Martin Czerny

Type B aortic dissection: patient identification, treatment decision process, and treatment modalities

Thoracic endovascular aortic repair (TEVAR) is a well established therapy option for patients with complicated type B aortic dissection (TBAD), where rapid diagnosis and treatment is essential for effective management of the disease. *Confluence* spoke with Dr Martin Czerny at University Heart Centre Freiburg, Germany to discuss optimisation of treatment for patients with TBAD, including the use of TEVAR in uncomplicated TBAD patients.

What is type B aortic dissection?

Dr Martin Czerny (MC): Aortic dissection belongs to the family of acute aortic syndromes, and is a highly fascinating disease with a variety of clinical courses. 'Type A' and 'type B' are fundamentally different. If you have 10 patients with Type A, over half will die if they do not have access to treatment. Conversely, in a group of 10 patients with TBAD, 9 out of 10 will survive without access to treatment, hence the clinical course of TBAD is more benign than type A.[1] This is the reason why physicians tend to underestimate the lethal potential of TBAD. However, this is likely to be a misconception, as recent work has shown that many TBAD patients will develop complications sooner or later.

What factors define complicated vs uncomplicated TBAD?

MC: The literature tells us that just 1 out of 10 cases of TBAD is complicated or becomes complicated in the initial phase.[1] Patients with uncomplicated TBAD mostly present under stable clinical conditions, with acute pain occurring hours or days before the dissection is identified. However, the disease can rapidly lead to severe complications, so it is extremely important to anticipate who will develop complications and who will remain uncomplicated.

Having a complicated TBAD means to sustain malperfusion or any kind of staged rupture or having uncontrolled hypertension, which is actually often related to a pseudo-coarctation. The disease process may also potentially lead to a transition from type B to retrograde type A, where the patient's dissection moves into their aortic arch and even into the ascending aorta. These clinical scenarios are very likely to happen within the first 14 days after the onset of the disease and are very rare afterwards, so the critical period are the first 14 days.

How is complicated TBAD detected?

MC: Morphological parameters are used to anticipate complications if they have not already occurred with a main focus on the site of primary entry tear. Recent work has clearly shown that this parameter is one of the most important independent predictors of the presence of or development of complications in the first 14 days of TBAD.[2]

In terms of daily practice, when a clinically uncomplicated patient with TBAD is referred to our centre, we follow a diagnostic algorithm to confirm that complications are definitely not present. To do this we look at the site of the primary entry tear and the distance from this tear to the left subclavian artery. It is important to understand that the dissection not only follows the blood flow downstream, but also propagates in a retrograde fashion within the aortic wall. If the primary entry tear is located at the concavity, retrograde propagation can occur and the patient has a substantially elevated risk of complications.

There is a clear association between the primary entry tear at the lesser curvature of the distal arch and the development of malperfusion, intramural haematoma or retrograde type A aortic dissection.[3] If we observe an entry tear at the lesser curvature of the aortic arch with or without a short distance to the left subclavian artery, these patients will

fig. 1

undergo prophylactic thoracic endovascular aortic repair (TEVAR), as the likelihood that they will develop complications is extremely high.

Primary diagnostics should be done via CT scan. The European Society for Cardiology (ESC) guidelines clearly recommend CT angiography (CTA) as a first-line diagnostic modality; in addition, ECG triggering is a very important component to reduce motion artefacts. MRI may be used to learn on the functionality of the membrane. However, this is optional and CTA should be considered as the first-line diagnostic modality.

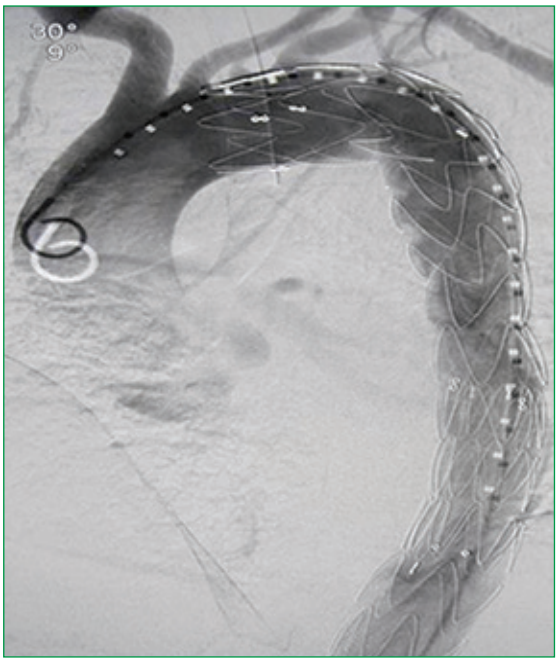
What are the current treatment options available for patients with TBAD?

MC: The initial target for therapy is always to keep blood pressure low, under a limit of 120 to 70 mmHg. Medical therapy remains the first-line treatment option, but where invasive treatment is necessary, TEVAR is the first option and, in certain clinical scenarios, the use of the 'frozen elephant trunk technique' can also be used.[4]

TEVAR always aims to achieve closure of the primary entry tear. The procedure requires a landing zone of at least 2 cm in order to land in a segment where safe and stable deployment of the stent-graft can be performed. This is the reason why we are pretty liberal in having a carotid-to-subclavian bypass or subclavian-to-carotid transposition to maintain supra-aortic perfusion in our patients if the primary conditions for such a kind of landing zone are not given due to a short distance to the left subclavian artery.

In the last 10 years, there has been a shift from over-stenting the left subclavian artery towards prophylactic transposition, because clinical data have clearly shown that the remaining risk of developing any kind of neurological injury is higher when the left subclavian artery is over-stented.[5] If there is any time to plan the procedure, this is strongly recommended.

An important point to reflect on when TEVAR is performed in patients with TBAD is what I would call the 'black box' of retrograde type A aortic dissection (RTAD). RTAD is an adverse effect of TEVAR, with a higher incidence in TBAD than any other thoracic aortic pathology.[6] The reason for this is most likely that the tissue of the proximal thoracic aorta in patients with TBAD is still inherently diseased, despite regular diameters.



What type of patient subgroup is TEVAR most appropriate for?

MC: TEVAR is most appropriate for patients with morphological characteristics that allow you to anticipate complications. I would divide these potential complications into different time slots. The first is early complication, which mostly occurs within the first 2 weeks after the acute event. This includes the development of malperfusion and retrograde Type A aortic dissection, as well as recurring pain and contained rupture. The second group is patients developing complications at a later timepoint, which, for 98% of patients, consists of an increase in aortic diameter leading to aneurysmal formation. One way to catch these complications and prevent them may be to perform prophylactic TEVAR. This could be considered if the initial aortic diameter is at least 4 cm. Patients who have the primary entry tear at the lesser curvature of the distal aortic arch, or have a very short distance from the primary entry tear to the left subclavian artery, are the high-risk subgroup. My opinion is that these patients should always have TEVAR, despite being nominally uncomplicated.

The efficacy of TEVAR in patients with post-dissection aneurysm formation is still a very large discussion point. In this cohort, our personal preference is to go for classical surgery, as this clearly provides the best results in the long-term. Branch technology also has its place in this cohort

of patients, and we will need to obtain robust clinical data to define what subgroups will also benefit from extended endovascular therapy.

Has the TEVAR target patient cohort changed in recent years?

MC: It definitely has – the 5-year results from the INSTEAD-XL trial showed that aortic specific mortality and disease progression were significantly lower with TEVAR vs optimal medical treatment alone in uncomplicated patients (P=0.04 for both).[7] These results changed the field and led to important modifications for the recent ESC 2014 Guidelines on the Diagnosis and Treatment of Aortic Diseases.[8] As a result, there is now a Class IIa recommendation with level of evidence B (Class IIaB) for TEVAR in uncomplicated TBAD. This has been supported by the ABSORB trial, which was also recently published.[9] The main difference between the two trials was that INSTEAD-XL recruited between 2–52 weeks, and ABSORB recruited from Day 0–14 after onset. We are still awaiting the long-term data from ABSORB, but it is likely that the results will be similar to INSTEAD-XL. For complicated TBAD patients, there remains a Class I recommendation with level of evidence C.

How can TEVAR be applied to patients with uncomplicated TBAD?

MC: As retrograde Type A aortic dissection can be a consequence of the TEVAR procedure, physicians have to think twice before applying prophylactic therapy in an uncomplicated patient with type B aortic dissection. Our personal algorithm includes critical evaluation of these so-called uncomplicated patients, as many of them – according to the before-mentioned risk-factors – are highly likely to sustain complications, sooner or later. These parameters are then taken into consideration and then TEVAR is performed prophylactically if even just one of these before-mentioned risk-factors is applicable.

What are the main barriers preventing the scientific community from adopting TEVAR for uncomplicated TBAD?

MC: I think the main barrier is that TEVAR is an invasive therapy and applying this to patients who subjectively don't appear to have any problems, and who are unlikely to have problems within the years to come, is challenging. TEVAR is thought of as a prophylactic therapy, showing its clinical benefits 5 years after treatment, as observed in the INSTEAD-XL study. While TEVAR was shown to benefit patients, the fact that these were 5 years down-the-line may preclude this type of intervention in many settings. However, I am convinced that the results from the INSTEAD-XL study should cause physicians to consider using TEVAR in uncomplicated patients.

Outside of clinical studies, is there anything that companies can do to help increase the adoption of TEVAR?

MC: Industry can make an impact by improving the technology, as branched grafts addressing the left subclavian artery could make a difference, since they would lower the threshold to treat lesions in proximity to the left subclavian artery for patients who would otherwise need any kind of supraaortic transposition.

Additionally, there is always a discussion around optimising stent-graft tapering, especially in a more chronic clinical setting, where stent graft-induced new entry occurs. This is a new kind of TEVAR-induced disease where the distal end of the stent graft erodes the dissection membrane, thereby creating a new primary entry tear immediately distal to the stent-graft (Janosi RA, et al. *Catheter Cardiovasc Interv* 2015;85:E43–53). This pathophysiological mechanism is a new finding, which has supported the need for tapered grafts and radial forces moving proximally to distally. Companies are essential to helping the field to advance through optimising conformability of devices.

How important are the ESC guidelines for practising physicians?

MC: The ESC guidelines are essential for practising physicians. Imagine a scenario where a clinical course of a patient ends up otherwise than expected and the case goes to court. The first step a reviewer logically takes is to refer to the guidelines to identify if the physician has acted either inside or outside current recommendations. While these recommendations are not dogmatic, they should be regarded as a document made by specialists to advise others to choose the right kind of treatment. However, the final responsibility always lies with the individual treating physician.

The next update to the current guidelines is not fixed. There was an 11-year period between the first and second aortic guidelines, but knowledge in the field has increased so much in the meantime that

it is highly unlikely that it would take that long for further updates. I think the next round of updates will also include morphological parameters such as the ones mentioned.

There are still gaps in knowledge with regard to the natural course of the disease and in particular with regard to pressure distribution between lumina. Any kind of non-invasive means to measure blood pressure in the false lumen would be a major step in predicting dilation and understanding the natural course of the disease. In terms of the dynamics of the disease, many of us would like to have a standardised functional protocol and be able to note the number of communications between lumina, because this also seems to be a major determinant between an uncomplicated and a complicated natural course of the disease.

How do you think that the number of undiagnosed cases of TBAD can be decreased?

MC: The first question is to identify how many undiagnosed cases there are. For instance, in the city of Vienna, everybody who dies outside hospital without a clear diagnosis will undergo autopsy. However, if you don't have a complete autopsy setting in your region you will never know how many undiagnosed cases there are. We need to raise awareness in emergency departments as for patients who come in with acute chest pain, merely 4 out of every 1000 will have an aortic dissection. To help diagnose these cases it is important to listen to the patient, as they will tell you their development of pain and therefore the development of dissection. For example, "it started in-between my shoulders and the pain went downwards", or "the pain went upwards and came across to the anterior chest". This is what patients tell you when they have sustained an aortic dissection, but you have to ask the right questions and you have to listen closely. Then after having raised suspicion, it is is all about the threshold to perform or to not perform a CT scan.

What can be done to optimise the pathway of treatment for patients with TBAD?

MC: I am convinced that the main important task is the creation of aortic centres where patients are centralised and subjected to routine checks in a clearly structured programme. What often happens is that when a patient develops TBAD he is hospitalised somewhere and images are sent to a referral centre. The centre replies saying that treatment is currently not necessary, as the patient is at that stage uncomplicated, and they are subsequently discharged and never seen again. Five or 10 years later, a massive post-dissection aneurysmal formation may be detected by chance as many of these patients undergo CT scans for an other reason later during their life. These frequently observed clinical scenarios are one of the many reasons to substantiate the plea for aortic centres.

The creation of these aortic centres, where the aorta is treated entirely from the aortic root down to the aortic bifurcation by a dedicated team – providing knowledge of the natural course of the disease, classical therapy and interventional therapy – is the key to success. This would greatly help to decrease the number of patients who lose the benefit of having early therapy.

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DISCLOSURES: Martin Czerny is a consultant for Medtronic and Boston Medical.