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Safety and efficacy of remote ischemic preconditioning in patients with severe carotid artery stenosis before carotid artery stenting: A proof-of-concept, randomized controlled trial

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Keywords
Ischemic Preconditioning; Stroke; Carotid Arteries; Stents; Brain Infarction; Angioplasty

Abstract

Background: Remote ischemic preconditioning (RIPC) has been proposed as a possible potential treatment for ischemic stroke. This study aimed to investigate the frequency of micro-embolic brain infarcts after RIPC in patients with stroke who underwent elective carotid artery stenting (CAS) treatment.

Methods: This study was managed at Shiraz University of Medical Sciences in southwest Iran. Patients undergoing CAS were randomly allocated into RIPC and control groups. Patients in the RIPC group received three intermittent cycles of 5-minute arm ischemia followed by reperfusion using manual blood cuff inflation/deflation less than 30 minutes before CAS treatment. Afterward, stenting surgery was conducted. Magnetic resonance imaging (MRI), including diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC), was acquired within the first 24 hours after CAS.

Results: Seventy-four patients were recruited (79.7% men, age: 72.30 ± 8.57). Both groups of RIPC and control

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Table 2. Comparison of factors describing microinfarcts based on magnetic resonance imaging (MRI) in two groups

Parameters	MRI positives group		P
	RIPC (n = 15)	Control (n = 19)	
Lesion surface area (mm^2) (mean ± SD)	101.24 ± 111.52	99.12 ± 94.66	
Maximum	387.72	398.89	0.580**
Minimum	11.50	11.61	
Average surface area (mm^2) (mean ± SD)	30.07 ± 19.85	30.00 ± 31.50	
Maximum	90.63	150.00	0.420**
Minimum	11.50	8.73	
Number of lesions (mean ± SD)	3.40 ± 3.62	3.94 ± 3.99	
Maximum	12.00	18.00	0.280**
Minimum	1.00	1.00	
Largest lesion diameter (mm) (mean ± SD)	10.93 ± 5.02	11.89 ± 6.08	
Maximum	23.00	29.00	0.620**
Minimum	5.50	5.00	
Contralateral infarct (%)	40.00	33.30	0.690*
Ipsilateral infarct (%)	100	94.40	> 0.999*
Cortical infarct (%)	46.70	33.30	0.430*
Subcortical infarct (%)	80.00	100	0.080*
Bilateral infarct (%)	40.00	55.60	0.370*

*Chi-square test; **Mann-Whitney test

MRI: Magnetic resonance imaging; RIPC: Remote ischemic preconditioning; SD: Standard deviation

The duration of the pre-procedural interval for preempted RICP differed from several days to several months.[8,17,18] As an instance, Zhao et al. documented that RICP could diminish both incidence and the average surface area in patients who underwent CAS.

Their RIPC method was done with synchronous bilateral upper arm ischemia using an electric auto-control device with cuffs. It consisted of five rounds of five-minute ischemia and five-minute reperfusion, which were repeated two times a day for two weeks before CAS, that obviously differed from our method.[8]

We did not observe serious local or systemic adverse effects following the RIPC procedure, except in one participant in the RIPC group who experienced cuff extrusion-related petechiae on the arm. This complication has similarly occurred in some previous studies.[8,13] Besides, since most patients tolerated the RIPC method, it seems to be a low-cost, safe, and accessible strategy to apply to those undergoing CAS. However, mainly due to the small sample size, we could not detect a better outcome after RIPC.

The most substantial drawback of the current study was the small sample size. Moreover, using manual cuff pressure may cause an operator error. Hence, using digital cuff pressure may be better. For further follow-up in the next six months, it is better to do another DWI MRI.

Conclusion

Although RIPC was a safe and non-invasive modality before CAS to decrease infarcts, this study did not show the advantage of RIPC in the prevention of infarcts following CAS. However, further large-scale trials may be worthwhile to determine the efficacy of RIPC in the prevention of symptomatic or asymptomatic embolic stroke after CAS. Furthermore, the optimal treatment protocol for RIPC needs further investigation.

Conflict of Interests

The authors declare no conflict of interest in this study.

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