Long-Term Causes of Death and Excess Mortality After Carotid Artery Ligation

Tarik F. Ibrahim[1,2], Behnam Rezai Jahromi[2], Joonas Miettinen[2], Rahul Raj[2], Hugo Andrade-Barazarte[2], Felix Goehre[2], Riku Kivisaari[2], Hanna Lehto[2], Juha Hernesniemi[2]

OBJECTIVE: **Carotid artery ligation (CAL) is used to treat large and complex intracranial aneurysms. However, little is known about long-term survival and causes of death in patients who undergo the procedure. This study was intended to evaluate if patients who have undergone CAL have long-term excess mortality and what the causes of death are.**

METHODS: **All patients were treated at Helsinki University Hospital between 1937 and 2009. Patients who had undergone CAL and survived ≥1 year after the procedure were included in the cohort. Follow-up was until death or 2015 (2711 patient-years). Causes of death were reviewed and relative survival ratios calculated using the Ederer II method and a matched population.**

RESULTS: **There was 12% excess mortality in all patients 20 years after CAL and 22% after 30 years. A higher proportion of the patients who had subarachnoid hemorrhage (SAH) died during follow-up compared with unruptured patients undergoing CAL. Cardiovascular disease and cerebrovascular accident were the leading causes of death.**

CONCLUSIONS: **Patients with unruptured aneurysms did not experience as much excess mortality as those who had an SAH. The higher proportion of deaths observed in ruptured patients may be partly because of long-term excess mortality conferred by the SAH itself or SAH risk factors. Although the entire population did display excess mortality compared with the general population, this may be because of shared risk factors for aneurysm development and rupture and the cause of death.**

INTRODUCTION

Therapeutic carotid artery occlusion has been used as an effective treatment in the management of proximal giant or complex intracranial aneurysms (IAs). The development of microneurosurgical approaches as well as modern endovascular techniques has decreased the number of carotid artery ligations (CALs) performed, but they still have a viable role in IA management. Although the modalities for CAL have evolved from the days of silk ligature, clips, the Selverstone clamp, and the Crutchfield clamp,[1] so have the safeguards by which patients are deemed candidates for the treatment. Many centers now use a balloon test occlusion (BTO) with a variety of adjunctive modalities to predict CAL tolerance,[2-7] although there are other techniques as well.

Proximal ligation is the simplest treatment for giant and complex aneurysms in patients who can tolerate the procedure.[8] However, there have been few data about long-term survival after this procedure. It is important to know how the long-term complications affect excess mortality so that patients and families can be counseled accordingly.

Although other series have reported their results and complications with CAL, the follow-up has not been lifelong. Because there are few emigrations from Finland, we have been able to

Key words
- Carotid
- Excess mortality
- Ligation
- Occlusion
- Stroke
- Subarachnoid hemorrhage

Abbreviations and Acronyms
BTO: Balloon test occlusion
CAL: Carotid artery ligation
CI: Confidence interval
CVA: Cerebrovascular accident
DNIA: De novo intracranial aneurysm
HUH: Helsinki University Hospital
IA: Intracranial aneurysm
RSR: Relative survival ratio
SAH: subarachnoid hemorrhage
SMR: Standardized mortality ratio

From the [1]Department of Neurosurgery, Loyola University Medical Center, Maywood, Illinois, USA [2]Department of Neurosurgery, Helsinki University Hospital, Helsinki, Finland

To whom correspondence should be addressed: Tarik F. Ibrahim, M.D. [E-mail: tarik.ibrahim@gmail.com]

*Citation: World Neurosurg. (2016) 90, C:116-122.
http://dx.doi.org/10.1016/j.wneu.2016.01.023*

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

1878-8750/$ - see front matter

follow nearly our entire population of patients with CAL until they died or until the present day.

In this report, we analyzed survival in 129 consecutive patients undergoing CAL for IA. The goal of this study was to analyze if these patients suffered from long-term excess mortality compared with the general population and in addition to identify risk factors that may have a role in early deaths.

METHODS

Patient Cohort

We retrospectively analyzed 129 consecutive patients who underwent CAL in the neck for IA treated at Helsinki University Hospital (HUH) Department of Neurosurgery between January 1937 and December 2009 (Figure 1). All patients in Finland with IAs are treated at public hospitals that keep comprehensive and accessible records. HUH is the lone provider to southern Finland, with a catchment area of 1.8 million people. The Finnish population is ideal for population-based epidemiologic studies.

Patients who also underwent an adjunctive procedure such as clipping or bypass were excluded from the study ($n = 1$). All types of occlusions were included (ligature, Crutchfield clamp, endovascular balloon). For many patients, it was not clear from the operative report whether the internal carotid artery or common carotid artery was occluded. Of the total cohort, 113 patients who survived greater than 1 year after the CAL represent the focal study population in this evaluation of long-term excess mortality.

Follow-Up Data

All patient charts and radiographic images were reviewed and the appropriate clinical and radiographic data were recorded in the Helsinki Cerebral Aneurysm Database. Although many of the patients underwent CAL before the advent of modern-day techniques for assessing carotid occlusion tolerance, only 1 patient who suffered a postprocedure stroke survived more than 1 year. Fifteen patients died in the first year because of subarachnoid hemorrhage (SAH)-related causes, procedure-related complications, or other reasons. Among the 113 patients who survived greater than 1 year, 6 patient dates of birth or dates of death could not be identified. These patients were born in the late nineteenth and early twentieth centuries and it is suspected that some of their records may have been lost or that the patients moved during World War I or World War II. Table 1 shows the remaining 107 patients' characteristics.

Ethics and Statistics

For the purpose of studying long-term excess mortality, we included only patients surviving greater than 1 year from the date of their procedure in our relative survival ratio (RSR) calculations. The RSR estimates the excess mortality that a patient undergoing CAL experiences compared with the age- and sex- matched general population. It does this regardless of whether the death is directly related to the initial illness or procedure. Confidence intervals (CIs) (95%) for the curves were calculated using the delta method on the log cumulative hazard scale.

We also used the standardized mortality ratio (SMR) to estimate differences in mortality between the study cohort and the general Finnish population and to establish whether this was statistically significant. The SMR is calculated by observed deaths divided by expected deaths and is standardized by age, sex, and calendar year.

To test the differences in excess mortality between the genders and between ruptured and unruptured cases, we constructed a multivariate Poisson regression model for the excess mortality[9] using gender and rupture status as covariates. A constant excess hazard was assumed for the follow-up time intervals divided at the time points 15, 25, and 35 years. The 95% CIs for estimated (excess) hazard ratios were based on a log-normal assumption and P values computed using the Z test.

The Ederer II method was used to estimate relative survival for the cohort. Population mortality for relative survival estimation was based on annual data with 100 age groups from Statistics Finland. The estimates are plotted only up to 40 years after CAL because of uncertainty in Ederer II estimates after the 40-year mark. This is because of the low expected survival (a hypothetical survival of Finns similar to the cohort without brain aneurysms) after that mark.

RESULTS

Overall Survival and Causes of Death

Table 1 shows characteristics for 107 patients undergoing CAL at HUH between 1937 and 2009 who survived greater than 1 year postoperatively and had complete follow-up data. As of June 2015, 76 patients (67%) of the study population had died during a follow-up period of 2711 years for an annual mortality of 2.8%. The study group's mean age at death was 76 years (median, 81; range, 44–87 years). Table 2 displays all causes of death and the time frame in which they occurred. The leading cause of death was cardiovascular ($n = 17$, 22%) followed by cerebrovascular accident (CVA) ($n = 13$; 17%).

Early Mortality

Fifteen patients (12%) died within the first year after undergoing CAL. Most of them ($n = 14$) had ruptured IAs that caused 13 to die as a result of SAH-related issues. One patient with an SAH experienced acute neurologic deterioration shortly after the common carotid artery was occluded with a Crutchfield clamp and died. The only patient with an unruptured IA who died in the first year (giant paraclinoid aneurysm) did so after said aneurysm ruptured following application a Crutchfield clamp prior to discharge from the hospital.

Overall Long-Term Excess Mortality

The RSR curve for the entire population is displayed in Figure 2. There was long-term excess mortality for the entire study population at all time points greater than 1 year after CAL. The cumulative RSR was 0.95 (95% CI, 0.88–1.02) at 10 years, 0.88 (95% CI, 0.78–1.0) at 20 years, and 0.78 (95% CI, 0.64–0.95) at 30 years. This indicates excess mortality of 5%, 12%, and 22% at 10, 20, and 30 years after CAL, respectively. The SMR was 1.58 and showed the excess mortality difference compared with the general population to be statistically significant ($P < 0.001$; CI, 1.24–1.98).