The New York Islands AVM Study
Design, Study Progress, and Initial Results

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Background and Purpose—Prospective population-based data on the incidence of brain arteriovenous malformation (AVM) hemorrhage are scarce. We studied lifetime detection rates of brain AVM and incident AVM hemorrhage in a defined population.

Methods—The New York islands (ie, Manhattan Island, Staten Island, and Long Island) comprise a 9,429,541 population according to the 2000 census. Since March 15, 2000, all major New York islands hospitals have prospectively reported data on consecutive patients living in the study area with a diagnosis of brain AVM and whether the patient had suffered AVM hemorrhage. Patients living outside the ZIP code–defined study area were excluded from the study population.

Results—As of June 14, 2002, 284 prospective AVM patients (mean±SD age, 35±18 years; 49% women) were encountered during 21,216,467 person-years of observation, leading to an average annual AVM detection rate of 1.34 per 100,000 person-years (95% CI, 1.18 to 1.49). The incidence of first-ever AVM hemorrhage (n=108; mean age, 31±19 years; 45% women) was 0.51 per 100,000 person-years (95% CI, 0.41 to 0.61). The estimated prevalence of AVM hemorrhage among detected cases (n=144; mean age, 33±19 years; 50% women) was 0.68 per 100,000 (95% CI, 0.57 to 0.79).

Conclusions—Our prospective data, spanning 27 months, suggest stable rates for AVM detection and incident AVM hemorrhage. Approximately half of AVM patients may suffer intracranial hemorrhage. (Stroke. 2003;34:e29-e33.)

Key Words: cerebral arteriovenous malformations ■ epidemiology ■ hemorrhage

The New York Islands AVM Study is an ongoing prospective, population-based incidence and case-control study designed to determine arteriovenous malformation (AVM) detection rates, the incidence and prevalence of AVM-associated morbidity, mortality and case fatality rates. Predefined demographic and morphological variables are collected in a multicenter design to analyze their effect on AVM-associated morbidity and mortality.

Methods

The New York islands, ie, Manhattan Island, Staten Island, and Long Island (the latter including the New York City boroughs of Brooklyn and Queens and the counties of Nassau and Suffolk) comprise a 9,429,541 population according to the 2000 census. The geographic features of the 3-island territory favored our assumption that cases of fresh hemorrhage, and even those AVM cases discovered without hemorrhage, would not be transported long distances or across major bodies of water to reach a nearby hospital. Using the International Classification of Diseases, ninth revision (ICD-9)–coded discharge data from the New York Statewide Planning and Research Cooperating System, we identified the 19 major hospitals that, taken together, accounted for 95% of all New York islands residents diagnosed with a cerebrovascular anomaly (ICD-9, 747.81) between 1996 and 1999.1,2

Identification of Subjects

Subjects are eligible at any age and are enrolled in the ongoing incidence study if they are current residents of the ZIP code–defined study area and if they have been newly diagnosed with a brain AVM after March 15, 2000. Patients detected thereafter with a previously known AVM diagnosis are not considered as incidence cases but are included in the prevalence estimates. Referral patients living outside the ZIP code–defined study area, those moving to the study area to facilitate diagnosis and treatment, and formerly known AVM patients who had completed AVM treatment before March 15, 2000, are excluded from the study population.

An ongoing active surveillance program has been implemented to ascertain all cases of hospitalized and nonhospitalized AVM patients in the New York Islands AVM Study area. Routine weekly fax alert sheets collected from each participating site provide updated information on newly detected AVM patients eligible for the ongoing survey. Any diagnosis is classified on the basis of the imaging technique used: CT, MRI, MRA, cerebral angiography, or any combination (see variable definitions in the Appendix). Cases detected from CT only are not counted until the malformation has...
been confirmed by \geq 1 additional technique. Definite AVM mortality and case fatality estimates include data from institutional (neuro)pathology departments and the New York City Office of Chief Medical Examiner.

As a retrospective control for AVM detection rates, we asked all participating centers to retrieve from their patient files the number of hospitalized and nonhospitalized AVM patients seen in the years 1996 to 1999 at their institution.

Variable Definition and Statistical Analysis
Research definitions for clinical and morphological AVM characteristics have been established by the Columbia AVM Database project since 1989 and formed the basis for a recently published national consensus paper on reporting terminology in AVM studies. For the purpose of future case-control analyses, the New York Islands AVM Study adapted predefined study variables in accordance with the consensus definitions. Variable definitions used by the New York Islands AVM Study are outlined in the Appendix.

Average annual detection and incidence rates were calculated from the number of AVM patients detected on the New York islands (lifetime diagnosis) divided by the New York islands population according to the US Census 2000. A Poisson distribution was assumed in determining 95% CIs. The overall age distribution in the AVM cohort was further tested for differences between patient subgroups through the use of standard statistical models ($\chi^2$, $t$ test, Spearman’s rank correlation) at an $\alpha$ level of 0.05.

Results
Retrospective Estimates
During a 4-year interval including 1996 through 1999, the average number of cases detected per year was $110 \pm 4$ (SD). The retrospective average annual detection rate of brain AVMs was $1.2$ per 100 000 person-years (95% CI, 1.1 to 1.4).

Prospective Estimates
Since March 15, 2000, all major New York islands hospitals and their related hospital networks have cooperated prospectively to report weekly data on consecutive patients living in the study area with a diagnosis of brain AVM. Figure 1 illustrates cumulative absolute frequencies of detected AVM patients showing a steady increase during the ongoing study.

As of June 14, 2002, 284 prospective AVM patients (mean $\pm$SD age, $35 \pm 18$ years; 49% women) were encountered during 21 216 467 person-years of observation, leading to an average annual AVM detection rate of $1.34$ per 100 000 person-years (95% CI, 1.18 to 1.49). One hundred eight patients presented with intracranial hemorrhage (mean age, $31 \pm 19$ years; 45% women); the crude incidence rate for first-ever AVM hemorrhage in our population was $0.51$ per 100 000 person-years (95% CI, 0.41 to 0.61). The prevalence of AVM hemorrhage among detected cases ($n=144$; mean age, $33 \pm 19$ years; 50% women) was $0.68$ per 100 000 (95% CI, 0.57 to 0.79).

Overall, no age differences were found between women (mean age, $31 \pm 19$ years) and men ($32 \pm 16$ years). Patients presenting with incident AVM hemorrhage were significantly younger (mean age, $28 \pm 19$ years) than those with nonhemorrhagic AVM presentation ($38 \pm 16$ years; $t$ test, $P=0.003$).
Additionally, for incident AVM hemorrhage, a significant negative correlation was found with increasing age ($r=-0.192$, $P=0.001$). In a univariate model comparing relative frequencies of hemorrhagic versus nonhemorrhagic presentation across different age classes (in 10-year increments), a significant association between incident AVM hemorrhage and age at presentation was found ($\chi^2_{(df=6)}, P=0.009$; Figure 2).

### Discussion

The present article provides the study design, progress report, and initial results of an ongoing prospective, population-based survey. The reported stable recruitment rates lend credence to the applied epidemiological study design and the effectiveness of the implemented detection system. The prospective findings match our initial retrospective predictions and retrospective estimates from prior reports as summarized in Figure 3.

Our preliminary findings do not include estimates on AVM-related mortality and case fatality rates because of the relatively short 27-month follow-up period. To date, however, to our surprise, only 3 of all identified AVM patients have been reported dead since the study was initiated. Given the known high fatality rate of intracranial hemorrhage from other causes, this observation may raise concerns that our results underestimate the frequency of AVM hemorrhage (and its associated mortality). A systematic type I error with estimates trending toward falsely low values cannot be entirely excluded, mainly because no AVM-specific ICD-9 codes exist, no bedside AVM screening tool is readily available, and all diagnostic procedures were made at the discretion of the treating physicians. Cerebral angiography is the current diagnostic standard in patients presenting with subarachnoid hemorrhage, but it may not have been performed in cases in which the patient’s clinical state or advanced age precluded any invasive treatment option. As for intracerebral hemorrhage, current recommendations favor angiography for all cases without a clear cause of hemorrhage, particularly for young, normotensive patients.4 Nonetheless, the timing of cerebral angiography after acute intracerebral hemorrhage usually depends on the patient’s clinical state and the neurosurgeon’s judgment about the need for surgical intervention.

Clearly, the New York Islands AVM Study is not a prevalence study. Based on a hypothetical prevalence of 10 AVM patients per 100,000 population, prior calculations indicate that MR screening of 1 million people would be necessary to yield estimates with sufficiently narrow CIs.5 Any attempt to survey diagnostic brain imaging in the New York islands population on incident intracranial hemorrhage alone is defeated by the dimension of the study logistics necessary to identify and analyze the expected 3600 cases per year (predictions based on figures given elsewhere6). Prior observations from large MR brain imaging series did not lead to detection rates of previously unknown or asymptomatic AVMs.7,8 Reported estimates from hospital-based autopsy series also appear to be unreliable, with prevalence estimates ranging from 5 to as many as 613 AVM cases per 100,000.5

Sad to say, but the rarity of the disease, its presumed

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Figure 2. Age-related relative frequencies of incident hemorrhagic and nonhemorrhagic AVM presentation in 284 patients from the New York Islands AVM Study. Overall mean±SD age differed significantly between AVM patients presenting with hemorrhage (28±19 years) and those with nonhemorrhagic presentation (38±16 years; t test, $P=0.003$).

![Bar chart](image-url)
congenital nature, and its assumed long asymptomatic development period make it unlikely that an overall prevalence will ever be known.

For the reasons cited above, the number of AVM cases missed in our survey remains unknown. A larger sample size, longer follow-up, and inclusion of pathology and medical examiner data are necessary to address the issue of AVM-related morbidity and mortality in our ongoing study. In addition, the proportion of patients undergoing AVM treatment (ie, surgical, endovascular, and/or radiation therapy) will considerably influence rates of AVM hemorrhage, morbidity, and mortality on follow-up. Two prior reports—one retrospective series and 1 based on symptomatic patients only—suggested that once an AVM has been detected, the rate of hemorrhage is about 3% to 4% per year. To address this issue, our ongoing study continues to collect data on both natural history and treatment-related outcome of unselected patients as included in the incidence cohort. The prospective findings may set the stage for a proper clinical trial to determine appropriate AVM management plans with the least morbidity and mortality.

Appendix

The New York Islands AVM Study:
Variable Definitions

Demographic Variables
The patient’s birth date, residential ZIP code, sex (male/female), self-defined race/ethnicity (American Indian, Asian, black, Hispanic, white, other), current insurance status (Medicaid, Medicare, private insurance, any combination, other), and enrollment date are documented. Age at presentation is calculated as the patient’s age (in years) at the time of the initial AVM presentation (diagnostic event).

Clinical Variables
The diagnostic event (or initial AVM presentation) is defined as the clinical picture of the index event that brought the patient to a medical encounter and directly led to the discovery of the AVM. The date of the diagnostic event is documented, and the mode of clinical presentation is further stratified. Intracranial hemorrhage refers to bleeding into the brain or its surrounding spaces. A hemorrhagic presentation (or incident intracranial hemorrhage) is defined as a clinically symptomatic event with signs of fresh intracranial blood on head CT and/or MRI or in the cerebrospinal fluid. The primary bleeding location is further classified as parenchymatous, subarachnoid, intraventricular, or any combination.

Any event of clinical seizure activity is syndromatically stratified into simple focal, partial complex, and (primary or secondary) generalized seizures.

A focal neurological deficit refers to a functional deficit on examination and is stratified as to whether the deficit was persistent, progressive, or reversible at the time of evaluation.

Headaches are further stratified into sudden onset headache, migrainous headaches (typical features required, ie, with or without aura, typical course, vegetative symptoms), nonspecific remittent headaches, and chronic headaches (>4 d/wk).

Other modes of presentation include any other AVM-related symptoms (eg, a bruit) that eventually lead to the diagnosis of the malformation. Incidental or asymptomatic presentation refers to a clinical presentation that was clearly unrelated to the AVM regarding the indication for imaging, eg, pituitary gland dysfunction or chronic sinusitis.

Handedness (right-handed, left-handed, ambidextrous) is coded according to the patient’s self-definition in the neurological history. Measures of health-related dysfunction include Rankin Scale, Barthel Index, and EuroQol and are documented for each patient at the time of first clinical contact, within 24 hours after a procedure, at least weekly during admission for the first event, and at 3, 6, and 12 months.

Morphological Variables
The imaging source and date of CT, MRI, arterial MR angiography, diagnostic 4-vessel brain angiography, and/or superselective cerebral
angiography are documented. The nearest imaging source in time to the
patient’s presentation is the basis for the description of morphological
variables.

Brain AVM side (right, left, midline) refers to the topographic
location in cases in which 1 malformation has been detected. For those
harboring ≥1 brain AVM, each malformation is coded separately.

The AVM size (nidus size) is measured as the largest diameter in
millimeters based on pretreatment MRI and/or cerebral angiogram.
Anatomic AVM location is stratified into lobar (frontal, parietal, temporal, and/or occipital lobe), deep (basal ganglia, thalamus, internal capsule, corpus callosum), and/or infratentorial (midbrain, pons, medulla, cerebellum) location.

A so-called “eloquent” brain location (as defined by the Spetzler-
Martin scale) is coded positive in cases in which the AVM is located in
“the sensorimotor, language, and visual cortex; the hypothalamus
and thalamus; the internal capsule; the brain stem; the cerebellar
peduncles; and the deep cerebellar nuclei.”

An AVM feeding artery is defined as any intracranial vessel that
angiographically contributes arterial flow to the malformation. Feed-
ning arteries may be parent arteries that give rise to vessels that
directly or indirectly supply flow to the AVM. Coding of multiple vessels is possible. For documentation, single feeding arteries are
stratified into right or left internal carotid artery, anterior choroidal
artery, anterior cerebral artery cortical branches, anterior cerebral
artery penetrators, middle cerebral artery cortical branches, middle
cerebral artery penetrators, vertebral artery, posterior inferior cere-
bellar artery, basilar artery, anterior inferior cerebellar artery, supe-
rior cerebellar artery, posterior cerebral artery cortical branches,
posterior cerebral artery perforators, posterior choroidal artery, any
dural supply (via external carotid artery or vertebral artery branches).

Moyamoya-type changes are defined as any pattern of collateral
small-vessel recruitment resulting from proximal feeding artery
stenosis or occlusion.

Concurrent arterial aneurysms are defined as saccular dilatations
of the lumen ≥2 times the width of the arterial vessel that carried the
dilatation and further classified as feeding artery aneurysms, in-
tramural aneurysms, and aneurysms unrelated to blood flow to the
AVM. The number and vessel location of any aneurysm subtype are
documented. Intramural aneurysms are coded only when visualized
early after angiographic injection, eg, before substantial venous
filling occurs. Infundibula, arterial ectasias (ie, dilated feeding
vessels), and intramural aneurysmal dilations seen during the
venous angiographic phase only are not coded as arterial aneurysms.
Arterial aneurysms are coded as unrelated to the AVM when located
on intracranial arteries not contributing blood flow to the AVM.

The venous drainage pattern is categorized as angiographic
drainage into the superficial cortical veins (superficial venous
drainage), drainage into the deep venous system (deep venous
drainage such as the internal cerebral veins, basal veins, vein of
Galen), and combined superficial and deep drainage. “In the poste-
rior fossa, only cerebellar hemispheric veins that drain directly into
the straight sinus, torcula, or transverse sinus are considered to be
superficial.”

Venous stenosis/occlusion is defined as a ≥2-fold caliber narrow-
ning or occlusion of any draining vein outflow pathway seen in 2
angiographic views.

Venous ectasia is coded positive in cases with a ≥2-fold caliber
increase change in any draining venous channel.

Treatment Variables
The date of each treatment procedure is coded, along with the treatment
modality (ie, surgery, endovascular treatment, radiation therapy) and
treatment target (AVM treatment, aneurysm treatment). Each procedure
is labeled as being technically complete or incomplete.

Clinical variables and measures of health-related dysfunction as
outlined above are reassessed within 48 hours after a procedure.
Additional follow-up evaluation by the clinical coordinator at each
center is scheduled at 3, 6, and 12 months.
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