CBF Before and After Extracranial-Intracranial Bypass Surgery in Patients with Ischemic Cerebrovascular Disease Studied with 133Xe-Inhalation Tomography

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SUMMARY Cerebral blood flow (CBF) was studied by 133Xenon inhalation tomography in 22 patients with symptoms of ischemic cerebrovascular disease before and after establishment of an extracranial-intracranial bypass shunt. Selection of patients for shunting was based on angiographically demonstrated arterial occlusions and on the finding of focal low flow areas corresponding to the clinical symptoms, that consisted mainly of minor stroke with good remission and with or without subsequent TIAs. It was required that the area of low flow should clearly exceed the CT lesion present in practically all cases.

Following surgery, the permanent neurologic deficits remained unchanged, while the TIAs stopped in all but one case. Two patients showed a definite increase of CBF in the low flow area while another two showed a questionable increase. All the other cases, 18 of the 22, showed an unchanged tomographic flow map with no trend towards diminution in extension or severity of the focal hypoperfused area. A persistent low flow in areas with no corresponding CT lesion following alleviation of a possible flow impediment is interpreted to represent an incomplete infarction or diachisis.

MEASUREMENTS OF CEREBRAL BLOOD FLOW (CBF) have become an integrated part of the preoperative evaluation program when extracranial-intracranial bypass (EC-IC) surgery is considered in patients with cerebrovascular disease. Studies using the intracarotid technique,1, 2 and the interventional 133Xenon technique3 have suggested that patients with a focal decrease of CBF and with a normal or only moderately reduced overall level of CBF might in particular benefit. As a focal CBF decrease in chronic cerebrovascular disease may reflect a lowered metabolic demand of infarcted tissue, some authors have pointed out that preoperative measurements in addition to resting CBF measurements should include regional estimates of the cerebral vasoreactivity4, 5 cerebral metabolic rate,6 or cerebral blood volume,7, 8. The results of these studies indicated that it may be possible to identify the subset of patients with a compromised collateral circulation.

Single photon emission computer tomography (SPECT) of inhaled 133Xenon affords an atraumatic, rapid, and easily repeatable method for analysis of regional CBF. By its 3-dimensional approach, this technique is particularly well suited for the detection of low flow areas, and allows for a direct comparison with structural changes seen on CT scan. The present report deals with the findings in a consecutive series of patients finally selected for shunt surgery on basis of the finding of hypoperfused areas exceeding in size a focal CT lesion of complete infarction. In most patients, several CBF measurements were performed before and after shunting.

Methods

Clinical Material

The material comprises 6 women and 16 men with an age range from 27 to 66 years (mean 50 years). Five
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had mild or moderate arterial hypertension, well controlled by appropriate therapy. None had heart disease or diabetes mellitus. Most patients received antplatelet drugs and 9 were on anticoagulant therapy.

The patients were selected according to the clinical and angiographical criteria applied in the ongoing collaborative study on EC-IC anastomosis. The clinical symptoms from the relevant hemisphere are presented in table 1. Three patients had only experienced TIAs from the relevant hemisphere. Of 15 patients who had suffered a minor stroke 7 had subsequent relevant TIAs. Of 4 patients with sequelae after severe strokes, one had subsequent relevant TIAs.

Based on analysis of the clinical symptoms and symptom-provoking factors, the TIAs were classified as being either of hemodynamic or embolic origin. A hemodynamic pathogenesis was assumed, when postural changes provoked shortlasting symptoms. In all other cases distal embolism causing transient focal ischemia was considered the pathogenetic mechanism. Of the 11 cases suffering TIAs only one met the criteria of a hemodynamic pathogenesis. This patient (case LW) noted, some months after a minor stroke, almost daily attacks of difficulty of speech and weakness of her right arm in relation to postural changes, in particular during the morning hours, symptoms that promptly disappeared after shunting.

The angiographical findings indicating lesions possibly amendable by an EC-IC bypass were in 18 cases occlusion of one internal carotid artery and in 4 cases severe stenosis or occlusion of the middle cerebral artery or its major branches. Final selection for surgery was based on the results of CT scan and CBF measurements. The criteria were the findings of an asymmetrical flow pattern with a focal hyperperfused area on the tomographic flow map in agreement with the clinical and angiographical findings. Also it was required the size of the low flow area should be at least twice the size of the focal lesion seen on CT scan. It should be noted that two of the 22 patients showed a normal CT scan in the relevant hemisphere despite a focal low flow area on the CBF map.

Initially only one pre- and postoperative study was undertaken. But in the majority (18 patients) at least four studies were made: At the initial evaluation, immediately pre- and post-operatively, and a follow-up after more than 3 months.

The findings on the CT scan, the angiogram, and on the flow map are presented in table 1.

CBF Measurements

CBF was measured by 133Xenon inhalation and a rapidly rotating single photon emission computer tomograph, described in detail elsewhere. Briefly, the instrument consists of 64 separate NaI crystals, arranged in 4 banks of 16 each. One study lasts 4.5 minutes, during which 133Xenon is inhaled during the first 1.5 minute. During the 1.5 minute period of 133Xenon inhalation and during the 3 subsequent 1 minute periods a sequence of 4 tomographic pictures is recorded of the isotope distribution. Three slices of brain tissue are studied simultaneously each 2 cm thick with an unseen interslice distance of 2 cm. The sequence of tomographic pictures together with the input curve gathered from a single narrowly collimated detector positioned over the upper part of right lung is used to calculate CBF. This calculation is based on the bolus distribution principle applied to the sum of the first 2 tomographic pictures. Following reconstruction of the pictures, correction for background and tissue absorption of the radiation is applied.

The resolution is 1.5 to 1.7 cm in the plane and 2.0 cm perpendicular to the plane, measured as full width at half maximum (FWHM).

The patients were studied in the supine, resting state with eyes closed. The patient's head was positioned in the aperture of the instrument so that the 3 slices were centered 1 cm, 5 cm, and 9 cm above the orbitomeatal plane. Also, care was taken to center the patient's head in the aperture using an inflatable cuff, but otherwise no special measures were used for positioning. End tidal pCO2 was measured by an infra-red analyzer before, during, and immediately after each CBF study. Blood pressure was measured after the CBF study.

With a maximal lung concentration of 10 mCi 133Xenon per liter the radiation absorbed dose per study to the lung, being the organ receiving highest radiation, averages 6 mGy. The gonadal dose approximates 0.6 mGy. This radiation absorbed dose is in the order of a conventional X-ray of the chest.

Data Analysis

Calculation of the average CBF in a given region was performed by the computer after manually selecting the region. Average CBF in the symmetrical area in the contralateral hemisphere was also obtained. In the same way mean hemispheric blood flow was calculated in slice 2 and 3 (slice 1 represents mostly posterior fossa structures).

By direct comparison with the CT scan, the area of complete infarction could be delineated on the tomographic flow map. As the slices of the 2 CT-scanners used (EMI 1010 and Siemens Somatom, DR) were 1.0 cm and 0.8 cm, respectively, both the slice corresponding to the OM = 5 cm or OM = 9 cm and the slices sandwiching this level were used for measurement of the full extent of the CT lesion. Then delineation was done of low flow areas where no focal CT lesions were seen, in most cases at the OM plane without CT lesions. Calculation of flow in these areas, in the following referred to as the region of interest (ROI), was then performed. The CBF values from that region and the symmetrical contralateral region were obtained in all successive CBF measurements. Calculation of the degree of side-to-side asymmetry was performed by taking the difference of flow in the ROI and the symmetrical region as a per cent of the value of the symmetrical region (the highest value), i.e. in per cent of the flow in the presumed healthy side.

For comparison with the patients in the present study mean cerebral and regional flow values were obtained from a normal material of 10 persons (hospital staff.
mean age 43 years (52, 56) all studied three times with an interval of one week between studies. Average hemispheric CBF in this series as calculated from slice 2 was 55 ± 5 ml/100g/min. The standard deviation of changes in mean flow between the repeated measurements in a given subject averaged 3 ml/100g/min. The "ROIs" in these 10 normal cases were chosen from slice 2 and represented areas of arterial supply, i.e. territory of the anterior cerebral artery, middle cerebral artery (further subdivided in a cortical and subcortical region), and posterior cerebral artery.14, 15 The mean value of the left to right side difference in per cent of highest side ranged from -0.9% ± 2.8% (1SD) (subcortical region of middle cerebral artery territory) to 2.1% ± 3.2% (1SD) (posterior cerebral artery territory). The size of these areas ranged from 14.2 cm² to 25.7 cm².

In order to assess the variances2 of repeated measurements of the side-to-side asymmetry in the normal material, individual variances were calculated for each ROI again expressing the side-to-side difference in per cent of the flow of the side with highest flow. This yielded mean S² values for these regions in the 10 normal cases ranging from 4.78 (anterior cerebral artery) to 9.83 (posterior cerebral artery) with a mean value of 7.72. Calculating in the same way the S² for the ROI as defined for the patients from all the patients with at least 2 testing preoperative CBF measurements yielded a mean S² = 13.49 (n = 15). The higher variance in the patient material may reflect a truly higher day-to-day variation of regional CBF, but it should be noted that a somewhat smaller ROI was used in most patients. The effect of EC-IC on the side-to-side asymmetry was estimated by testing for the difference between two means.16 The average value of the side-to-side asymmetries in the ROI was calculated from all pre- and all late postoperative measurements, and the difference between these values in the individual patient DT, was used in the formula:

\[ t = \frac{\Delta D}{\sqrt{\frac{1}{n_{\text{pre}}} S^2 + \frac{1}{n_{\text{post}}} S^2}} \]

The denominator in this formula is an estimate of the standard deviation of the mean values obtained pre- and postoperatively, where S² = 13.49 and n_{\text{pre}} and n_{\text{post}} are the numbers of the pre- and postoperative measurements in the individual patient. The number of degrees of freedom was 14 (15 patients used to deter-
At the later clinical evaluation, only one patient, case JJ, seen 4 weeks after a left EC-IC showed some improvement. As shunting in this case was performed 8 weeks following a stroke after which improvement had been in progress preoperatively, the changes following shunting were interpreted as further spontaneous recovery (CBF map unchanged postoperatively). At the 3 months follow-up 5 patients reported improvement of intellectual function, viz. concentration, memorization, and less fatigueability. The two patients, described in detail later, who showed a postoperative improvement in CBF belonged to this group.

Operative Complications and Graft Patency

In the immediate postoperative period, one patient (case IL) suffered aggravation of her aphasia for some hours (see later for details). One additional patient (case AWP) suffered complications attributable to the shunt operation. Two months following surgery the patient noted weakness and dyscoordination of the right leg, and a CT scan showed a subdural hematoma localized around the craniotomy. Following evacuation the clinical symptoms subsided completely. CBF measurement one month later was unchanged compared to the preoperative findings. The angiogram showed a well-functioning shunt.

A total of 24 anastomoses were performed, two patients being operated bilaterally. Eleven patients un-
derwent postoperative angiography at the 3 months follow-up, confirming patency in all cases, but in two patients a narrow shunt lumen and poor contribution to the filling of the brain arteries was noted. In the remaining patients patency was assessed and confirmed by the palpation of a pulsating vessel at the border of the craniotomy. The neurosurgeon operating all patients in the present series has previously reported a patency rate of 95%. Antiplatelet and anticoagulant therapy was left unchanged postoperatively.

**Recurrence of Ischemic Symptoms**

In the observation period of 3 to 27 months (mean 12 months), only one patient suffered recurrence of symptoms of cerebral ischemia: Case BSP suffered two, presumably embolic, TIAs from the hemisphere of interest. In this patient the CBF measurement at the 3-months follow-up showed a focal improvement in CBF, and angiography showed a patent and well-functioning shunt.

**CBF Results Early After Shunting**

Fourteen patients were studied in the early postoperative period, 4 to 12 days (average 8 days) after surgery. Of the two patients who showed an increased CBF after 3 months only one showed a diminished side-to-side asymmetry at the early postoperative measurement after 8 days, and further improvement was seen at the 3 months follow-up. In the remaining 12 patients, the early postoperative CBF maps were essentially as the 3 months follow-up studies. No evident hyperemias or new ischemias were observed on the early pictures.

**CBF Results Later After Shunting**

In table 2, the time course of side-to-side asymmetry in the ROI is presented, and table 3 shows the averaged CBF value in the ROI for all pre- and postoperative studies. Based on the statistical analysis of changes in side-to-side asymmetry in the ROI, i.e. on the ΔD values, and on visual inspection, the patients were grouped in 3 categories according to the changes following surgery: Improved, questionably improved, and not improved.

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The D-values are calculated as the difference between the ROI and the symmetrical region taken as a percent of the value in the symmetrical region (healthy hemisphere).

**Patients with improved regional CBF (2)**

Two patients (cases 1 and 2) showed a significantly diminished side-to-side asymmetry, as evaluated from both statistical analysis and visual inspection.

**Case BSP**

This 35-year-old woman had suffered a severe stroke with left-sided hemiparesis. Two years later, the patient had several TIAs with pins and needles of the right side of her face and right arm, and two episodes of minutes lasting right-sided hemiparesis. Angiography showed normal neck vessels but bilateral occlusions of the anterior and middle cerebral arteries. CT scan showed a large infarct in the right parieto-occipital region but no lesion in the left hemisphere (fig. 1c). The CBF map (fig. 1a) showed low flow in the territories of both the anterior and the left middle cerebral arteries. In addition, low flow was seen corresponding to the infarcted area on the CT scan. Two months after a left-sided EC-IC bypass, she suffered two short lasting presumably embolic TIAs with right-sided paresthesias. However, a marked improvement in CBF was noted in the focal low-flow area in the left hemisphere one month later. A flow increase was also seen in the frontal region of the contralateral hemisphere (fig. 1b). This was the only patient, who postoperatively showed a normal flow map in the hemisphere shunted.

**Case LW**

This 55-year-old woman had suffered a minor stroke with a right-sided slight hemiparesis combined with slight aphasia, from which she practically recovered. Six months later she noted almost daily attacks of weakness of her right arm and of aphasia lasting for a few minutes. The symptoms occurred in particular during the morning in relation to postural changes. Angiography showed an occluded left internal carotid artery and a moderate stenosis of the right internal carotid artery (3 mm in diameter at the narrowest point). CT scan showed a small deepseated infarct in the left hemisphere (fig. 2c). The CBF map showed low flow in the regions of both anterior cerebral arteries, and in the territory of the left middle cerebral
 Patients with no improvement in regional CBF at rest (18 cases)

After surgery 18 patients showed a completely unchanged flow map at rest, as judged both from calculations of changes in side-to-side asymmetry and from visual inspection.

Case IS

This 55-year-old man suffered a moderate stroke with almost complete remission over 3 days. Angiography showed occlusion of the right internal carotid artery as well as of the right vertebral artery. CT scan showed a deepseated subcortical infarct in the right hemisphere (fig. 3c). CBF measurement showed a low flow in the region of the right middle cerebral artery in both slice 2 and 3 (fig. 3a), clearly exceeding in size the hypodense area on the CT scan. Three months following a right-sided EC-IC bypass, angiography showed a well-functioning anastomosis. However, the CBF study showed no changes in the flow distribution, i.e. the degree of side-to-side asymmetry persisted unchanged (fig. 3b), and the focal low flow areas persisted in the CT negative regions.

Discussion

In the present study, patients with ischemic cerebrovascular diseases were primarily considered for EC-IC bypass surgery on the clinical and angiographical criteria now generally agreed on for this surgical procedure, i.e. minor stroke and/or TIA combined with severely obstructive lesions of the cerebral arteries inaccessible to neck vessel surgery. In such patients, measurements of CBF and CT scans were undertaken, and the finding of focal low-flow, CT negative areas were used as final criterion for selection of candidates. To our surprise, 18 of the 22 patients showed a completely unchanged tomographic picture with persistent low flow in the shunted area. Shunt patency was verified by angiography in about half of these cases and could be surmised in the remainder.

This finding of a persisting hypoperfusion in areas without a CT lesion may either indicate a state of neuronal inactivity “diaschisis” or an ischemic tissue lesion “incomplete infarction”, also called “diffuse selective neuronal cell loss”. The neuropathology underlying the phenomenon of diaschisis has not yet been clarified, but it has been suggested, that diaschisis may result from deactivation due to interruption of activating afferent pathways. Diaschisis has been described in patients with ischemic cerebral infarction, where a reduction in CBF was observed in the contralateral cerebral or cerebellar hemisphere. However, in our present series of EC-IC bypass cases, one patient (KH) who only suffered TIAs had a persistent low flow following shunting and a normal CT scan. Although the CT scan might not have detected a lacunar infarct, undercutting of afferent fibers is not likely to be the reason for the low flow in this patient. Furthermore, in our previous study of TIA patients involving reconstructive surgery of the carotid artery, similar CT-normal/CBF-positive cases were seen that were un-

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ΔC denotes the improvement in asymmetry. End-expiratory CO₂ (FeCO₂) is also indicated. In patients with 2 preoperative and 2 postoperative CBF measurements, a change in ΔC of 7.9 or 6.5 is needed to reach statistical significant values of p < 0.05 and p < 0.10, respectively. The corresponding values for patients with 2 preoperative and 1 postoperative CBF measurement are 9.7 and 7.9, respectively.

artery (fig. 2a). On the assumption that the stenosing lesion of the contralateral internal carotid artery might have a hemodynamic significance, a right-sided carotid endarterectomy was first performed. However, the clinical symptoms (TIAs) did not subside, and CBF measurement 2½ months later was unchanged. A left EC-IC bypass was then performed after which the patient was free of TIAs.

CBF measurements 3 and 6 months after the bypass showed an improvement of CBF in the territories of the left anterior and middle cerebral arteries. This patient also showed an improvement in the frontal lobe of the right hemisphere, viz. on the side contralateral to the shunt (fig. 2b).

Patients with questionable improvement in regional CBF (2 cases)

Two patients (cases CR and NS) were included in this group. Both the statistical analysis and repeated visual inspections of the flow map indicated a minor increase of CBF in the ROI following the surgical procedure.

For Each Patient, the Average Value of CBF in the ROI for all Pre- and Postoperative CBF Measurements are Shown, both in Absolute Values (ml/100 g/min) and as Degree of Side-to-side Asymmetry.

In patients with 2 preoperative and 2 postoperative CBF measurements, a change in FeCO₂ of 7.9, respectively. The corresponding values for patients with 2 preoperative and 1 postoperative CBF measurement are 9.7 and 7.9, respectively.

Two patients (cases CR and NS) were included in our previous study of TIA patients involving reconstructive surgery of the carotid artery, similar CT-normal/CBF-positive cases were seen that were un-
changed by effective revascularization. Moreover, in most of the patients with a CT lesion, the anatomical localization of the infarcts could hardly alone explain the tomographically seen remote low flow area as undercutting of neuronal pathways.

Neuropathologic studies in man have demonstrated, that a selective neuronal cell loss, evident by a reduction in the neuronal density accompanied by microglia proliferation and slight reactive astrocytosis may occur in patients following a diffuse hypoxic insult. Also, these changes have been observed in regions surrounding areas of complete infarction. Experimental studies have documented an association between a low flow and a selective neuronal tissue damage. In a study on Macaque monkeys, temporary occlusion of the middle cerebral artery (MCA) was performed for a time interval ranging from 15 minutes to 3 hours. CBF was measured by implanted electrodes using the hydrogen clearance method prior to, during, and after the MCA occlusion. The findings were correlated to the neuropathological findings obtained 2 to 4 weeks after MCA occlusion. Incomplete selective tissue necrosis in the grey matter was observed in 13 of 19 animals. The study of Mies et al using a stroke model with MCA occlusion in the cat showed similarly regions of complete infarction surrounded by areas of low flow 8 weeks after infarction. Although the macroscopic inspection showed sharply demarcated infarcts, the microscopic examination revealed gradually decreasing

**Figure 1.** Preoperative tomogram of case BSP (slice 2) showed a low flow in the anterior part of both the left and the right hemisphere (1a). In addition, a low flow was seen in the posterior part of the right hemisphere, where CT scan showed a hypodense lesion (1c). Postoperatively, improvement of CBF was seen anteriorly in both hemispheres, and the flow distribution was normal in the left hemisphere (1b). The low flow area corresponding to the CT lesion in the posterior part of the right hemisphere persisted. The reference region of interest was chosen in the occipito-temporal region in the left hemisphere. The pictures are scaled according to the mean flow value obtained in this region and displayed from 4-164.
neuronal density on approaching the peri-infarct zone. A significant linear correlation was found between the decrease in neuronal density and the changes in CBF, measured by 14C-iodo-antipyrine autoradiography. In this study, low flow areas were also seen in some regions without structural changes, findings that were interpreted as functional inactivation.

In the light of our own observations and the studies mentioned, we propose that the lack of increase in a regional low CBF after revascularization is due to diaschisis and/or selective ischemic neuronal loss, lesions that are invisible on CT scan. Both lesions decrease regional metabolic demand and consequently cause a reduction of regional CBF which is unaltered by a successful shunt operation?

How to Identify Hemodynamic Cases?
It is implicit from the above discussion, that most of our patients had no evidence of a persisting hemodynamic impediment that could explain the low-flow CT-negative areas. Apparently collateral flow sufficed to supply a flow matching local metabolism. Thus, despite shunting no change in tissue flow occurred. In essence, all these cases had suffered a prior acute cerebrovascular disease, a stroke, plus in some cases TIAs caused by embolic events.

But our series, as that of most other surgically treated cerebrovascular-disease series, included a few hemodynamic cases, viz. patients in whom a chronic
hemodynamic impediment and poor collaterals coexist. Although it must be admitted, that the clinical efficacy of EC-IC shunting is still undocumented, and awaiting the results from the ongoing multicentre study, most investigators agree that hemodynamic cases represent a very important subset in whom a clinical benefit could be expected. In the following various approaches to identify such cases will be discussed.

In some patients a significant hemodynamic impediment may be diagnosed on clinical grounds alone, i.e. by TIAs occurring in relation to positional changes. In our study only one patient (case LW) suffered such symptoms. There are good reasons to suspect, however, that more cases should be classified as hemodynamic. First of all the anamnestic information is imprecise. Second, one may readily conceive of a marginally perfused brain area in which ischemia does not elicit overt symptoms that can be identified as a TIA. And, thirdly, even if a very significant hemodynamic impediment exists it could well be that no systemic hypotension has yet supervened to elicit an attack of frank ischemia with acute symptoms and with cell death permanently harming the patient. Antihypertensive treatment may here in particular be invoked as a provoking factor.

To identify the subset of patients with an impaired collateral capacity, Norrving and colleagues studied CBF and CO2-vasoreactivity with 133Xenon-inhalation and stationary equipment in patients with unilateral occlusion of the internal carotid artery. They observed a reduced CO2 response only in the patients with an
impaired collateral capacity as judged from the angiographic findings. In a similar way Halsey et al studied CBF in a series of 19 patients before and after EC-IC bypass. They concluded, that this operation did not affect the resting flow level but did augment the collateral reserve in patients where it has been most severely impaired by the arterial lesions preoperatively. The significance of a compromised collateral circulation was further evaluated by Spetzler et al. In 71 patients treated with an EC-IC bypass for symptomatic cerebrovascular occlusive disease, a definite correlation was established between the severity of the angiographically demonstrated vascular lesions and lower middle cerebral artery perfusion pressures.

Cerebral vasoreactivity may also be tested using acetazolamide (Diamox), which increase CBF by an effect similar to breathing air with an increased CO₂-content. Intravenous administration of the drug causes no discomfort, and furthermore, neither hyperventilation nor blood pressure changes are induced. We have previously reported on a case, where the hemodynamic significance of the arteriosclerotic lesions were disclosed by testing with Diamox. In this patient, with a thread-like internal carotid artery, CBF did not increase in the low flow area already present in the resting state in CT negative regions. Further validation of the Diamox test is ongoing, as studies on the cerebrovascular disease. In this case an EC-IC bypass was able to abolish the clinical symptoms and oxygen utilization in superficial middle cerebral artery anastomosis patients. An exploratory definition of clinical problems. Neurosurgery 3: 79–86, 1978

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SYNCOPE has been described as a relatively common, potentially dangerous problem that often remains unexplained despite extensive clinical evaluation. The possibility that syncope might at times represent an isolated manifestation of cerebrovascular disease has been raised. A recent one year prospective study of patients with syncope revealed a high overall mortality. An excess of sudden death was found among sub-
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The excess mortality was found in patients with evidence of underlying cardiovascular or life-threatening non-cardiovascular illnesses. There was no evidence

SUMMARY To obtain epidemiologic information regarding syncope, 2336 men and 2873 women aged 30 to 62 years at entry to the study were evaluated for syncope. During 26 years of surveillance, evidence of cardiac or neurologic morbidity and mortality was also recorded. At least one syncopal episode was

Epidemiologic Features of Isolated Syncope: The Framingham Study

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SYNCOPE has been described as a relatively common, potentially dangerous problem that often remains unexplained despite extensive clinical evaluation. The possibility that syncope might at times represent an isolated manifestation of cerebrovascular disease has been raised. A recent one year prospective study of patients with syncope revealed a high overall mortality. An excess of sudden death was found among subjects with syncope with mortality rates ranging from 3 to 24% in one year depending on patient subgroup. The excess mortality was found in patients with evidence of underlying cardiovascular or life-threatening non-cardiovascular illnesses. There was no evidence

From the Framingham Study, The National Heart, Lung and Blood Institute,* the Evans Memorial Department of Clinical Research and Department of Medicine, University Hospital, Boston University School of Medicine, the Section of Preventive Medicine and Epidemiology, and the Department of Neurology.‡

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