic (reactive) hyperemia and acute pathological hyperperfusion. First described on perfusion CT as a very often moderate CBF increase, MTT/TTP decrease within 30% like a temporary effect, according to a short-time deterioration of neurological symptoms (vestibular ataxia - 58%, vegetative dysfunction - 100%, anemic syndrome - 100%) in early postoperative period in patients with cardiac ischemia who had undergone coronary artery bypass surgery. The acute pathological hyperperfusion carotid revascularization is a casuistic phenomenon with two- or three-fold CBV and MTT/TTP increase and high hemorrhage risk. Besides, we detected similar exchanges via perfusion CT called benign hyperemia, which marks extension of MTT/TTP and an increase of CBV from 27% to 48% (average 30%), but with normal CBV-parameters, indicating that venous stasis in acute venous ischemic stroke due cerebral venous sinus-trombosis (68%), only 6% in cardiogenic stroke and appears never in arterial stroke. Territorial coincidence registered for perifocal of necrosis zones of benign hyperemia and vasogenic edema accompanied on MRI (DWI, ADC). Secondary hemorrhagic transformation registered for primary non-hemorrhagic venous stroke in 27%, only in 9% for arterial stroke and in 60% for cardiogenic stroke. Probably, congestion is an increasingly predisposing factor secondary hemorrhaging than necrosis.

1. Introduction
Cerebral hyperperfusion syndrome (CHS) after cerebral revascularization is a well-described rare phenomenon after carotid endarterectomy, carotid artery stenting or after intravenous tissue plasminogen activation [1, 2]. There were described increased relative cerebral blood flow (CBF, ml/100g/min) and also relative cerebral blood volume (CBV, ml/100g); decreased mean transit time (MTT/TTP, s) like a temporary effect with recovery rates to normal and called the post-ischemic (reactive) hyperemia and acute pathological hyperperfusion - CHS [3, 4]. The most important pathophysiological factor in pathological hyperperfusion is apparently lowered cerebrovascular reserve as a result of prolonged and severe hyperperfusion [5]. There have been reports of cerebral perfusion studies with venous infarction in the experiments with ligation [6] and in the clinical practice as an example of a single event with dural sinus sagittalis superior thrombosis on the young men [7]. Acute venous stroke (VS) in contrast to the patterns with arterial acute ischemic stroke (AIS) is characterized by an increase in regional CBF and CBV when also the MTT/TTP is prolonged, indicating venous stasis [8]. A similar picture in the perfusion maps has areas of so-called benign hyperemia, which marks extension of MTT/TTP and an increase CBV, but normal CBF during perfusion tomographic studies [9].

2. Questions and objects of investigation
We did not meet the quantitative data on the deviation indicators CBF, CBV, MTT / TTP, which would characterize the boundary between the reactive hyperperfusion, CHS and benign hyperemia or contradictory opinions about the changes of MTT/TTP. The types of perfusion and diffusion of brain tissue disorders, were studied by us in patients with cerebral venous sinus-trombosis (CVST) with the
development of venous stroke without primary hemorrhage (VS, n=39), venous infarction due CVST with primary hemorrhage (n = 9), with atherothrombotic ischemic stroke (AIS, n = 56) and cardioembolic stroke (CS, n = 46), as well as in patients with ischemic heart disease with arterial hypertension, underwent coronary artery bypass grafting (n=47).

3. Benign hyperemia
Areas of hypoperfusion (penumbra) and aperfusion (necrosis/infarction) in patients with primary non-haemorrhagic stroke of AIS and CS on CBV maps with CTP, done within the therapeutic window is almost always accurately territorially correlated (r = 0.97) with signs of cytotoxic edema on diffusion-weighted images (DWI) and maps of the apparent diffusion coefficient (ADC) with magnetic resonance imaging (MRI). Territorial coincidence is registered for zones benign hyperemia and edema according to DWI, ADC at VS (Figure 1). Signs of benign hyperemia we met more often at the VS, but also, though rarely with CS. In perifocal zone of infarction we observed as a congestion on the map at CBV of CTP and images non-contrast MR perfusion (ASL). A distinctive feature of venous stroke from arterial lesions is the less frequent development of necrosis (55% vs. 79%), and also not oligemia in the perifocal infarction zone, but benign hyperemia with exceeding perfusion parameters compared with a healthy tissue on the opposite side from 27% to 48% (An average of 30%).

![Figure 1](image_url)

**Figure 1.** Hypodense right occipital zone on the initial CT in acute right transversal dural sinus thrombosis case (a). Congestive hyperperfusion on computed tomography perfusion: increased up to 25-30% mean transit time (b); (c) cerebral blood flow; (d) cerebral blood volume. Diffusion-weighted magnetic resonance imaging (e) and apparent diffusion coefficient (f) on MRI confirms focal acute ischemia territory of right occipital zone.
In these areas, we noted an inversion of MR signal on DWI and ADC-mapping, indicating the early development of vasogenic edema in the background of cytotoxic edema in the hyperperfusion areas [10].

We [11] agree with opinion [12], that the phenomenon of hyperperfusion is associated with the development of vasogenic edema, which by venous stroke often comes within 24 hours, while by arterial stroke associated with the subacute period (from 3 to 7 days). “Crosshair” curves signal DWI and ADC seems to AIS usually in 5-7 days period, when there is a vasogenic edema. The signal on DWI begins to decline, while ADC-mapping, on the contrary - to rise. For venous ischemia zone crosshairs DWI and ADC curves shifted closer to the clinic manifestation (for 1 day). If the projection VS earlier inversion of foci is observed in 68% of cases, a similar inversion in arterial stroke is marked only in 6% at CS.

4. Acute cerebral hyperperfusion syndrome
Model CHS may be hemorrhagic venous infarction resulting CVST. When CTP notes almost two- or even threefold increased CBV in the affected area with a slight increase of CBF due to two- or three-fold prolonged MTT/TTP (Figure 2).

Figure 2. Edema of the superior parietal lobule and the SAH on the rightside on routine CT (a) in thrombosis superior sagittal sinus case. CTP marked almost three times larger of blood volume in the affected area (d) in an equally pronounced elongation contrast transit time (b), but a slight increase in blood flow (c).
Secondary hemorrhagic transformation registered on a control routine CT during the primary non-hemorrhagic VS 27%, only in 9% for AIS and in 60% for CS. A distinctive feature of secondary hemorrhage when VS is the development of congestion in the area, combined with the difficulty of outflow at vasogenic edema area. Hemorrhagic transformation at AIS develops in the area of necrosis and cytotoxic edema and it happens rarely. Probably, congestion is increasingly predisposing factor secondary hemorrhage than a necrosis. When CS combination of necrosis and hyperemia with elements of the early development of vasogenic edema in perifocal zones leads to secondary hemorrhage more frequently than in VS and AIS. Why is this happening? Since the constrictor response of the arteries is a compensatory protective nature, in its absence or reduction of the capacity for such a reaction in violation of cerebral haemodynamic autoregulation, the blood continues to flow in the cerebral vessels under ordinary or elevated pressure and hyperemia zone forms background of venous congestion. This results in an overflow of intracranial microcirculation, rise in intracranial pressure and brain-threatening consequences.

5. Reactive (post-ischemic) hyperperfusion
The phenomenon of reactive (post-ischemic) hyperperfusion observed by us in the early postoperative period in patients with cardiac ischemia and arterial hypertension with the duration more than 10 years who had undergone coronary artery bypass surgery (n = 47). There has been noted a moderate (up to 22-25%), same as significant change of cerebral perfusion (decrease of TTP, CBF and an increase of CBV) in areas perfused MCA on both sides. These changes were accompanied by a temporary deterioration of neurological symptoms: vestibular ataxia syndromes (58%), vegetative dysfunction syndrome (100%), asthenic syndrome (100%). Clinical manifestations of reperfusion syndrome in 8 days after the operation is not detected, whereas signs of cerebral hyperperfusion still persisted. Patients with an anamnesis of arterial hypertension (duration less than 10 years) or without hypertension significant changes in brain perfusion in the postoperative period were not found, which indicates the safety of cerebral haemodynamic autoregulation mechanisms.

6. Conclusion
In our opinion, changes TTP/MTT is not less informative data than the CBF and CBV (Table 1).

| Type of disorders of brain tissue perfusion | rMTT/TTP | rCBF | rCBV |
|--------------------------------------------|----------|------|------|
| Cerebral hyperperfusion syndrome            | ++       | ±    | ++   |
| Benign hyperemia                           | ±        | ±    | +    |
| Reactive postischemic hyperperfusion        | -        | +    | ±    |

Extension of time with a decrease in blood flow - a sign of hypoperfusion. A moderate increase in the time at moderately elevated blood volume - a sign of benign hyperemia. The shortening of the time with a moderate increase in blood volume - a sign of post-ischemic reactive hyperperfusion. Significant prolongation of transit time combined with a significant increase in blood volume are signs of cerebral hyperperfusion syndrome according with a high risk of hemorrhage. Close to each other benign hyperemia and reactive post-ischemic hyperperfusion have different mean transit time or time to peak (a small increase or a slight shortening, respectively).
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