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Comparison of Early Outcomes and Restenosis Rate Between Carotid Endarterectomy and Carotid Artery Stenting Using Propensity Score Matching Analysis

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WHAT THIS PAPER ADDS

This propensity score matched analysis of unselected patients with carotid stenosis reconfirms the findings of previous randomised controlled trials (RCT) that carotid endarterectomy was associated with a lower 30 day incidence of major adverse clinical events and restenosis than carotid artery stenting. This suggests that RCT findings from selected study populations can be generalised to clinical practice.

Objective/Background: Despite randomised evidence, the debate continues about the preferred treatment strategy for carotid stenosis in routine clinical practice. The aim of this study was to compare early outcomes and restenosis rates after carotid endarterectomy (CEA) and carotid stenting (CAS) in unselected patients using propensity score matching (PSM).

Methods: The 30 day incidence of major adverse clinical events (MACE; defined as stroke, transient ischaemic attack, myocardial infarction, or death) and procedure related complications, as well as restenosis rates during follow-up were compared between unselected patients undergoing CEA or CAS between January 2002 and December 2015 at a single institution. PSM was used to balance the following factors between the CEA and CAS cohorts: age, sex, hypertension, diabetes, dyslipidaemia, smoking, atrial fibrillation, previous percutaneous coronary intervention or coronary artery bypass grafting, valvular heart disease, contralateral carotid occlusion, degree of carotid stenosis, and symptomatic status. Statistical comparisons of outcomes were based on logistic regression analysis and log rank test.

Results: Of 1184 patients (654 CEA and 530 CAS), 452 PSM pairs of CEA and CAS patients were created. The CAS group showed a relatively higher 30 day incidence of MACE (7.5% vs. 2.4%; odds ratio [OR] 3.261, 95% confidence interval [CI] 1.634–6.509; $p = .001$) but a lower incidence of procedure related complications (1.5% vs. 5.3%; OR 0.199, 95% CI 0.075–0.528; $p = .001$). During a mean follow-up of 49.1 months (range 1–180 months), restenosis rates were higher after CAS than after CEA (1.5% vs. 1.0% at 12 months and 5.4% vs. 1.2% at 24 months, respectively; $p = .008$).

Conclusion: This PSM based observation reconfirmed previous trial results in both asymptomatic and symptomatic patients with carotid artery stenosis in routine clinical practice: CEA showed lower 30 day MACE and mid-term restenosis rates than CAS.

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INTRODUCTION

Atherosclerotic stenosis of the internal carotid or intracranial arteries is associated with 8–16% of ischaemic strokes.[1–3] Carotid endarterectomy (CEA) and carotid artery stenting (CAS) have been compared as treatment modalities of internal carotid artery (ICA) stenosis in many studies. Previous meta-analyses demonstrated that CAS significantly increases the risk of minor stroke but decreases the risk of myocardial infarction (MI).[4,5] In addition, recent randomised controlled trials (RCTs) with long-term results showed no significant differences in the risk of 30 day post-operative stroke, MI, or death between the two procedures.[6,7] Despite many reports, the efficacy debate continues between these two treatment modalities. Can these results be

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uniformly applied to an individual institution? The aim of this study was to evaluate early outcomes of CEA versus CAS and restenosis rate during the follow-up period. To balance demographic and clinical characteristics and to adjust for selection bias and confounding factors between the two groups, propensity score matching (PSM) was applied in the analysis.[8–10]

MATERIALS AND METHODS

Study enrollment and data collection

This study was approved by the Institutional Review Board of Samsung Medical Centre. Informed consent was waived for this retrospective review. From January 2002 to December 2015, 1488 cases of CEA or CAS were performed at a single institution and were included in this study. Demographic and clinical data of enrolled patients were retrospectively collected from electronic medical records.

Among the 1488 cases of CEA ($n = 840$) or CAS ($n = 648$), 47 cases of CEA co-performed with a coronary artery bypass grafting (CABG) operation and 38 cases of CAS performed without embolic protection devices (EPD), three cases of technical failure, and 109 patients who received sequential treatment with CEA or CAS for each of two carotid arteries were excluded from this study.

Procedures

Indications for treatment of ICA stenosis at the authors' institution are ICA stenosis $>$ 50% in symptomatic (presence of neurological or ocular symptoms) patients and $>$ 70% in asymptomatic patients, unless totally occluded. All patients who underwent carotid revascularisation had computed tomography angiography, magnetic resonance angiography, or conventional angiography before the procedure. The degree of stenosis was calculated according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) measurement criteria.[11,12]

When deciding treatment modality between CEA or CAS, CAS was selected for patients with an unfavourable carotid anatomy for CEA (prior ipsilateral radiation therapy to neck, previous ablative neck surgery, contralateral vocal cord paralysis, presence of a tracheostomy stoma, high lesion above the C2 vertebral body), high surgical risk of CEA (old age, severe heart failure, severe pulmonary function disorder), the preference of the patient, and for the purpose of the clinical trial.

All CEAs were conducted using conventional endarterectomy technique under general anaesthesia, and carotid shunts were used routinely (Pruitt-Inahara® Carotid Shunts; LeMaitre Vascular, Burlington, MA, USA). In symptomatic patients, antiplatelet agent was continued before the CEA procedure and all CEA procedures were performed with intravenous unfractionated heparin (50–60 units/kg body weight) during the CEA procedure. The carotid artery was closed primarily or with processed bovine pericardial patch (Vascu-Guard; Synnovis Surgical Innovations, St. Paul, MN, USA) according to the surgeon's preference. CAS was performed under local anaesthesia with antiplatelet therapy (100 mg aspirin and/or 75–300 mg clopidogrel) before the procedure and intravenous unfractionated heparin (50–60 units/kg body weight) during the procedure. Several types of EPD were applied for all CAS during the study period. After CEA or CAS, single or dual antiplatelet therapy or warfarin was continued unless contraindicated.

Endpoints and definition

The primary endpoint for this study was the 30 day postoperative incidence of a major adverse clinical event (MACE), a composite outcome that defined any clinical stroke, TIA, MI, or death. Any clinical stroke was defined as an acute neurological event with focal symptoms and signs, lasting for 24 hours or more, that were consistent with focal cerebral ischaemia. MI was defined as one or more of the following: documentation of electrocardiographic changes indicative of acute MI; new elevation in troponin more than three times the upper level of the reference interval in the setting of suspected myocardial ischaemia. Secondary outcome included the 30 day incidence of procedure related complication, such as cerebral hyperperfusion syndrome, bleeding required re-operation, cranial nerve injury, and restenosis rate during the follow-up period. Cerebral hyperperfusion syndrome was included with severe ipsilateral headache with hypertension, seizures, and intracranial haemorrhage on image study,[13,14] without any further confirmative examination by transcranial Doppler.[15] For patients complaining of unusual prolonged headache or showing abnormal neurological signs after CEA or CAS, neurological examinations and further management were performed by neurologists. Cranial nerve injury was determined on the basis of the symptomatic presentation after the revascularisation procedure showing injury of hypoglossal, recurrent laryngeal, superior laryngeal, and marginal mandibular branch of facial nerve.[16,17]

Duplex ultrasonography was routinely performed at 1, 6, 12, and 24 months after revascularisation and then every year during the follow-up period. Seventy percent or more diameter reducing stenosis or occlusion and peak systolic velocity above 300 cm/s detected by duplex ultrasonography were considered restenosis.[18,19]

Statistical analysis

The primary predictive variable for the analysis was revascularisation technique (CEA vs. CAS). Because this study was designed as a retrospective observational study and there were likely to be non-random differences between the CEA and CAS groups, the PSM technique was used to reduce possible selection bias and confounder effects and to create two balanced groups.

PSM matching using zero matching tolerance, and a 1:1 matching algorithm without replacement was conducted by a professional biostatistics team. Matching factors were as follows: age, sex, hypertension, diabetes, dyslipidaemia, smoking, atrial fibrillation, previous percutaneous coronary intervention or CABG, valvular heart disease, contralateral

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