protocol, surely contributed to the higher risk of developing a thrombosis anyway.

In conclusion, compared with the other study results, our data suggest that a notably mild anticoagulation protocol does not increase the risk of severe thrombo-embolic events in the early and late postoperative period after the implantation of the HM II CW LVAD. Furthermore, this mild regime is helpful in reducing the still unacceptably high incidence of bleeding episodes in the use in this patient group.

Conflict of interest: none declared.

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APPENDIX. CONFERENCE DISCUSSION

Dr Edmunds (Philadelphia, PA, USA): I want to know why you did not measure some of the markers of thrombin formation and fibrinolysis. There are no data about what happened to the blood during this mean of 8 months of perfusion. Do you have any data about what was going on with the blood other than the platelet count?

Dr Menon: We tested the thrombocyte function in the two patients who were not anticoagulated.

Dr Edmunds: Well, that is 2 of 40. Let’s get to the 38.

Dr Menon: We analysed the von-Willebrand factor, and all patients developed von-Willebrand syndrome. Nearly all patients, whether they take aspirin or not, will have impaired thrombocyte function.

Dr Edmunds: I am going to comment because all who are working with these devices on a chronic basis know that blood is traumatized as it goes through the machine. You need to measure F.1.2 to find out how much thrombin is being generated, and you need to measure D-dimer, or some other measure of fibrinolysis, because that is also going on. Just saying you did not have any stokes depends on how fine you are able to see a stroke or find a stroke. And if I have to have one of these devices, and I am closer to it than anybody else in the room probably, I do not want to lose my head.

Dr Menon: Yes, that is absolutely right.

Dr Edmunds: There is not much left anyway.

Dr Menon: Every 4 weeks, we have a close examination of every patient during the whole period, and we define stroke as having a neurologic deficit persisting for more than 24 h according to the CT scan findings.

Dr D. Loisance (Paris, France): I still do not understand how you can say that there is no thrombus formation in your patients. You do not show us any evidence about thrombus formation, and we are wondering, as was stated before, about the D-dimers. It is at least the minimum you should show us.

Dr Menon: In every patient, we tested the free haemoglobin and LDH of course, and it was almost within normal levels. And even the parameters of the LVAD pump seem to be very okay in every patient. We are testing it every 4 weeks.

A breakthrough in the use of ventricular assist device (VAD) therapy was achieved when the pilot trial of Thoratec’s novel HeartMate II was launched in the US and Europe in 2004. Rotary blood pump technology was about to replace pneumatic driven pulsatile devices. The continuous flow mode promised more mechanical stability, noiseless operation and much smaller devices.

Since there had been problems with the first version of the HeartMate II, as well as with the earlier DeBakey device in terms

EDITORIAL COMMENT


Adverse events in long-term ventricular assist device therapy

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Keywords: Ventricular assist device · HeartMate II · Adverse event
of pump thrombosis, the start of the pilot trial was under the impression that, for the new technology, anticoagulation and antiplatelet therapy should be as strong as possible.

In hindsight, this was not necessary and was causing harm to the patients. Therefore, in subsequent recommendations, anticoagulation therapy became less and less aggressive. Following the current guidelines, the group from Aachen reports favourable results in this journal in terms of bleeding and thrombosis in patients implanted with the HeartMate II.

In the meantime, it was recognized that these rotary blood pumps cause an acquired von Willebrand Syndrome. Shear stress, which seems unavoidable, when energy is transferred to the blood with miniature impellers at high speed, is the cause of the largest monomers of the von Willebrand factor (vWF), being the biggest molecule in the blood, to change their tertiary structure exposing the cleaving sites to a hydrolytic enzyme. Thereby, a substantial decrease of the largest monomers without changing the total amount of vWF is found. This leads to a clinical condition that is well known in patients with severe aortic stenosis: an impairment of primary haemostasis and the Heyde syndrome: Patients suffer from minor bleeding from the mucosa that may lead to nose and mouth bleeds. In addition, major bleeding episodes may occur at arteriovenous malformations in the small bowel [1]. These are not easy to find and to treat.

These findings triggered some programmes, like ours, to withdraw antiplatelet medication and just use coumadin. In most programme antiplatelet therapy is continued, but the target international normalized ratio was further decreased.

There were reports that in bleeding episodes anticoagulation was withdrawn completely without any adverse events (AEs). So the question arose, is anticoagulation at all necessary in HeartMate II patients?

Currently it seems, pump replacements for pump thrombosis have become more frequent. One reason, of course, is the increased number of implants, but in addition it leads to the conclusion that anticoagulation is necessary in VAD therapy. We have reached the other end of the spectrum - going from ‘as much as possible’ in 2004 to ‘almost nothing at all’ 8 years later. In this debate, the paper of Dr Menon et al. [2] is leading the way, and in a direction that most experienced centres would agree with: the pendulum swinging back to a moderate anticoagulation protocol.

But is this the end of this story?

VAD therapy proved in the last 8 years that the long-term stability of the pumps is not an issue anymore. Patients can be supported not only as a bridge to transplantation, but as a definitive therapy for end-stage heart failure. The devices have been in numerous trials to show that. Therefore, the use of this technology has increased substantially, because the number of heart transplant procedures no longer matches the demand of patients in heart failure.

Despite the success of VAD therapy, given the number of patients in need, why is the number of implants still at a relatively low level? One factor is reimbursement, the others are AEs in VAD therapy.

These are linked in the way that future reimbursement of chronic support with VADs can only be expected when a gain in quality-adjusted life years is proven.

What are the most limiting AEs in long-term therapy? There is an incidence of bleeding and thrombosis, possibly leading to cerebrovascular accidents (CVAs) or pump thrombosis. Still Menon et al. describe a low incidence of CVAs, although the mean follow-up was limited to only 240 days. Truly, it is much less than years ago, but is it at an acceptable level? I have my doubts: the follow-up in this article as well as in most publications is too short to give definitive answers: what is the incidence of CVAs in a 5-year perspective?

In addition, a driveline infection is still the other major AE: the incidence is high and requires dedicated outpatient care to decrease injury to the driveline. Recently, most investigators in this field have agreed to find correlations of infections with subsequent CVAs. It seems there is a delicate balance between thrombosis and bleeding in VAD patients that can be challenged by many factors.

So what is the bottom line? Moderate anticoagulation protocols are currently state-of-the-art in VAD patients with rotary blood pumps. In addition, this technology allowed for the first time to consider VAD as a real treatment option in heart failure. But can we show a gain in quality-adjusted life years [3]? We have proven a survival benefit [4], but the quality of life and the absence of serious AEs in a 5-year perspective remain to be shown.

Conflict of interest: Martin Strueber was a primary investigator in the HeartMate II Pilot and is member of the European Advisory Board of Thoratec, Inc.

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