Five-year neurological and EEG outcome after open-heart surgery

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SUMMARY A five-year neurological and EEG follow-up was carried out on 55 patients who had undergone open-heart surgery for valve replacement in order to investigate the long-term results of the treatment. The five-year survival rate was 89%. The prevalence of permanent neurological abnormalities after operation was 9%. Transient ischaemic attacks occurred in five patients but no more severe cerebrovascular accidents were encountered. The rate of embolic events was 2.8 per 100 patient-years. Various subjective symptoms and complaints showed a highly beneficial outcome. Also the five-year EEG outcome was encouraging; the prevalence of abnormal EEG had fallen from the value before operation of 45% to 25%. The harmful influence of long perfusion time (extracorporeal circulation) during operation was found to be reflected in the long-term EEG outcome and, significantly, not only in the patients who had, but also in those who had not developed clinical abnormalities complicating the immediate course after operation. Although a valvular surgery patient faces a number of CNS problems before, during and after operation, the overall long-term outcome of successful surgery seems highly beneficial in neurological terms.

The vast literature devoted to the central nervous system (CNS) effects of open-heart surgery has emphasised the multiplicity of potentially harmful factors to which patients are exposed before¹⁻³ and during⁴ the operation. In particular, the risks of CNS dysfunction during the operation, mostly related to extracorporeal circulation, have been thoroughly scrutinised⁶⁻¹⁴ and due to the attention paid to them they have diminished strikingly.^{4, 5, 15, 16} However, cardiac surgery patients face many problems even after the correction of the major circulatory disturbance; for example they are exposed both to embolisation from the artificial valve and to the side-effects of the life-long anticoagulant therapy¹⁷⁻²¹ required with most of the types of prostheses. Thus far, neurological studies in open-heart surgery patients have been limited to describing the immediate results after operation while the later outcome has been passed over. Indeed, because most of the occasional clinical complications have been mild and reversible, investigators seem to have

been content with observing events during the critical early phase after surgery. The resultant lack of knowledge concerning the long-term course is not limited just to the clinical aspects but also includes any subclinical features of CNS abnormality. Now the major clinical problems seem to be in the process of being solved and, as investigatory methods are developed even further, the subclinical level events are being given increasing attention. Thus, 24 neuropathological,¹⁴ neuroradiological,²⁵ biochemical^{26, 27} and electroencephalographical (EEG)^{10, 28-32} measures have indeed revealed post-operative CNS dysfunction even in the absence of clinical manifestations. Since the information available on the long-term neurological outcome after surgery is limited to a few brief statements in surgical reports,¹⁷⁻²⁰ the present study was carried out. It is a continuation of a previous series of investigations dealing with pre- and postoperative clinical³³ and EEG^{31, 32} aspects of cardiac surgery up to the first year after surgery. The follow-up period now has been extended to 5 years.

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Patients and methods

Of the 65 consecutive patients who had undergone valvular replacement surgery and clinical and EEG investiga-

Table 1 Subjective symptoms, case histories and vocational status before and after operation.

	During the last year before operation No of pat.	During the first postoperative year No of pat.	During the 5th postoperative year No of pat.	
Headache				
Migraena	8	5	3	
Other forms	8	8	3	
Vertigo	9	6	3	
Syncope	6	0	0	
Epileptic attacks	1	2	1	
Sleep disturbances	3	3	1	
Neurovegetative symptoms	2	3	1	
				During the whole postoperative 5-year period
				All
TIA	4*	1	5	4
Stroke	4*	0	0	0
Complications of anticoagulant treatment‡	0	0	2	2
Able to work	34	29	27	—
Sick-leave	19	23	23	—
Retired (age)	2	3	5	—

*includes all the occurrences before operation

†No of patients with no preoperative history

‡intestinal bleeding

tions before and after operation,^{31 55} were available for re-evaluation 5 years post-operatively. Five patients had died during the first year after operation (three operative and two late deaths), and two further patients had died later of cardiac causes. There were three additional patients who did not wish to participate in the study because they had moved far away but they gave a written description of their subjective outcome, reporting good health and no neurological problems, and this information agreed with the reports given by their doctors. The case mortality rate was 8% for the first postoperative year and 3% for the following 4 years, the 5-year survival rate thus being 89%.

The timing of investigations ranged from 4 years 6 months to 5 years 9 months (mean 5.1 ± 0.3 years). There were 49 men and 16 women whose ages ranged from 21 to 71 (mean 46 ± 10) years. Aortic valve replacement had been performed in 40 patients, mitral valve replacement in 10 and both of the valves in five. The Björk-Shiley tilting disc prosthesis had been used in all the operations. The details of the pre-, intra- and postoperative care and arrangements have been presented previously.^{31 32 33} All the patients had a complete clinical neurological investigation performed by the author. The EEG recordings were performed using a 16-channel machine and standard conditions and four different electrode montages. The EEG recording time was at least 30 minutes. The EEG evaluation was performed using conventional methods, and using the same grading system as described in our previous reports.^{31 32}

All the patients had been under regular cardiological surveillance and their optimal medication had been carefully adjusted. All had continuous anticoagulant (warfarin) therapy, the effect of which had been regularly controlled. The cardiological outcome had been assessed as optimal or highly satisfactory in all except one patient who had developed intractable cardiac failure unrelated to the pros-

thesis. One further patient suffered from a declining general condition due to advanced gynaecological malignancy.

The patients were grouped according to their clinical outcome 10 days after operation: NC group (no clinical signs of CNS dysfunction) and CC group (clinical complications present).³³

Results

Table 1 presents the course of the reported subjective symptoms and complaints. There was a distinct decrease in headache and vertigo. None had had syncopal attacks after operation in contrast to six cases preoperatively. Five patients had developed transient ischaemic attacks (TIA) (three carotid, two vertebrobasilar); only one of these five patients had had TIA before operation. Angiography of the precerebral vessels which was performed in the three patients with carotid symptoms (the remaining two patients refraining from the examination) showed normal findings. None of the 55 patients had developed stroke or suffered from other kinds of more severe cerebrovascular accidents (CVA).

Clinical findings Table 2 shows the clinical neurological findings. One of the five patients who had residual abnormalities related to a CVA before operation had recovered, while the preoperatively present disturbances remained unaltered in the others. The two patients who had shown motor residual signs of operative complications one year after surgery, still displayed these signs at 5 years. One additional patient who had had aphasia complicating the operation had recovered completely. Two further patients who had developed slight

Table 2 Clinical findings

	Before operation No of pat.	1 year after operation No of pat.	5 years after operation No of pat.
Preoperatively present signs related to preop. CVAs	5*	3	3
other causes	6†	6	6
Residual signs of disorders developed intraoperatively			
motor	—	2	2
cognitive	—	2	1
peripheral	—	2	0
Renewed signs (appeared during operation, recovered within the first year)	—	—	2
New signs (developed after the first postop. year)	—	—	1‡

*one operative death included

†anisocoria 2, partial oculomotor palsy 1, essential tremor 1 and femoral neuropathy 2

‡polyneuropathy in a patient who had sustained a gynaecological malignancy (treated with radiotherapy and chemotherapy)

Table 3 General EEG normality grade before and 5 years after operation.

		Before operation N	%	5 years after operation N	%
All patients N = 55	Normal EEG	30	55	41	75
	Abnormal EEG	25	45	14	25
	R abnormal only	2	3	0	0
	L abnormal only	8	15	4	7
NC patients N = 30	both hemisph. abn.	15	27	10	48
	Normal EEG	17	57	24	80
	Abnormal EEG	13	43	6	20
	R abnormal only	2	7	0	0
CC patients N = 25	L abnormal only	4	13	2	7
	both hemisph. abn.	7	23	4	13
	Normal EEG	13	52	17	68
	Abnormal EEG	12	48	8	32
	R abnormal only	0	0	0	0
	L abnormal only	4	16	2	8
	both hemisph. abn.	8	27	6	24

R = right hemisphere

L = left hemisphere

Fig 1 Follow-up of the prevalence of abnormal EEG in the patient groups with (CC) and without (NC) neurological complications present 10 days after operation.

brachial plexus injury at operation and who had had residual signs at one year were now found completely normal. There were two patients who showed renewed signs, that is signs similar to those which had appeared at operation but which had disappeared within the first postoperative months.

EEG results

General EEG evaluation Table 3 gives the general normality grade of the EEG. The preoperative prevalence of abnormal EEG was 45%, which contrasts with 25% 5 years after operation. The left hemisphere dominated in the appearance of abnormalities both before and after operation. The proportion of bilaterally abnormal EEGs showed a slight increase, comprising 60% of the preoperative and 71% of the 5-year postoperative abnormal EEGs;

Table 4 Mode of EEG change from the preoperative state to 5 years after operation in the cardiological groups.

	Prevalence of abnormal EEG in %		The nature of the 5-year postoperative EEG when compared with the preoperative EEG					
	Before operation	5 years after operation	improved		impaired		unchanged	
			N	%	N	%	N	%
All (N 55)	45	25	18	33	4	7	33	60
Aortic (N 40)	48	22	10	25	2	5	28	70
Mitral (N 10)	70	30	6	60	3	30	1	10
Aortic + mitral (N 5)	80	40	2	40	0	0	3	60

improved/impaired: change from abnormal to normal or vice versa

this increase was due to the relatively more frequent recovery of unilateral disturbances.

The follow-up of the prevalence of abnormal EEG in the NC and CC groups is shown in fig 1. Corresponding to the clinical differences, the groups also displayed EEG differences after operation, the CC group experiencing EEG deterioration more often and slower recovery than the NC group. At 5 years, the CC group had a trend towards renewed impairment in contrast to continuing in the NC group. In all, 18 patients (33%) had EEG improvement during the 5 postoperative years while four patients (7%) had deterioration, the remaining 33 patients (60%) remaining unaltered (table 4). The respective numbers for the first year after operation had been 20, 0 and 35.

Nature of EEG abnormalities Figure 2 shows the nature of the main EEG abnormality. Theta range disturbances, which were usually episodic and appeared in the temporal regions in the great majority of cases, were the most common abnormalities both before and after operation. Slow wave abnormalities were found preoperatively and immediately

after operation but not thereafter. Instead, sharp wave disturbances appeared at 5 years in three patients, all of whom had a clinical complication of the same hemisphere as the late EEG abnormality. **Perfusion time and EEG outcome** The patients were divided into a short (<2 h; number of patients 25) and a long (>2 h; number of patients 30) perfusion time group. The prevalence of abnormal EEG fell from the preoperative value of 40% to 20% at 5 years in the short perfusion time group, in contrast to a less marked improvement from 50% in the long perfusion time group. Within the NC group, the prevalence of abnormal EEG fell from 39% to 11% in those patients whose perfusion time had been short while the change was only from 50% to 30% in those who had had a long perfusion.

Other EEG findings Age, sex, degree of valvular calcification, presence or absence of syncope or atrial fibrillation, occurrence of pre- or postoperative TIA, and the presence of residual signs related to operative complications had no detectable effect on the EEG course. Instead, differences were found between the valvular groups. During the first postoperative year, the aortic patients had a more marked EEG improvement than the mitral and multiple valvular groups.³² Thereafter, the mitral group still continued with improvement and at 5 years the proportion of the improved EEGs when compared with the preoperative state was the greatest in the mitral group (table 4).

Discussion

The observed 5-year survival of 89% (the operative and late deaths are included) compares favourably with previous studies. Ross *et al*³⁴ reported a 73% 4-year survival; Björk and Henze¹⁷ an 82% survival for 5 years in aortic, 66% in mitral and 66% in aortic + mitral replacement patients; and Lewang²⁰ reported an 86% survival rate for 7 years in aortic replacements. Thus it is concluded that our patients and the surgical and cardiological results did not differ from those in other series, despite the

Fig 2 Nature of the main EEG abnormality before and after operation.

relatively high prevalence of CNS disorders after operation in the present series.^{31,32} The importance of taking account of even the slightest degree of clinical disturbance³⁵ is emphasised. Apart from the complications related to anticoagulant medication (table 1), treatment seemed to bring improvement in all aspects other than in the occurrence of TIA (table 1.). Serious bleeding did not occur in contrast to the 6.3 cases per 100 patient years reported previously.¹⁷ The occurrence of TIAs even exceeded the TIA prevalence observed before operation despite the continuous anticoagulant treatment. Angiography of the extracerebral vessels did not reveal any lesion in those three patients with carotid TIAs who were investigated, and the remaining two patients displayed no cervical bruits. The most probable reason was the artificial valve, as has become apparent from surgical reports.¹⁷ All the TIA patients were given additional medication with dipyridamole (75 mg tid). All of them have now been followed for over two additional years during which none has developed recurrent TIAs. This gives additional support to the reported³⁶ usefulness of a combination of warfarin and dipyridamole in preventing embolism associated with prosthetic heart valves. In all, the number of embolic episodes was 2.8/100 patient-years which is in agreement with previous studies reporting rates of 2.4 episodes/100 patient-years³⁷ with anticoagulants, and contrasts with the rates of 22.8³⁷ and 8.7²¹ per 100 patient-years with acetylsalicylic acid + dipyridamole regimen.

Although the treatment of the prolonged cardiac disease improved many aspects of life, its effect on the vocational status was slight (table 1). In agreement with previous studies^{34,38} return to work usually occurred in the first postoperative year. Neurological disturbances induced at operation contributed markedly to incapacity to work in two patients: one patient had cognitive disorders, the other patient did not recover from motor disturbances.

In previous reports^{8,31,39,40} some preoperative factors with predictive importance have been recognised. For the present long-term results, however, only the preoperative occurrence of CVAs was found significant. Four of the five patients who had residual or renewed signs of 5 years' investigation (table 2) had a history of CVA which had occurred 1-4 years before operation. What is important is that all these patients had sustained their CVA during the period when the operative treatment was being considered, but postponed because the cardiological condition had not yet advanced to the point where the operation was thought necessary. This not only emphasises the importance of careful

preoperative assessment but also indicates that more attention should be paid to the evaluation of the CNS instead of considering the heart alone.

The importance of preoperative measures may also be reflected in the EEG course of the patients. The mitral patients seemed to gain greatest postoperative EEG benefit later than the aortic patients. This might be attributed to the well-known later timing of operation in the mitral patients. This agrees with the observed differences in the course of the neuropsychological outcomes between the mitral and aortic patients.²³ Thus it seems that operative treatment of valvular disease should not be postponed in patients who display coexistent factors indicating potential risks for CNS dysfunction, unless critical overriding arguments indicate the advantages of a delay.

Besides certain preoperative factors, the duration of perfusion is one of the major determinants of CNS outcome.^{4,5,8,9,23,27,30-33} The harmful effect of long perfusion time was evident also in the long-term EEG outcome; the EEG difference between the short and long perfusion time groups was accentuated with advancing follow-up time. Significantly, the influence of perfusion time was also seen in the clinically non-affected patients and not solely in the patients who had sustained clinical complications at operation. This discloses the cumulative nature of the harmful factors effective during extracorporeal circulation and underlines the need for protecting the CNS from prolonged perfusion, the effects of which may have much widespread and long-term consequences than we have supposed so far.

The correspondence between the clinical and EEG course established immediately after operation remained also in the later course (fig 1, table 3). Impairment of the EEG when comparing the 5-year result with the preoperative EEG was observed in four patients, three of whom were CC cases and the remaining one NC patient appeared to be the only patient who suffered a deteriorating cardiac dysfunction. The recovery of the EEG abnormalities which appeared after operation (figs 1 and 2) reflects the mostly reversible nature of the intraoperative changes. What is most encouraging is that improvement of the basic preoperative abnormalities provides evidence that the treatment has indeed improved the cerebral circulatory and metabolic conditions.

To conclude, the postoperative process of recovery from the strains of operation and, particularly, from the prolonged circulatory disturbance, seems to be a much longer process than has been supposed thus far. Therefore, operative treatment of valvular disease should not be postponed unnecessarily. The intraoperative conditions seem to have long-term

effects on the CNS, despite the major technical advances which have been made. Furthermore, if both optimal outcome and greater safety are desired, then consideration of the cardiologic condition of the patient alone is not sufficient: closer attention must be paid to the evaluation of the CNS.

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