Impact of Preoperative Ultrasonography Screening for Carotid Artery Stenosis in Lung Cancer Patients

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Background. Stroke is a major cause of morbidity or death after lung operations. Carotid artery screening (CAS) is useful for detecting carotid artery stenosis, which is one of the causes of stroke. This study investigated the frequency of and risk factors for preoperative carotid artery stenosis to determine whether CAS with ultrasonography contributes to preventing postoperative stroke or cardiovascular comorbidities in lung cancer patients.

Methods. This retrospective study included 1,676 consecutive lung cancer patients who underwent surgical resection.

Results. Of the 1,342 patients who underwent CAS, 173 (12.9%) had carotid artery stenosis. Significant associations with carotid artery stenosis were found for older patients ($p < 0.0001$), men ($p < 0.0001$), smoking history ($p < 0.0001$), history of stroke ($p = 0.0037$), cardiovascular diseases ($p < 0.0001$), hypertension ($p = 0.0353$), diabetes mellitus ($p = 0.0037$), and peripheral vascular diseases ($p < 0.0001$). Patients with the three independent risk factors of age, male sex, and history of cardiovascular diseases had a 6.43-fold higher prevalence of carotid artery stenosis (odds ratio, 6.43; 95% confidence interval, 3.80 to 10.89) than those with none of these factors. Propensity score–matched analysis showed that incidences of postoperative stroke and cardiovascular comorbidities were both lower in patients who underwent CAS and received appropriate anticoagulant therapy than in those who did not ($p = 0.0619$ and $p = 0.0319$, respectively).

Conclusions. Preoperative CAS is a simple and useful tool for detecting carotid artery stenosis. Administration of perioperative anticoagulant therapy to preoperative patients with lung cancer and carotid artery stenosis identified by CAS may prevent postoperative stroke and cardiovascular events.

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Postoperative stroke occurs in 0.6% to 0.9% of patients undergoing thoracic operations [1] and is thus a rare complication but a major cause of morbidity or death after lung operations. The main causes of postoperative stroke are cerebral atherothrombosis, lacunar stroke, cardiac embolism associated with atrial fibrillation, dehydration, hypotension, and perioperative systemic hypercoagulability [2]. In particular, atherosclerotic stenosis of the carotid artery impairs cerebral blood flow [3], and thromboembolic events associated with it are a frequent cause of ischemic strokes [4]. Carotid artery disease is therefore a risk factor for stroke [4]; indeed, approximately 10% of strokes are attributable to thromboembolic events associated with atherosclerotic carotid artery disease [4].

The prevalence of asymptomatic carotid artery stenosis ranges from 0.1% to 7.5% [5]. In addition, Kallikazaros and colleagues [6] reported a high prevalence of combined aortic and carotid plaques in patients with no clinical evidence of atherosclerotic cardiovascular disease. Thus, the condition of the carotid artery may reflect the general state of the cardiovascular system, even in asymptomatic patients.

In our institution, all patients with lung cancer are routinely screened preoperatively by ultrasonography of carotid artery for risk of preventable cerebrovascular events in the perioperative period. However, to our knowledge, no published studies have clarified the frequency of or risk factors for carotid artery stenosis or investigated the utility of ultrasonographic carotid artery

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screening (CAS) of patients with lung cancer. The present study investigated the frequency of and risk factors for preoperative carotid artery stenosis and whether CAS contributes to preventing stroke or cardiovascular comorbidities in postoperative lung cancer patients.

Material and Methods

Patients

The National Hospital Organization Kyushu Medical Center Ethics Committee approved this study (approval number: 17C210). Between November 1984 and May 2017, 1,676 consecutive patients with primary lung cancer underwent surgical resection in the Department of Thoracic Surgery, Clinical Cancer Institute, National Hospital Organization Kyushu Medical Center. Preoperative ultrasonographic CAS was performed routinely on these patients from January 2001. Data of the 1,342 patients who had undergone preoperative CAS after January 2001 were compared with the remaining 334 patients who had undergone operations before December 2000 without preoperative CAS.

Preoperative CAS

Carotid artery stenosis was evaluated by using ProSound Alpha 6 and 7 ultrasonography system (Hitachi Aloka Medical, Tokyo, Japan). The degree of stenosis was calculated based on the method described in the European Carotid Surgery Trial [7], and the calculated percentage of stenosis of the linear carotid artery was classified as mild (30% to 49%), moderate (50% to 69%), severe (70% to 99%), or occluded, as previously described [8] (Fig 1).

Perioperative Treatment of Carotid Artery Stenosis

Patients were treated according to their grade of carotid artery stenosis as follows: patients with no or mild carotid artery stenosis without a history of stroke had no treatment, those with mild carotid artery stenosis and a history of stroke or moderate carotid artery stenosis without a history of stroke started intravenous anticoagulant therapy using unfractionated heparin (10,000 U) postoperatively, and those with moderate carotid artery stenosis with a history of stroke or severe carotid artery stenosis started intravenous anticoagulant therapy using unfractionated heparin (10,000 U) 7 days before the operation. Patients receiving heparin were monitored by measuring activated partial thromboplastin times, and anticoagulant therapy was discontinued 3 days after the operation.

Histopathologic Evaluation

Formalin-fixed and paraffin-embedded surgical specimens were retrospectively collected, and sections were stained with hematoxylin and eosin and reviewed. Pathologic staging was based on the TNM classification of the International Union against Cancer [9]. For Seventh Edition TNM staging, all patients underwent computed tomography (CT) scans of the thorax and upper abdomen, bone scintigraphy, and brain CT or magnetic resonance imaging or fluorodeoxyglucose-positron emission tomography.

Patients Without Preoperative CAS

Between November 1984 and December 2000, 334 consecutive patients with primary lung cancer had undergone complete surgical resection in our institution without CAS. This control group was retrospectively matched with the group that had undergone CAS according to sex, preoperative comorbidities, surgical procedure, intraoperative blood loss, and pathologic stage. Selected outcomes were compared between these groups to evaluate prevention of postoperative comorbidities by CAS.

Statistical Analysis

Patients' clinical and pathologic profiles were summarized using descriptive statistics or contingency tables. The Student t test, the χ^2 test, or the Fisher exact test was used to compare variables between the two groups. Propensity score matching was performed to reduce the potential for bias introduced by the nonrandom
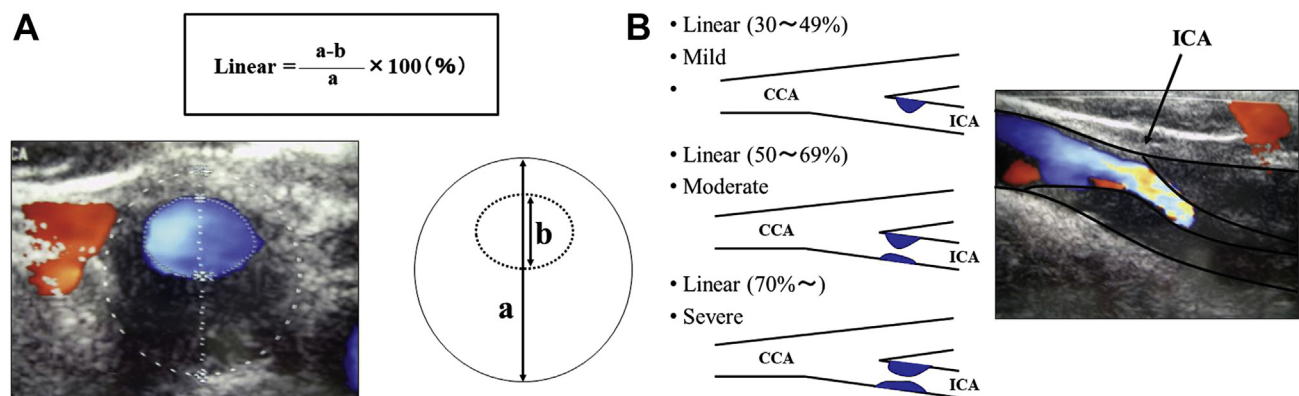

Fig 1. (A) Ultrasonographic assessment of the carotid artery and the severity of stenosis calculated as a percentage. (B) Classification of the severity of stenosis. (CCA = common carotid artery; ICA = internal carotid artery.)