Is anti-platelet therapy needed in continuous flow left ventricular assist device patients? A single-centre experience†

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Abstract

OBJECTIVES: We report our 5-year experience of continuous flow left ventricular assist device (LVAD) implantation without the use of anti-platelet therapy.

METHODS: Between February 2006 and September 2011, 27 patients (26 men; 1 woman) were implanted with a continuous flow LVAD (HeartMate II, Thoratec Corporation, Pleasanton, CA, USA). The mean age was 55.7 ± 9.9 years. The mean duration of support was 479 ± 436 (1–1555) days with 35.4 patient-years on support. Twenty-one patients were implanted as a bridge to transplantation and 6 for destination therapy. The anticoagulation regimen was flupidone for all patients, with aspirin for only 4 patients. At the beginning of our experience, aspirin was administered to 4 patients for 6, 15, 60 and 460 days. Due to gastrointestinal (GI) bleeding and epistaxis, aspirin was discontinued, and since August 2006, no patients have received anti-platelet therapy.

RESULTS: At 3 years, the survival rate during support was 76%. The most common postoperative adverse event was GI bleeding (19%) and epistaxis (30%) (median time: 26 days) for patients receiving flupidone and aspirin. The mean International Normalized Ratio (INR) was 2.58 ± 0.74 during support. Fifteen patients have been tested for acquired Von Willebrand disease. A diminished ratio of collagen-binding capacity and ristocetin cofactor activity to Von Willebrand factor antigen was observed in 7 patients. In the postoperative period, 2 patients presented with ischaemic stroke at 1 and 8 months. One of these 2 patients had a previous history of carotid stenosis with ischaemic stroke. There were no patients with haemorrhagic stroke, transient ischaemic attack or pump thrombosis. The event rate of stroke (ischaemic and haemorrhagic) per patient-year was 0.059 among the patients without aspirin with a normalized ratio of 2.0–3.0, but the recommendation was later reduced to 1.5–2.5 plus aspirin in an analysis of the BTT patients by Boyle et al. [4]. On the other hand, five different protocols were applied, including vitamin K antagonist with or without aspirin, or with or without Clopidogrel in the early European experience [1].

A number of studies have confirmed the encouraging results and the most experienced centres reduced the amount of anticoagulation therapy [5]. At the beginning of our experience with HM2 support, aspirin was administered to 4 patients, but due to gastrointestinal (GI) bleeding and severe epistaxis, aspirin was discontinued. Therefore, no new patients have received anti-platelet therapy. The aim of this study was to report the safety and effectiveness of the anticoagulation protocol using only a vitamin K antagonist without any anti-platelet therapy in managing a continuous flow LVAD.

INTRODUCTION

The treatment of refractory heart failure with a left ventricular assist device (LVAD) is now a widespread method for bridge to transplant (BTT) or destination therapy (DT) patients. Early in the HeartMate II (HMII) European experience [1, 2] as well as in the HMII BTT trial [3], the initial results revealed a very low incidence of thrombotic occurrence with a higher incidence of bleeding. However, despite similar results of ischaemic and haemorrhagic stroke in these two studies, the antithrombotic regimens were different. In the BTT trial, a protocol constituted of aspirin and warfarin was initially used with a targeted international

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PATIENTS AND METHODS

Patients

A retrospective review was done of the clinical and biological data of all patients implanted with a HMII LVAD in our institution between February 2006 and September 2011. A total of 27 patients have been implanted by a LVAD (HMII, Thoratec Corporation, Pleasanton, CA, USA). Twenty-six (96%) patients were men (26 men/1 woman) and the age ranged between 30 and 71 years with a mean age of 55.7 ± 9.9 years. Eighteen (67%) patients presented a clinical history of smoking and 5 (19%) with diabetes mellitus. The body surface area ranged from 1.61 to 2.33 m² with a mean of 1.91 ± 0.2 m². The majority of patients had ischaemic cardiomyopathy (16, 59%) and 11 (41%) had dilative cardiomyopathy. Four patients had a previous history of coronary artery bypass surgery. Mean left ventricular ejection fraction was 21 ± 9.0. All patients were in New York Heart Association (NYHA) class IIIb or IV. Fourteen (52%) patients were in interagency registry for mechanical assisted circulatory support (INTERMACS) level 1 or 2. Eighteen (66%) patients were supported on inotropic support. Fifteen (56%) patients presented in cardiogenic shock, and 2 (7%) had a recent previous history of cardiac arrest. Twelve (44%) patients were supported by extracorporeal membrane oxygenation (ECMO) with a mean duration of 6.4 ± 2.9 days (4–19 days). One patient was supported for 10 days by Impella 5.0 (Abiomed, Danvers, MA, USA). One patient was supported with intra-aortic balloon pump (IABP). Twelve (44%) patients were mechanically ventilated. Intention to treat was BTT in 21 (78%) patients, DT in 6 (22%). One patient was converted from BTT to DT due to pulmonary metastases of renal cell carcinoma. Table 1 summarizes clinical and biological patient baseline data.

Surgical procedures

All the implantations of HMII were performed under cardiopulmonary bypass (CPB) with aortic cross-clamping only during the implantation of the inflow cannula into the apex of the left ventricle. Concomitant surgical procedures were tricuspid annuloplasty in 3 patients and closure of the permeable foramen ovale in 4. A full dose of protamine was administrated to antagonize heparin at the end of CPB. ECMO, Impella and IABP were weaned in 7 patients and ECMO was continued for right-sided support in 6 for a mean duration of 6 (4–20) days.

Anticoagulation protocol

For all patients, an intravenous infusion of unfractionated heparin was initiated when mediastinal tube drainage was <50 ml/h. For the first postoperative day, heparin was titrated to maintain a partial thromboplastin time between (1.5 and 2) times of that of control. Once patients were weaned from artificial ventilation, anticoagulation with fluindione was initiated to obtain a target INR of 2–2.5, and then heparin was discontinued. At the beginning of the experience, aspirin was administered to 4 patients for 6, 15, 60 and 460 days. Due to GI bleeding and epistaxis, aspirin was discontinued, and since August 2006, no patients have received anti-platelet therapy.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range) (years)</td>
<td>55.7 (30–71)</td>
</tr>
<tr>
<td>Sex: men (%)</td>
<td>26 (96%)</td>
</tr>
<tr>
<td>BSA, mean (range) (m²)</td>
<td>1.91 ± 0.2 (1.61–2.33)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>5 (19%)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>6 (22%)</td>
</tr>
<tr>
<td>Tobacco, n (%)</td>
<td>18 (67%)</td>
</tr>
<tr>
<td>Ischemic aetiology, n (%)</td>
<td>16 (59%)</td>
</tr>
<tr>
<td>Dilative aetiology, n (%)</td>
<td>11 (41%)</td>
</tr>
<tr>
<td>Previous coronary by-pass surgery, n (%)</td>
<td>4 (15%)</td>
</tr>
<tr>
<td>Sodium (mean ± SD)</td>
<td>133 ± 8.2</td>
</tr>
<tr>
<td>Potassium (mean ± SD)</td>
<td>4.1 ± 0.6</td>
</tr>
<tr>
<td>Urea (mean ± SD)</td>
<td>12.7 ± 7.8</td>
</tr>
<tr>
<td>Creatinine (mean ± SD)</td>
<td>117.8 ± 58.2</td>
</tr>
<tr>
<td>LVEF, mean ± SD ( %)</td>
<td>21 ± 9.0</td>
</tr>
<tr>
<td>INTERMACS level 1 or 2, n (%)</td>
<td>14 (52%)</td>
</tr>
<tr>
<td>Mechanical support</td>
<td>n = 14</td>
</tr>
<tr>
<td>ECMO, n (%)</td>
<td>12 (44%)</td>
</tr>
<tr>
<td>IABP, n (%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Impella 5.0, n (%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Intention to treat</td>
<td></td>
</tr>
<tr>
<td>BTT, n (%)</td>
<td>21 (78%)</td>
</tr>
<tr>
<td>DT, n (%)</td>
<td>6 (22%)</td>
</tr>
</tbody>
</table>

BNSA: body surface area; LVEF: left ventricular ejection fraction; INTERMACS: interagency registry for mechanical assisted circulatory support; ECMO: extracorporeal membrane oxygenation; IABP: intra-aortic balloon pump; BTT, DT, BTC: bridge to transplantation, destination therapy, bridge to candidacy.

Von Willebrand factor analysis

Beginning in June 2006, patients were tested for Von Willebrand disease after a surgical procedure when they presented with non-surgical bleeding. Since August 2008, patients were systematically tested before and after implantation of the LVAD. Plasma Von Willebrand factor antigen (vWF:Ag) was measured by immunoturbidimetry (Siemens Healthcare Diagnostic, Marburg, Germany). Functional analysis of Von Willebrand factor (vWF) was performed using a ristocetin cofactor assay (vWF:RCo, Siemens Healthcare Diagnostic, Marburg, Germany) and collagen binding (CB) assay (vWF:CB, Diagnostica Stago, Asnières, France). The ratio vWF:RCo/vWF:Ag >0.65 was considered as normal. The ratio vWF:CB/vWF:Ag was measured by the capacity of vWF to bind to collagen and was considered as normal for a value of >0.7. The closure time was measured with a platelet-function analyser (PFA-100, Siemens Healthcare Diagnostic, Marburg, Germany) using the collagen/adenosine diphosphate (ADP) and collagen/epinephrine cartridges.

Statistical analysis

Data were expressed as mean ± SD. Survival analysis includes data as of March 2012 and was performed with the use of the Kaplan–Meier method with censoring for heart transplantation or cardiac recovery. Calculations were performed with Abacus Concepts StatView statistical software (SAS Institute, Inc., Cary, NC, USA). Adverse events were presented both as the percentage of patients who had the event, and as event rates per
patient-year. For this analysis, we have excluded the period during which the 4 patients were treated with both anti-platelet therapy and vitamin K antagonist.

RESULTS

Patients outcomes

All patients were followed until either transplantation or death up to March 2012. Median length of stay in the intensive care unit was 32 days, with a total median hospital stay of 67 days. This duration included the rehabilitation period of the patients, and at the end of the hospital stay, they were directly discharge home. The mean duration of support was 479 ± 436 (1–1555) days with a cumulative 35.4 patient-years on support. Two patients were supported >4 years, 2 >3 years, 3 patients >2 years and 9 >1 year.

In the BTT group of patients, 5 (19%) died on support postoperatively after a mean duration of 32 days due to multi-organ failure. One patient died after 340 days of support of an internal rupture of the driveline. In the DT group of patients, 1 died after 3 years of support due to end-stage right heart failure. Nine (33%) patients underwent heart transplantation after a mean duration of support of 1.44 ± 0.63 year. One patient died 4 days post-transplantation due to a septic shock. One patient was weaned for recovery at 330 days but died postoperatively of heart failure.

The survival rates during support of BTT and DT patients at 1 and 6 months were 85 and 82%, and at 1 and 3 years, it was 76 and 76%, respectively (Fig. 1). The overall survival for patients either transplanted, weaned or on-going at 1, 3 and 5 years were 77, 65 and 58%, respectively.

Bleeding complications

The mean INR for all patients during support was 2.59 ± 0.74. Surgical rethoracotomy due to postoperative bleeding was observed in 18 (66%) patients after a mean duration of 10 ± 8.2 postoperative days.

Non-surgical bleeding defined as epistaxis, haemoptysis or GI bleeding was observed in 10 patients (37%) (Table 2). Two of them were being managed with fluindione and aspirin. The most common non-surgical bleeding event was upper respiratory tract bleeding (epistaxis and haemoptysis) in 8 (30%) patients after a mean time of 25 ± 20 days of support. One patient (fluindione and aspirin) died at 67 days of suffocation after a massive epistaxis. Arterial embolization was necessary in 2 patients. GI bleeding was present in 4 (15%) patients with recurrent episodes in 2. Two patients presented both epistaxis and GI bleeding.

vWF profile results

Fifteen patients have been tested for acquired Von Willebrand disease (AvWD). A diminished ratio of collagen-binding capacity and ristocetin cofactor activity to vWF antigen was observed in 7 (47%) patients. Five (71%) of these 7 patients presented severe non-surgical bleeding (epistaxis and GI bleeding).

Table 3 summarizes the vWF profile, platelet function and anticoagulation protocol for patients with non-surgical bleeding complications.

Thromboembolic events

Two patients presented with ischaemic stroke at 1 and 8 months, leading to an incidence of 0.059 ischaemic stroke per patient-year. One of the 2 patients had a previous history of carotid stenosis with ischaemic stroke. There were no patients with haemorrhagic stroke, transient ischaemic attack or pump thrombosis (Table 2). Therefore, the overall event rate of stroke (ischaemic and haemorrhagic) per patient-year was 0.059 among the patients with fluindione regimen only (no aspirin). One patient presented a progressive aortic insufficiency due to a retraction of an aortic cusp linked to the presence of a thrombus adherent to the left-coronary cusp. This thrombus was diagnosed by computed tomography scan in the early postoperative phase. Another patient presented with a chronic obstruction of the inflow cannula due to progressive migration of the inflow cannula into the septum. These 2 patients were transplanted uneventfully.

Other complications

Percutaneous lead fracture at the pump housing occurred in 3 patients. The first caused the death of the patient, the second required a pump replacement and the third was asymptomatic.
and was discovered during transplantation. Severe infection of the driveline occurred in 2 patients. These patients were listed emergently and successfully transplanted.

**DISCUSSION**

The HMII is an axial-continuous-flow LVAD and has progressively become a widespread therapy for patients with refractory heart failure. The HMII is the most frequently used LVAD with >13 000 implantations worldwide and >5000 patients on-going (Thoratec data). At the beginning of the US HMII II clinical trial, the anticoagulation protocol was considered aggressive [5]. However, more recent studies have shown a low risk of thrombotic events during HMII support [4, 6, 7]. In a recent analysis of 281 patients supported by the HMII, the overall rate of stroke was 0.08 event years, with a rate of ischaemic and haemorrhagic stroke of 0.05 and 0.03 event years, respectively [8].

The early European experience yielded similar results [1, 7]. A recent analysis of Boyle et al. [9] analysing outpatient anticoagulation concluded that the small number of thrombotic events was offset by a larger number of bleeding events [4]. Moreover, although the recent clinical results indicate that there is a low rate of thrombotic events during HMII support, bleeding was the most frequent adverse event, occurring in ~50% of all cases. These results are consistent with data from INTERMACS, the national registry in the USA.

Our initial experience highlighted the high incidence of haemorrhagic complications resulting in numerous morbidities or even death, leading to our decision to stop aspirin and use fluindione as the only anticoagulant (monotherapy). This experience, cumulating 35.4 patient-years of support, showed a low incidence of ischaemic stroke and an absence of haemorrhagic stroke resulting in a very low overall incidence of stroke of 0.059 events/patient-years. Backes et al. [10], in a review of the literature, found a mean incidence of 0.17 (range: 0.06–0.29) strokes per patient-year with a postoperative regimen including heparin converted to coumarins, acetylsalicylic acid and dipyramidole. This series, however, does not describe the risk factors for stroke such as diabetes mellitus, smoking or previous history of stroke. It can be questioned which proportion of strokes is related to the presence of the device. In our series, the high level of patients who smoked (67%) and had diabetes mellitus (19%) could have led to a high number of stroke events. Despite these risk factors, our study exhibited a very low incidence of stroke events.

To our knowledge, this study is the first to report the long-term results of the safety of a monotherapy regimen solely constituted of a vitamin K antagonist. Moreover, we have used fluindione, a treatment never reported in the literature, but one derived from 1,3-indandione and its pharmacokinetic activity is characterized by a long half-life. The role of the molecule (coumarin vs warfarin vs fluindione) used for the anticoagulant regimen has never been studied, but could have a direct effect on the incidence of stroke events. Additionally, despite a recommended INR target of 2–2.5, we were surprised, in retrospectively analysing our INR data to find a mean INR of 2.59 corresponding to the higher limit of our target. Recently, Menon et al. reported a reduced anticoagulation regimen with a lower INR target (2–2.5) and aspirin in patients <55 years or in those with severe atherosclerosis of the right coronary artery [11]. This regimen did not increase the thromboembolic events, even in patients without aspirin. However, as pointed out in an editorial by Strueber [12], the mean duration of support was only 241 days. The mean duration of 479 days, in our patients, could suggest that the withdrawal of aspirin is an acceptable safety method for long-term support.

**Table 3: The vWF profile, platelet function and the anticoagulation therapy in patients with non-surgical bleeding complications**

<table>
<thead>
<tr>
<th>Patient</th>
<th>vWF profile: FvW (RCO/Ag)</th>
<th>PFA-ADP(s)</th>
<th>Anticoagulation</th>
<th>INR/PTT(s)</th>
<th>Non-surgical bleeding</th>
<th>First episode postoperative (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NA</td>
<td>NA</td>
<td>Aspirin fluindione</td>
<td>INR = 1.44</td>
<td>Epistaxis</td>
<td>34</td>
</tr>
<tr>
<td>2</td>
<td>NA</td>
<td>NA</td>
<td>Aspirin fluindione</td>
<td>INR = 2.68</td>
<td>Epistaxis</td>
<td>67</td>
</tr>
<tr>
<td>3</td>
<td>1.14</td>
<td>NA</td>
<td>Fluindione</td>
<td>INR = 1.48</td>
<td>Epistaxis</td>
<td>35</td>
</tr>
<tr>
<td>4</td>
<td>0.42 (AvWD)</td>
<td>86</td>
<td>Fluindione</td>
<td>INR = 1.8</td>
<td>Gl</td>
<td>30</td>
</tr>
<tr>
<td>5</td>
<td>0.56 (AvWD)</td>
<td>&gt;300</td>
<td>Heparin</td>
<td>PTT = 68</td>
<td>Epistaxis/Gl</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>1.06</td>
<td>56</td>
<td>Heparin</td>
<td>PTT = 59.3</td>
<td>Epistaxis</td>
<td>10</td>
</tr>
<tr>
<td>7</td>
<td>0.56 (AvWD)</td>
<td>&gt;300</td>
<td>Heparin</td>
<td>PTT = 52.7</td>
<td>Epistaxis</td>
<td>16</td>
</tr>
<tr>
<td>8</td>
<td>0.64 (AvWD)</td>
<td>206</td>
<td>Aspirin fluindione</td>
<td>INR = 3.41</td>
<td>Gl</td>
<td>133</td>
</tr>
<tr>
<td>9</td>
<td>0.59 (AvWD)</td>
<td>&gt;300</td>
<td>Heparin</td>
<td>PTT = 63.1</td>
<td>Epistaxis/Gl</td>
<td>21</td>
</tr>
<tr>
<td>10</td>
<td>0.55 (AvWD)</td>
<td>&gt;300</td>
<td>Heparin</td>
<td>PTT = 66.2</td>
<td>Haemoptysis</td>
<td>22</td>
</tr>
</tbody>
</table>

NA: non-available; Gl: gastrointestinal; INR: international normalized ratio; PTT (s): partial thromboplastin time (seconds); FvW (RCO/Ag): Von Willebrand (Ristocetin cofactor activity/antigen); AvWD: acquired Von Willebrand disease; PFA-ADP: platelet-function analyser with collagen; PFA-Epi: platelet-function analyser with epinephrine.
Bleeding complications during support with a continuous flow LVAD are induced by multiple factors, including the AvWD, fibrinolysis and anticoagulant therapy [13]. High-molecular Willebrand (HMW) multimers, which are the most effective form of vWF, play a key role in primary haemostasis by mediating platelet adhesion and aggregation. These HMW multimers are subject to high shear stress, leading to them being cleaved as they pass through the device [14]. AvWD appears in the early postoperative phase [15] and probably explains the high level of rhabdomyolysis in our series. Moreover, 44% of our patients, prior to the LVAD implantation, were supported with ECMO, which is known to contribute to AvWD [16]. On the other hand, the use of a low dose of aspirin inhibits the enzyme Cox-1, which produces thromboxane A-2, necessary for platelet aggregation. The high frequency of the development of AvWD in patients with continuous flow LVAD and the concomitant anti-platelet therapy may lead to an increased risk of bleeding [17]. The low incidence of thromboembolic events in our study, without the use of anti-platelet therapy, may be explained by a variable but systematic alteration of the platelet function in patients with axial-flow LVAD. Steinlechner et al. [18] demonstrated that platelet dysfunction is only partly attributable to low vWF activity.

Anti-platelet therapy with aspirin is largely given to patients with HMII LVAD, but the risk/benefit balance of this practice has not been well determined. In all cases, the monitoring of the platelet function with thromboelastogram may probably aid in assessing the need for anti-platelet therapy [12].

In conclusion, this single-centre study suggests that monotherapy using only a vitamin K antagonist (fluindione) without anti-platelet therapy in long-duration LVAD support appears to not increase thromboembolic events and could lead to a diminished risk of haemorrhagic stroke. Moreover, due to the difference between this approach and numerous other anticoagulation protocols, further randomized and controlled studies evaluating a monotherapy regimen with vitamin K antagonist are needed to confirm our findings.

ACKNOWLEDGEMENT

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Conflict of interest: Pierre-Yves Litzler is proctor for Thoratec, Inc.

REFERENCES


APPENDIX. CONFERENCE DISCUSSION

Dr C. Heilmann (Freiburg, Germany): Some groups consider acquired von Willebrand syndrome to be a prophylactic issue or situation. Do you have any data? What is your opinion about that?

Secondly, previous publications associate age with the appearance of non-surgical bleeding, and I would like to add that I consider the majority of intrathoracic bleeding also to be non-surgical. Of course, you close the wound very carefully, and the incidence of bleeding is higher in LVAD patients than in other patients. So it should be a patient-related problem rather than technique-related. Did you analyse your incidence of bleeding with regard to association with age?

Dr Litzler: For the age, no. Despite a median age of 55 years in our population, we observed a lot of bleeding, surgical and non-surgical, but because of our very small population, it was difficult to analyse the association. However, because of the relatively young age of our population, bleeding is probably not related to age but probably multifactorial.

For the acquired von Willebrand syndrome, I was also surprised to see that only half of our patients tested presented with acquired von Willebrand disease, seven patients out of 15 patients tested, compared with the 100% of patients with acquired von Willebrand disease reported for some series in the literature. So it is surprising for us not to have all of our patients with acquired von Willebrand disease, and we don’t know why. There is a link between acquired von Willebrand disease and nonsurgical bleeding, but we don’t exactly know the hypothetical impact on the platelet function to avoid the use of aspirin. I don’t know your opinion on this.
Dr Heilmann: Perhaps my question was not well phrased. The first question was to comment on the diagnosis of acquired von Willebrand syndrome. What algorithm do you use to diagnose it?

Dr Litzler: What kind of test?

Dr Heilmann: Yes.

Dr Litzler: Ristocetin and collagen-binding versus antigen ratio, and for some patients we used multimer analysis, too.

Dr Heilmann: You used all three measures for one patient?

Dr Litzler: Yes.

Dr Heilmann: So that is surprising for me, too. But did you observe thrombotic events in patients with acquired von Willebrand syndrome?

Dr Litzler: No. The two patients with thrombosis had no particular alteration of their platelet function.

Dr Heilmann: Did they have acquired von Willebrand syndrome? Acquired von Willebrand syndrome is something different from platelet dysfunction.

Dr Litzler: For the first patient, the test was not available in our laboratory at that time; this was a patient with a carotid stenosis with a previous history of stroke.

Dr M. Morshuis (Bad Oeynhausen, Germany): I think your results are excellent, but it is quite courageous to start such a trial, because you don’t know beforehand what the result will be in six years. But you were very successful and someone has to try. So the reason that you started was that you saw too much epistaxis, you lost one patient because of that, or cerebral bleeding, and then you thought, okay, we have to try something else?

Dr Litzler: At the beginning it was exactly the same for biventricular patients when we implanted PVAD and IVAD devices. We started in 1998, and at the beginning of our experience when we tried to give aspirin to our patients, it was a total nightmare because of major bleeding. So we stopped using aspirin without problem with PVAD and IVAD, and we don’t understand exactly why in Rouen we have no thromboembolic events. Possibly it is the use of fluindione; I think I have discussed that before, and I think maybe it is one of the key points, because it is a vitamin K antagonist with a longer half-life. It may be that with its use we have some protection from thromboembolic events. I don’t know. There are no reports in the literature about the use of fluindione. There are a lot of questions but no answers.

Dr G. Whitman (Baltimore, MD, USA): It seems to me that the question you are asking is can you treat patients who have continuous flow devices with just a vitamin K antagonist without antiplatelet therapy. Are you following them simply by symptoms? Or are you looking for something biochemical that might suggest that there is subclinical clot formation like bilirubin or LDH, because I, too, find this fairly courageous?

Dr Litzler: Yes, it was only clinical. We have a very long mean duration of support of more than 400 days. So with such a long period of support, I can’t imagine the formation of clots and so on, without clinical incidence. We have patients with more than five years without taking aspirin. So if you have a repeated clot, thrombus in the pump or in the brain, I think you will have a clinical event one day.

Dr B. Torfason (Reykjavik, Iceland): Have you decided on a list of exclusion criteria like, for instance, coronary stents?

Dr Litzler: For the moment, no. It is very hard to decide to stop aspirin when you have a patient with a coronary stent, because you don’t know if you will have a problem with the stent. Until now we have no problem with stents in these patients. So maybe it is like protection with a pump.

Dr Torfason: Maybe I missed it. Did you have some patients with stents?

Dr Litzler: We had patients with coronary stents in this series.