Neurocognitive deficit following mitral valve surgery

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Abstract

Objective: Neurocognitive deficit is an important complication in patients undergoing open heart surgery. The aim of this prospective, contemporary study was to objectively measure neurocognitive brain function following mechanical mitral valve replacement and mitral valve repair. Methods: Forty consecutive, unselected patients (mechanical valve replacement \( n = 20 \), mean age 65 ± 14; valve repair \( n = 20 \), mean age 64 ± 7, \( P = 0.896 \)) entered this prospective, contemporary study. Neurocognitive function was objectively measured by means of P300 auditory evoked potentials (peak latencies, ms) and two standard psychometric tests (Mini Mental State Examination, Trailmaking Test A (TTA)), preoperatively, 7 days and 4 months postoperatively. Results: Before operation, neurocognitive brain function was comparable in both patients groups (mechanical valve replacement versus valve repair: P300 potentials 374 ± 25 versus 378 ± 46 ms; \( P = 0.791 \) and TTA 57 ± 15 versus 54 ± 10 s; \( P = 0.552 \)). Following mechanical valve replacement, neurocognitive function continuously worsened (7 day-follow-up: P300 potentials 392 ± 28, \( P = 0.001 \) versus preop and TTA 65 ± 17, \( P = 0.0001 \); 4-month follow-up: P300 potentials 406 ± 39, \( P = 0.0004 \); TTA 69 ± 17, \( P = 0.0001 \)). Interestingly, neurocognitive brain function was unaffected in patients undergoing valve repair (7-day follow-up: P300 potentials 386 ± 40, \( P = 0.890 \) versus preop and TTA: 53 ± 10, \( P = 0.644 \); 4-month follow-up: P300 potentials 374 ± 36, \( P = 0.166 \) and TTA 54 ± 11, \( P = 0.147 \)). At 4-month follow-up, patients with mechanical prostheses performed worse as compared to valve repair (P300 potentials: \( P = 0.024 \); TTA \( P = 0.014 \)). Conclusion: As shown by P300 auditory evoked potentials and Trailmaking Test A, there is marked neurocognitive damage related to mechanical valve replacement, whereas mitral valve repair does not affect neurocognitive function. This finding supports the beneficial effect of mitral valve repair over mechanical valve replacement in the decision-making tree of borderline cases, which are suitable for both types of procedure.

Keywords: Neurocognitive function; Mitral valve surgery; Mechanical valves; Reconstruction

1. Introduction

Neurocognitive deficit after open heart surgery with cardiopulmonary bypass (CPB) is intensively discussed to have tremendous social and economical impact. It is accused to affect quality-of-life and to prolong in-hospital stay as well as to increase use of resources [1,2]. Despite technical improvement of CPB circuits – resulting in less systemic activation and consecutively less systemic inflammatory response – neurocognitive deficit is described to appear in 30–80% of patients undergoing open heart surgery with CPB [2–5].

From the beginnings in the 1970s with the introduction of annuloplasty rings by Carpentier et al. and Duran and Obago, mitral valve repair today accounts for 75% of mitral valve surgeries [6]. When considering the major series, despite its greater technical complexity, mitral valve repair is associated with a lower surgical mortality rate than prosthetic mitral valve replacement, provides better survival rates, better postoperative left ventricular function (as a result of preserved subvalvular apparatus) and lower rate of reoperations [6,7]. By performing mitral valve repair, prosthesis related problems such as thromboembolic events, endocarditis, structural valve failure and paraprosthetic leakage can be avoided.

For measurement of neurocognitive dysfunction we used a previously described diagnostic tool, consisting of two standard neuropsychometric tests (TTA and Mini Mental State Examination) and objective P300 auditory evoked potential measurement [8–11]. Evoked potential measurements detected by cortical leads, representing stable
sequences of negative and positive electroencephalogram peaks within a period of several hundred milliseconds, are a highly sensitive and reproducible tool for evaluation of cognitive and neuronal brain dysfunction caused by various disorders, such as cerebrovascular disease, metabolic disorders (kidney, liver failure, diabetes) and surgical trauma [12–15]. Cognitive P300 auditory evoked potentials, elicited by a tone discrimination paradigm, are objective measures related to information and cognitive processing, which, therefore allow a quantification of cognitive brain dysfunction [15]. P300 measures were shown to be much more sensitive in detecting metabolically induced brain dysfunction than psychometric tests or electroencephalograms [12,16]. Furthermore, the low coefficient of intra-individual test-retest variation of below 2% in cognitive P300 auditory evoked potential measurement, which is of particular importance in follow-up assessments, demonstrates its usefulness in patients following cardiac surgery [8,9,12].

The aim of this prospective, contemporary study was to objectively measure neurocognitive brain function following mechanical mitral valve replacement and mitral valve repair.

2. Materials and methods

2.1. Patients

After approval was obtained by the Ethics Committee of the University of Vienna 20 consecutive patients undergoing mechanical mitral valve replacement with a mechanical prosthesis (mean age 65 ± 14 years) and 20 consecutive patients, undergoing mitral valve repair (mean age 64 ± 7), were enrolled in this prospective study. Exclusion criteria were: (1) a hemodynamically relevant carotid artery stenosis (of more than 75%) and a history of one of the following medical conditions; (2) prior stroke with residual deficit; (3) uncontrolled hypertension; (4) psychiatric illness requiring treatment; (5) alcoholism; (6) renal disease (defined as a creatinine more than 2.0 mg/dL); (7) active liver disease; or (8) presence of significant aortic sclerosis in routinely performed intraoperative TEE. Narcotics for pain relieve were restricted to the time of chest tube drainage. Chest tubes were removed on postoperative day 2. All investigations were performed by the same investigator who was blinded to the group classification (single blind, prospective design).

2.2. Preoperative risk stratification

Preoperative risk stratification was performed using the EuroSCORE. EuroSCORE stands for European System for Cardiac Operative Risk Evaluation. The EuroSCORE is a risk stratification system to help in the assessment of quality of cardiac surgical care. The score consists of Patient-, Cardiac- and Operation-related factors [17].

2.3. Neuropsychological testing

Neuropsychological testing and physical examinations were completed preoperatively, 7 days and 4 months after surgery, respectively. All examinations were performed by the same investigator who was blinded to the group classification of each patient. Neuropsychological testing consisted of P300 auditory evoked potentials, Mini Mental State Examination and TTA. To avoid any influences due to biorhythm, all investigations were performed in the afternoon under comparable conditions.

2.4. Auditory P300 evoked potentials

Cognitive P300 auditory evoked potentials were recorded with Ag/AgCl electrodes on a ‘Nicolet 2000’ (Nicolet, Madison, WI). P300 evoked potentials were generated following a binaurally presented tone discrimination paradigm (odd-ball paradigm) with frequent (80%) tones of 1000 Hz and rare (20%) target-tones of 2000 Hz at 75 dB HL. Filter bandpass was 0.01–30 Hz. Active electrodes were placed at Cz (vertex) and Fz (frontal), respectively, and referenced to linked earlobe A12 electrodes (10/20 international system). During the paradigm, the subjects were instructed to keep a running mental count of the rare 2000 Hz target tones. To verify attention, P300 recordings with a discrepancy of >10% between the actual number of stimuli and the number counted by the subjects were rejected and repeated. P300 evoked potential recording resulted in a stable sequence of positive and negative peaks. Latencies (ms) of the cognitive P300 peak were assessed. To confirm reproducibility, two sets of P300 measurements were recorded in all patients. Special care was taken that studied patients were free from narcotics or sedatives for at least 48 h.

2.5. Psychometric tests

Immediately after P300 recording, the standard psychometric tests TTA and Mini Mental State Examination were performed to test cognitive impairment and psychometric performance. To minimize learning effects, five different Trailmaking Tables were randomly used. The Trailmaking Test (part A) requires subjects to connect, by drawing a line, a series of numbers and letters in sequence (i.e. 1-2-3) as quickly as possible [18]. The Mini Mental State Examination is a widely used method for assessing cognitive mental status. It assesses orientation, attention, immediate and short-term recall, language, and the ability to follow simple verbal and written commands. Furthermore, it provides a total score that places the individual on a scale of cognitive function [19].

2.6. Follow-up

In addition to the neuropsychological testing, patients were studied by means of echocardiography, ECG, blood tests and clinical investigation at all points of follow-up.
Special attention was paid to the incidence and development of atrial fibrillation Table 3. Echocardiography was used to assess functional state of heart valves and to assure that all patients were free of LV-thrombus during the period of follow-up.

2.7. Surgical procedure

All patients underwent mildly hypothermic CPB (35°C) with intermittent cold blood cardioplegia with a hot shot before opening the cross clamp. The CPB circuit consisted of a hollow-fiber oxygenator (Bard HF 5701, C.R. Bard Inc, Havorhill, MA) and a lining system primed with ringer lactate, mannitol, heparine and apoproteine. Flow during CPB was maintained at 2.5 l/min per m². Blood cardioplegia was maintained at 4:1 ratio. Hematocrit was kept above 20% with packed red blood cells if necessary. Perfusion pressure during CPB was kept above 50 mmHg with phenylephrine if necessary. In all patients undergoing mechanical mitral valve replacement the posterior leaflet was preserved. Before opening of cross-clamp as well as weaning from cardiopulmonary bypass careful deairing was performed via the apex of the heart and the ascending aorta under continuous inflation of the lungs. This was vigorously controlled by TEE monitoring. Mean arterial pressure after CPB was kept above 60 mmHg with volume and vasoactive drugs as appropriate. ICU treatment was performed according to institutional standards.

2.8. Anticoagulation

2.8.1. Mechanical valve replacement

Perioperative 2 × 7500 IE/d low molecular weight heparin Dalteparin-Natrium (Fragmin®, Pharmacia & Upjohn GmbH; Vienna, Austria), on day 5 start with Phenprocoumon (Marcumar®, Roche Austria GmbH; Vienna, Austria) for 4 months (targeted INR range 1.4–2.5; targeted INR 2.0). After that Aspirin (Thrombo Ass®; Lannacher Heilmittel GmbH; Lannach, Austria) life long; in case of persistent atrial fibrillation Phenprocoumon (Marcumar®, Roche Austria GmbH; Vienna, Austria) life long (targeted INR range 1.4–2.8, targeted INR 2.0).

2.8.2. Valve repair

Perioperative 2 × 5000 IE/d low-molecular-weight heparin Dalteparin-Natrium (Fragmin®, Pharmacia & Upjohn GmbH; Vienna Austria); in case of atrial fibrillation 2 × 7500 IE Dalteparin-Natrium. On day 5 start with Phenprocoumon (Marcumar®, Roche Austria GmbH; Vienna, Austria) for 4 months (targeted INR range 1.4–2.5; targeted INR 2.0). After that Aspirin (Thrombo Ass®; Lannacher Heilmittel GmbH; Lannach, Austria) life long; in case of persistent atrial fibrillation Phenprocoumon (Marcumar®, Roche Austria GmbH; Vienna, Austria) life long (targeted INR range 1.4–2.8, targeted INR 2.0).

2.9. Statistical analysis

Data are reported as mean ± SD. Comparison of P300 auditory evoked potentials and standard psychometric test were performed using analysis of variance after testing for normality of distribution. The time course of cognitive brain function was analyzed by means of paired t test for the different groups. Categoric variables were compared using the Chi-Square test or Fisher’s exact test as appropriate. P-values <0.05 were considered as significant, two sided. The study was analyzed using SAS, version 8. Since this is a non-randomized, prospective study and there was no intraoperative conversion form repair to replacement group, statistical analysis was not performed on an intention-to-treat, but treatment basis.

3. Results

Forty elective consecutive patients undergoing mitral valve surgery (mechanical valve replacement n = 20, valve repair n = 20) at our institution were prospectively followed. Preoperative risk measured using the EuroSCORE (valve repair 4.1 ± 2.1 versus mechanical valve replacement 3.8 ± 1.5, P = 0.681), as well as patient characteristics were comparable. Patient characteristics are given in Table 1. Detailed information on the used mechanical mitral valves and Annuloplasty bands is given in Table 2.

3.1. Clinical outcome

In the period of follow-up there was no death in either group. Operative data were comparable in both groups.

2.7. Surgical procedure

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Valve repair</th>
<th>Valve replacement</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>20</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>65 ± 14</td>
<td>64 ± 7</td>
<td>0.896</td>
</tr>
<tr>
<td>Age range (years)</td>
<td>(39–86)</td>
<td>(46–75)</td>
<td></td>
</tr>
<tr>
<td>Sex (f:m)</td>
<td>12:8</td>
<td>12:8</td>
<td>0.478</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>57 ± 8.3</td>
<td>60 ± 11</td>
<td>0.408</td>
</tr>
<tr>
<td>Mitral valve stenosis (n)</td>
<td>0</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>–</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Mitral valve insufficiency (n)</td>
<td>20</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Degree</td>
<td>3.2 ± 0.5</td>
<td>3.5 ± 0.5</td>
<td></td>
</tr>
<tr>
<td>Combined valve disease</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>EuroSCORE</td>
<td>4.1 ± 2.1</td>
<td>3.8 ± 1.5</td>
<td>0.681</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Valve types</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCRI On-x® mechanical mitral valve</td>
<td>8</td>
</tr>
<tr>
<td>Carbomedics mechanical mitral valve</td>
<td>7</td>
</tr>
<tr>
<td>Baxter MIRA mechanical mitral valve</td>
<td>5</td>
</tr>
</tbody>
</table>

Annuloplasty bands

| Baxter Physio Annuloplasty Band | 11 |
| Carpenter Edwards Annuloplasty Band | 9  |
3.2. P300 auditory evoked potentials

In preoperative measures, P300 auditory evoked potentials were comparable (mechanical valve replacement 374 ± 25 ms versus valve repair 378 ± 46 ms, P = 0.791; Fig. 1). In patients undergoing mechanical valve replacement, P300 auditory evoked potentials were markedly impaired (= prolonged) versus preoperative measures (7-day follow-up: 392 ± 28, P = 0.001 and 4-month follow-up: 406 ± 39, P = 0.0004). In contrast, P300 auditory evoked potentials remained unchanged in patients undergoing valve repair (7-day follow-up: 386 ± 40 ms, P = 0.890 and 4-month follow-up: 374 ± 36, P = 0.166). At 4-month follow-up difference between patients mechanical mitral valve replacement and mitral valve repair was significant (P = 0.024).

3.3. Standard psychometric tests

TTA was comparable in preoperative measures (mechanical valve replacement 57 ± 15 s versus valve repair 54 ± 10 s, P = 0.552; Fig. 2). In patients undergoing mechanical valve replacement TTA was markedly impaired (= prolonged) after the operation (7-day follow-up: 65 ± 17, P = 0.0001 and 4-month follow-up: 69 ± 17, P = 0.0001). In contrast, there was no change in patients undergoing valve repair (7-day follow-up: 53 ± 10 s, P = 0.644 and 4-month follow-up: 54 ± 11 s, P = 0.147). At 4-month follow-up difference between patients mechanical mitral valve replacement and mitral valve repair was significant (P = 0.024).

In Mini Mental State Examination all patients scored normal (scoring from 24 to the maximum of 30). This just indicates that all patients were free form clinically overt neurologic symptoms throughout the whole study period.

In order to firmly establish a strong correlation between objective P300 auditory evoked potentials and Trailmaking Test A a Pearson correlation was calculated (R² = 0.868, P = 0.0001).

4. Discussion

As shown by P300 auditory evoked potentials and TTA, successful mitral valve repair results in preserved neurocognitive function. In contrast, successful mechanical mitral valve replacement adversely affects neurocognitive brain function.

The latter findings add additional information to the intensively described phenomenon of neurocognitive deficit after cardiac surgery [1–3] It is accepted that deficits in memory, learning, concentration and visual motor response – known as neurocognitive deficit – affect up to 80% of patients undergoing coronary artery bypass grafting (CABG) with CPB [2–5]. Knowledge with regard to valve surgery is rare and there are no data with regard to mitral valve repair. The clinical impact of neurocognitive deficit has been subject of intensive discussion in the past. There is clear evidence that neurocognitive deficit prolongs in-hospital stay and the process of rehabilitation and therefore affects return to work and daily life of patients [1]. This has been associated with a tremendous use of resources [1]. Neurocognitive deficit has also been shown to be demoralizing for the patient and his family [3]. Due to a lack of long-term data, many clinicians have minimized the
importance of perioperative neurocognitive deficit in the past, because the decline appeared to be of only transient nature in the majority of patients. However, as Newman et al. have only recently shown that neurocognitive deficit at hospital discharge is an independent predictor of neurocognitive deficit 5 years after surgery, it seems crucial to underestimate the long term impact of neurocognitive deficit [3].

Neurocognitive function was objectively measured by a previously described diagnostic tool consisting of P300 auditory evoked potentials and two standard psychometric test (Mini Mental State Examination, TTA) [8–10,12]. Objective P300 peak latencies of auditory evoked potentials have widely been used to evaluate cognitive brain function in different diseases and have proven their usefulness for measurement of cognitive brain function in patients undergoing heart surgery [8–10,13–15]. Cognitive P300 evoked potentials, elicited by a tone discrimination paradigm, represent an objective and valid measure of cognitive brain function. P300 peak latencies, increasing with age in healthy subjects. There is clear evidence that P300 auditory evoked potentials relate to cognitive impairment rating, rapid evaluation of cognitive function test, orientation, stimulus evaluation, selective attention, visual pattern recognition, and digit span were shown to be much more sensitive in detecting neurocognitive deficit than psychometric tests or electroencephalograms [10,12,14,16,20–22]. It is generally accepted that psychometric tests are not without bias, e.g. in part because of long performance times (stressing attention), visual impairment, influence of psychomotor function, level of education, or learning effects [23,24]. Moreover, the P300 technique has a very low intra-individual test-retest variability, with a coefficient of variation of below 2%, which further stresses its usefulness for follow-up studies [8,9,12].

To confirm reproducibility of measurements all P300 recordings were taken repeatedly (double tracing). The high SDs of mean P300 peak latencies are the result of age dependency of cognitive P300 peak latencies. Mini Mental State examination, a standard test of cognitive impairment, was normal in all patients (scoring from 24 to the maximum of 30) in preoperative measures and at all points of follow-up. This indicates that only patients without clinically overt neurological symptoms entered the study and that all patient were free of clinically overt neurological symptoms throughout the period of follow-up. More discriminating were the findings in psychomotor TTA. Using Pearson correlation we were able to establish a strong correlation between TTA and P300 auditory evoked potentials. To minimize learning effects five sets of Trailmaking Tests were randomly used.

Neurocognitive function continuously worsened in patients undergoing mechanical mitral valve replacement throughout 4-month follow-up. In contrast, it remained unchanged in patients undergoing valve repair. Two major observations need to be discussed: First, difference in immediate postoperative damage and second, different course of cognitive brain function throughout 4-month follow-up. Concerning the first observation, it was surprising to us, that there is lack of immediate postoperative damage in valve repair patients, despite the fact of an invasive, open heart procedure (potential risk in both type of procedures: e.g. use of CPB, aortic cross-clamp, opening of heart chambers with risk of air embolism). It seems most likely, that this is a result of standardized treatment of different valve pathologies in mechanical valve replacement and valve repair, respectively. Patients receiving mechanical valve replacement generally present with more complex pathologies (e.g. combined vitiump with progressive valve destruction with more severe calcification of ring, leaflet and subvalvular apparatus). In contrast, patients receiving valve repair, present with less severe destruction of valvular structures. It seems plausible that resection of calcified leaflets or manipulation with calcified subvalvular apparatus during valve insertion, may serve as potential source for particular matter, embolizing to the brain. The latter fact may well explain the different amount of neurocognitive damage between mechanical valve replacement and valve repair immediately postoperative. Nevertheless, it remains to be stressed that valve repair patients seem to perform much better than the vast majority of CABG patients, despite the increased risk of air embolism (as a result of the open heart procedure) [3,8,9]. This discrepancy may best be explained by different underlying diseases, generalized atherosclerosis in CABG patients and isolated valve destruction in mitral valve repair patients. Progressive cerebrovascular disease and consequent pathologic autoregulation in CABG patients seems to render these patients particularly vulnerable to cerebral malperfusion during CPB.

The second – maybe clinically more relevant observation – is the fact that patients with mechanical valve replacement take a completely different course of cognitive brain function throughout 4-month follow-up as compared to valve repair patients. Two possible mechanisms – questionably additive – may be discussed. On the one hand in the mechanical valve replacement group this may be persistence or even worsening of initially embolic damage by particular matter in the brain, independent whether there is ongoing embolization. On the other hand this may be
ongoing damage related to blood/mechanical valve surface interaction, as mechanical heart valves have been shown to produce microemboli entering the cerebral blood circuit [25]. Both particular matter as well as cavitation phenomena (causing gas embolism) seem feasible. It may speculated whether microembolic events might especially occur during phases of suboptimal anticoagulation, which fail to cause clinically overt complications, but result in neurocognitive damage.

4.1. Limitations

The primary limitation is the fact we compare different pathologies (although basic patients characteristics were comparable) and therefore, patients did not receive the surgical procedure in a randomized fashion. Since mitral valve repair is the definitive method of choice for all correctable pathologies, randomization of these particular patients would be questionable. Mitral valve repair was performed whenever technically feasible. This is in well line with other institutional standards. Another important limitation is the fact that no transcranial doppler measurements were obtained in this study. The reason for this is that inability of currently available transcranial doppler systems to differentiate between size and nature (gaseous, particualr) of microemboli. Particular matter are likely to cause more server damage as compared to gaseous microemboli. Therefore, data obtained by the currently used transcranial doppler systems might be misleading. The presented measures of P300 potentials and standard psychometric tests are only valid for patients undergoing mitral valve repair/replacement in the age-range of mean 65 years undergoing mildly hypothermic cardiopulmonary bypass. These data can not be extrapolated to other age ranges, different comorbidities (e.g. diabetes, presence of significant carotid artery stenosis) and perfusion protocols, respectively. From the present data we are unable to exclude an extremely delayed return of cognitive brain function in patients undergoing mitral valve repair with a mechanical prosthesis.

4.2. Conclusion

Taking these limitations into account, we conclude that neurocognitive damage related to mechanical valve replacement is striking, whereas mitral valve repair does not affect cognitive brain function. Despite the fact of generally different underlying pathologies, our data support the benefit of valve repair over mechanical replacement in borderline cases.

Acknowledgements

We thank Daniela Dunkler, MSc (Stat), for the statistical analysis of the work.

References

Appendix A. Conference discussion

Dr D. Taggart (Oxford, United Kingdom): I’m somewhat confused about what you’ve told us today. If I understand from previous papers you’ve published in the European Journal and Annals of Thoracic Surgery, you have demonstrated with P300 latency and reaction time. rolling out on normal 4 months after surgery in patients undergoing coronary artery bypass grafting. Yet you’re telling us today, if I understood your data, that patients undergoing mitral valve repair with cardiopulmonary bypass, they still have impaired recovery in the P300. And wonder if you could speculate and put those two observations together for me.

Dr Grimm: You’re fully right. And the problem is that gaining knowledge is an evolving process. And what we have learned for the cohort of coronary surgery patients is that we have included an extremely broad range of pathologies, ranging from diabetes, insulin-dependent diabetes for more than 10–15 years, including patients with significant cerebrovascular disease. So I think in the particular field of patients after coronary surgery, we have to break down the numbers and focus on selected patient groups. Like patients with the diabetics, they do perform completely different than a simple otherwise healthy patient with just having 3-vessel disease and no cerebrovascular or peripheral disease. I think that just putting all coronary patients into one pot, I think that maybe not appropriate anymore, we have to break it down and focus on specific subgroups.

Dr A. Moritz (Frankfurt, Germany): I’m also puzzled by the results we’ve heard in these three papers dealing with neurocognitive dysfunction after valve surgery.

The first actually showed that if you take the wrong valve, you get a problem with your neurocognitive function.

The second, from your group, we heard that there is an age difference in the reaction, but the mechanical valve is pretty perfect, it returns to normal.

Now, in the second group, where the patient age is somewhat higher than in the first group, for the mitral valves now, the repair behaves like the mechanical valve in the aortic position, but the mechanical valve in the mitral position is bad.

So what do we see now? I mean, only by changing the position of the mechanical valve, you have a completely different neurocognitive outcome.

Dr Grimm: Maybe answering backwards. I hope I can remember everything. I think that we have learned from our clinical doings, and if we look at the ACC recommendations for anticoagulation of the patients, there is another target range in INR mitral valve patients than for aortic valve patients. So I think we cannot put together patients carrying a mechanical aortic valve and patients carrying a mechanical mitral valve, at least from our experience.

The second point is we cannot give you an answer on which type, whether they did, taking the Medtronic heart valve, for example, that really performed better than other valves. We didn’t focus our study on this. And I think now, following several hundred of patients following coronary surgery, to me it turns out that predominantly it’s age and extent of comorbidities, and we are having all those patients presenting always this, that make those patients vulnerable. So if the patient is old and he is diabetic, I think whatever you do, even if you do a MIDCAB on him, he will have damage. Whereas if you have a rather healthy 50-year-old man, just having aortic insufficiency, he will have much better outcome than older one. I think we are just learning and gaining more and more information and learning that maybe we have to rethink things that we published 3, 4 years ago. I think this is an ongoing process.