Omental Approach to Functional Recovery After Cerebrovascular Disease

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Key words
- Cerebral revascularization
- Moyamoya
- Omentum
- Stroke

Abbreviations and Acronyms
bFGF: Basic fibroblast growth factor
EDAS: Encephalo-duro-arterio-synangiosis
EMS: Encephalo-myo-synangiosis
MCA: Middle cerebral artery
MMD: Moyamoya disease
NGF: Nerve growth factor
non-MMD: Ischemic stroke of other etiology
OT: Omentum transplantation and transposition
rCBF: Regional cerebral blood flow
STA-MCA bypass: Superficial temporal artery and middle cerebral artery
TIA: Transient ischemic attack
VEGF: Vascular endothelial growth factor

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■ OBJECTIVE: **To review and synthesize the clinical literature regarding risks and benefits of omentum transplantation and transposition surgery in patients with ischemic stroke of other etiology (non-MMD) and Moyamoya disease (MMD), and to evaluate the evidence for biological underpinnings of the presumed physiologic effects of omentum transplantation and transposition on vascularization of brain parenchyma.**

■ METHODS: **Articles were searched on scientific databases using predefined key terms. Data abstraction was based on the clinical course as reported in the articles. For further analysis, patients were divided into groups according to their diagnosis (MMD or non-MMD). Descriptive statistics were computed for better integration of the results.**

■ RESULTS: **The final literature review contained 15 articles (11 case series, 4 single case studies) with data on 93 patients (29 non-MMD, 64 MMD). At post-assessment 56% of patients showed substantial gains in functional domains (24% in the non-MMD group, 71% in the MMD group) and 92% demonstrated improvements of cerebral vascularization (55% in the non-MMD group, 98% in the MMD group). Differences in improvement became apparent with regard to the initial symptomatology wherein transient ischemic attacks were related to superior recovery rates and language pathologies showed least improvement.**

■ CONCLUSIONS: **Surgical revascularization using omental tissue has shown good success rates, particularly for recurrent transient ischemic attacks and prevention of further strokes and should be considered as treatment option for selected patients. Experimental data on the physiologic basis for postoperative improvement delivered convincing evidence for its arteriogenic potential and recent developments in omental stem cell research suggest a role in recovery from long-standing neurological deficits.**

INTRODUCTION

Ischemic stroke is a major public health concern, being the second most prevalent cause of death after myocardial infarction and one of the leading causes of disability.[1] In contrast to the socioeconomic burden, availability of effective treatment approaches is scarce, with recombinant tissue plasminogen activator as the only Food and Drug Administration-approved drug in acute ischemic conditions.[2] Later, in the subacute phase, many patients show functional improvement after physical therapy, speech therapy, or another rehabilitative modality according to their individual needs.[3] In addition to these conservative approaches, neurosurgical revascularization can be a treatment option for certain ischemic conditions, as for example, moyamoya vasculopathy, which is a chronic cerebrovascular disease characterized by occlusion of cerebral arteries and formation of abnormal vascular networks proximal to the lesion side, mainly affecting pediatric and adult cohorts of Asian origin.[4] Affected individuals are considered for surgical interventions in case no improvements are visible after drug therapy or endovascular treatment.[5] These methods were developed during the past century and can be broadly divided into indirect and direct revascularization approaches. The former type provides immediate augmentation of blow flow by establishment of anastomosis between, for example, the superficial temporal artery and middle cerebral artery (STA-MCA bypass).[6] Indirect procedures, in contrast, do not provide instantaneous relief of vascular insufficiency but instead require additional time for collateral outgrowth and synangiosis. They include encephalo-duro-arterio-synangiosis (EDAS), encephalo-arterio-synangiosis, encephalo-myo-synangiosis (EMS), encephalo-duro-arterio-myo-synangiosis, and encephalo-myo-arterio-synangiosis. An important commonality in all indirect procedures is that cerebral blood flow is enriched through extracranial arteries feeding into a periosteal connective tissue flap (EDAS), a cranial muscle flap (EMS), or another procedurespecific tissue flap that eventually forms collaterals with underlying parenchyma.[7]

A more controversial indirect approach for surgical revascularization is accomplished using the greater omentum either by transposing a pedicled flap subcutaneously to the lesion side or transplantation and microanastomosis with extracranial blood vessels. The omentum is an intra-abdominal, sheet-like structure originating from the greater curvature of the stomach and covering the ventral side of the intestines and parts of the colon. This peritoneal fold consists of mesothelial cells and connective tissue and has a supportive function for abdominal organs by provision of vascular, lymphatic, and peripheral nerve innervation.[8] The first surgical approach using an omental pedicle flap was performed in patients suffering from peripheral lymphedema. The underlying rationale was based on the observation that introduction of omental tissue with functional lymphatic vessels would lead to drainage of accumulated interstitial fluid.[9] Subsequently, laboratory work showed beneficial effects of omental transposition on vascularization of the underlying parenchyma, which stimulated interest on its effectiveness in the central nervous system.[10] Confirming evidence came from primate studies, where it was shown that heterotopic transplants penetrated the cortical surface leading to blood vessel formation. In these early experiments omental flaps were placed on the left temporoparietal junction, before occlusion of the middle cerebral artery (MCA). In contrast to monkeys in the experimental condition, control animals developed contralateral hemiparesis after arterial occlusion.[11] The investigators concluded that omental transplants are capable of vascularizing healthy brain tissue and preventing ischemia formation during subsequent induction of cerebral hypoperfusion.[12] The extension of laboratory results into clinical practice was suggested to be of particular relevance for patients at risk of ischemic events (i.e., those who experienced previous transient ischemic attacks [TIA]), but was discarded due to its invasive nature and the uncertainty of recurrent strokes in the clinical population.[9] Nevertheless, omental revascularization procedures were performed and evaluated in a variety of cases with cerebral hypoperfusion and, according to the studies, the overall results have been favorable.

This review will systematically summarize and synthesize case reports and case series data on omental transposition and transplantation (OT) in patients with Moyamoya disease (MMD) and in patients with ischemic stroke of other etiology (non-MMD), provide an overview of key neurobiologic factors underlying OT-induced angiogenesis, and review recent developments in stem cell research of omental tissue.

REVIEW OF CLINICAL CASES AND METHODS

A literature review was undertaken in general scientific databases (PubMed, Web of Science) and key journals using the search terms: omentum OR omental AND stroke AND/OR Moyamoya (last accessed March 1, 2015). The literature search was restricted to English, German, Polish, and Japanese languages. No constraints were made with regard to publication date. All relevant articles were further searched by their reference list. Studies were excluded if in addition to omental procedures, treatment involved simultaneous surgical revascularization by other direct or indirect approaches, patients showed primary lesions in non-cerebral regions (cerebellum, brainstem, medulla oblongata), or diagnosis revealed neurodegenerative disorders (Alzheimer's dementia, Parkinson disease). When the obtained data was considered insufficient or missing key information the first author was contacted. In case no further details were obtained and the study was considered to provide insufficient details, defined as missing a tabular listing or written description of patient characteristics and clinical course the article was discarded.

Data Extraction

Most included studies used generic terms for evaluation of postoperative outcomes (i.e., no improvement, minor improvement, improvement, complete resolution of symptoms) that was taken as primary outcome measure. In case no such categorization was provided or a narrative description of patients' course did not include a comparable evaluation, we compared the presenting symptomatology with status at follow-up assessment to classify the outcome accordingly. The postoperative imaging outcome was classified as success if the reported results conveyed sufficient supply of the affected cortical area through omental collaterals. Furthermore, patients were grouped across studies by their primary diagnosis into either MMD or non-MMD. Data syntheses was conducted for a better between-study comparison with regard to patients initial symptoms grouped into the following classifications: motor, language, neuropsychiatric, visual, TIA. Motor symptoms included hemiparesis, paraparesis, monoparesis, tetraparesis, facial paresis, limb weakness, plegic syndromes, and spasticity. Language symptoms included aphasia, dysarthria, and dysphasia. Neuropsychiatric symptoms included memory loss, learning problems, mental retardation, confusion, and emotional disturbance. Visual symptoms included hemianopsia, scintillating scotoma, visual field defects, blindness, and diplopia.

Statistical Analysis

The statistical analysis was performed using SPSS (IBM, version 21.0; Armonk, New York, USA), figural representations of data were obtained by Excel (Microsoft Cooperation, 2013; Redmond, Washington, USA). Calculation of descriptive statistics included univariate (mean, standard deviation, percentage) and bivariate (Pearson's correlation, P; Spearman's rank correlation, r) indices. For reason of methodologic constraints (see Limitation section) bivariate results were considered only if correlations were of medium size (P or $r \geq 0.3$).

RESULTS

The sequential steps of the review process with the corresponding number of articles is outlined in **Figure 1**. The initial search process yielded 46 hits of which 25 were regarded as relevant after screening for exclusion criteria. In the next step, 15 articles were extracted that contained sufficiently detailed patient characteristics for inclusion. The resulting literature sample was compromised of 11 case series and 4 single case studies, and included 6 articles from Japanese institutions, 6 from North American, and 2 from European facilities. An overview of the final literature is provided in **Table 1**.