ordered in advance. Off-the-shelf devices have been introduced during the last few years, with the potential to enable acute endovascular treatment of complex juxta- and suprarenal aneurysms or even thoracoabdominal aneurysms. In some centres, the ambition to treat most patients with ruptured AAA by way of EVAR has entailed more frequent use of parallel grafts for preservation of flow to the reno-visceral arteries in complex aneurysms. Using this method, an observational study from Zurich, Switzerland, and Örebro, Sweden, demonstrated excellent results.[18]

In 2014, 30-day outcome of the Immediate Management of Patients with Rupture: Open Versus Endovascular Repair (IMPROVE) trial was published.[19] The objective was to assess whether an EVAR strategy (in suitable anatomy) would reduce early mortality in patients with suspected ruptured AAA compared with open repair. It was designed as a randomized trial. In the primary outcome of 30-day mortality, no difference between the groups was reported. In sub-group analysis, women were found to benefit more from an EVAR strategy, due to high mortality in the open repair group among women. Moreover, more patients in the EVAR group were discharged directly to home. Many questions remain unanswered, such as if there are any differences between the two groups in the long run, and if that would infer any cost differences. We are anxious to see further results.

In conclusion, the year 2014 brought about important technical and methodological improvements and refinements, as well as epidemiological data on patients with aortic aneurysms. Elective repair of the standard infrarenal AAA, in most patients, has become a fairly safe procedure, and there is a trend towards a higher proportion of patients undergoing endovascular treatment. Even complex pathologies of the suprarenal and thoracoabdominal aorta can be managed endovascularly, and patients previously considered unfit for surgery can be offered repair to a higher degree. With the new imaging processing techniques, both patients and surgeons are exposed to less radiation, and improved imaging together with preoperative simulation can even further reduce the contrast load. Further developments in basic science and pharmacology may be additional amendments to the technical progress. We look forward to an exciting 2015!

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Interventional treatment of venous thromboembolism

A review and update of treatments in 2014

Venous thromboembolism (VTE) encompasses pulmonary embolism (PE) and deep vein thrombosis (DVT) and has an approximate annual incidence of 1 in 1000.[1] Venous thromboembolism contributes to death in more than half a million cases each year in the European Union.[2] Pulmonary embolism is a potentially life-threatening disease, particularly if systemic hypotension and right ventricular dysfunction are present.[3]

Although DVT is usually not life-threatening, its long-term sequelae have been underestimated for many years. Up to 40% of patients develop the post thrombotic syndrome (PTS), which often reduces quality of life due to venous claudication, skin changes, and ulcerations.[4] The risk of PTS is greatest in patients with thrombosis of the ilio-femoral veins, or the inferior vena cava.

Of note, anticoagulation therapy is associated with poor venous patency rates and the majority of ilio-femoral DVT do not recanalize, despite therapeutic levels of anticoagulation therapy.[5]

An early revascularization strategy in PE patients aims at restoring flow in pulmonary arteries, reversing right ventricular dysfunction, reducing the risk of circulatory collapse, death, and chronic thromboembolic pulmonary hypertension. In addition to anticoagulation with heparin, systemic thrombolysis is considered the standard therapy for PE patients at increased risk of death, but it is withheld in the majority of cases mainly due to the fear of life-threatening bleeding complications including intracranial haemorrhage.[3] Catheter interventions have evolved as a promising alternative to systemic thrombolysis or surgical embolectomy.

An early revascularization strategy in patients with ilio-femoral DVT aims at restoring venous flow and preserving venous valvular function, thereby improving symptoms and signs of acute DVT and preventing the development of the post thrombotic syndrome.[6] Catheter-directed thrombolysis followed by routine stenting of residual venous stenosis has replaced open surgical thrombectomy for the majority of ilio-femoral DVT cases. [7]

Recommendations and techniques for interventional treatment of acute VTE are summarized in this article.

Recommendations on interventional treatment

Pulmonary embolism

The 2014 European Society of Cardiology (ESC) guidelines on the management of PE recommend systemic thrombolytic therapy in high-risk patients who present with cardiogenic shock or systemic hypotension.[8] Owing to the risk of intracranial bleeding, systemic thrombolysis is no longer recommended as first-line therapy for haemodynamically stable patients at intermediate risk, i.e. in the presence of right ventricular dysfunction and a positive troponin test. Systemic thrombolysis is recommended as rescue therapy in intermediate-risk patients who suffer haemodynamic deterioration during the initial phase of anticoagulation treatment.

Catheter-directed treatment or surgical embolectomy should be considered for patients at intermediate or high risk, in whom systemic thrombolytic therapy is contraindicated or has failed.

Deep vein thrombosis

The 2012 guidelines of the American College of Chest Physicians recommend emergent thrombus removal by catheter intervention or surgical thrombectomy in patients with impending venous gangrene.[6]

Additionally, patients presenting with an ilio-femoral thrombosis, symptoms for <14 days, a good functional status, a life expectancy of at least 1 year, and a low risk of bleeding should be considered for catheter-directed thrombolysis.

Similarly, the 2011 American Heart Association (AHA) guidelines recommend catheter-directed thrombolysis or pharmacomechanical thrombolysis as a first-line treatment for patients with ilio-femoral thrombosis in patients at low risk for bleeding.[9]

Methods of interventional treatment

Overall, interventional treatment options are classified into those with or without the use of thrombolysis.

Catheter interventions without thrombolysis

For patients with absolute contraindications to thrombolysis therapy, the following techniques of intervention therapy are performed.[10, 11]

1. Thrombus fragmentation
   This technique disrupts obstructing thrombus into smaller fragments by manual rotation of a pigtail catheter or by inflation of a balloon catheter. There is a risk of distal embolization and worsening haemodynamic status when used in patients with centrally located PE.
2. Rheolytic thrombectomy
   Rheolytic thrombectomy (AngioJet®, Boston Scientific, USA) uses the Venturi effect and is enabled by a high-pressure saline jet inside the catheter.
3. Suction thrombectomy
   Suction of thrombus using large-lumen catheters (8–12 French) is performed manually by inducing a negative pressure with an aspiration syringe.
4. Rotational thrombectomy
   Rotational thrombectomy by an 8 or 10-Fr Aspirex® catheter (Straub Medical, Switzerland) can be used to establish flow in thrombotic occlusions. It macerates and removes thrombus by an incorporated high-speed rotational coil.
5. Vacuum-assisted thrombectomy
   Vacuum-assisted thrombectomy (AngioVac®, Angiodynamics, USA) is another option for patients with massive vena cava thrombosis or PE who cannot receive thrombolytics due to high risk of bleeding. It includes an extra corporal veno-venous bypass with a 22-Fr suction cannula, a 16-Fr re-infusion cannula, and a filter.[12]

Catheter interventions with thrombolysis

Catheter interventions with thrombolysis are the most commonly used techniques for the treatment of patients with PE and DVT.

Conventional catheter-directed thrombolysis
Thrombolytic agents, for example, recombinant tissue plasminogen activator (rtPA) at a dose of 1–2 mg/h for up to 24 h, are infused through side-hole catheters which are placed at the side of the thrombotic occlusion.
Pharmacomechanical thrombolysis
Pharmacomechanical thrombolysis refers to catheter-directed thrombolysis combined with a mechanical catheter technique. In addition to the thrombectomy mode, the AngioJet® system (Boston Scientific, USA) enables a high-pressure intrathrombos injection of thrombolytic agents (PowerPulse® technique).
Ultrasound-assisted thrombolysis is another type of pharmacomechanical thrombolysis which aims to accelerate thrombolysis success. It consists of a thrombolysis catheter with a microsonic core wire that uses high-frequency low-power ultrasound waves (EKOS Corporation; Bothell, WA, USA). In a randomized trial of PE patients at intermediate risk, ultrasound-assisted catheter-directed thrombolysis was superior in reversing right ventricular dilatation without an increase in bleeding rates compared with patients who received only anticoagulation.[13]

Summary and perspective

Catheter intervention is an evolving and promising minimal-invasive therapy for patients with acute VTE. The most commonly used techniques for patients with PE and DVT are catheter-directed thrombolysis and pharmacomechanical thrombolysis. Various mechanical thrombus removal therapies are available for patients who cannot receive thrombolytic agents due to an increased risk of bleeding.

While most PE patients do well with anticoagulation therapy alone, catheter interventions may be considered for selected PE patients at intermediate or high risk. Since systemic thrombolysis should no longer be used as a primary reperfusion therapy for PE patients at intermediate risk, it is likely that many centres will offer catheter-directed therapy to their patients in the future.

Patients with acute ilio-femoral DVT are at risk of developing the post-thrombotic syndrome if managed conservatively with anticoagulation therapy alone. Catheter-directed thrombolysis followed by stenting of underlying venous obstruction has emerged as standard treatment in many centres.

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From academia to industry

Working in industry requires wanting to make medicines

Patrick Vallance, head of Research & Development at GlaxoSmithKline, discusses his move from academia to industry and advises dropping personal research interests

Patrick Vallance, credit GSK

Patrick Vallance MD FRCP FMedSci has never been one for career planning. The decision to leave academia for industry was made overnight, following dinner with the then chairman of Research & Development (R&D), Dr Tadataka (Tachi) Yamada, who said, 'Why don't you come and join GlaxoSmithKline (GSK)?'

At the time Vallance was head of the division of medicine at University College London, UK. He was practising as a general and cardiovascular physician, teaching at the university, and had his own research group. 'I had very little to do with industry and all of my research money came from peer reviewed grants and other places', he says.

Vallance's clinical pharmacology background led to involvement with formularies and access to medicines, and Yamada had asked him to become part of the research advisory board for GSK. 'I did that and it was a massive eye opener for me about what went on in industry, the quality of the science, the breadth of the science, and the potential to impact human health', says Vallance. But he adds: 'I still had no intention of joining industry'.

After the dinner with Yamada he went home and thought, 'Am I going to spend the rest of my career trying to do something a bit like this in academia, trying to make chemicals and interfere with processes and write the occasional critical article about industry, or go in there and try and do something about it. I decided overnight that I would make the swap'. The decision came down to the observation that it's not possible to make medicines in academia. 'Medicines are made in industry and that's what I wanted to be involved with', says Vallance. 'A process that allows you to go from an idea through to something which is going to be given to millions of people and improve lives of patients across the world'.

As head of R&D at GSK he is involved in the whole process of making medicines, from the very early stage of ideas through to approval. In common with academia, he works with smart scientists who are extremely motivated and enthusiastic. Vallance says: 'It is in some ways a challenge of fostering individual and team creativity and delivery, which is a very similar thing to leading an academic department'.

He adds: 'What's different is it needs to be marshalled towards very clear, big outputs that need many, many people involved over multiple years'.

The science is much broader than at UCL, ranging from chemistry through to clinical science and crossing all therapy areas. 'I know enough to ask the questions of people and push things a bit', he says.

Much of the job is about leadership. While the department at UCL was large, with 400 or so people, at GSK he leads 10 500 staff. 'People who come from academia sometimes don't understand how important it is to get that leadership bit right', says Vallance. 'A lot of academia remains a very individualistic exercise. This is much more about getting teams working well together'.

He is also seeking to collaborate with scientists outside GSK's own walls through the company's 'open innovation' approach. It was developed to encourage innovation in diseases of the developing world, where there is no same potential commercial return and research has stalled. In 2010 GSK opened up access to its compounds that show activity against malaria and in 2012 did the same for TB.

When Vallance made the move to industry he thought he would miss seeing patients, but that has not been the case. He loved being a clinician, but explains: 'I'd become so busy in that job I'm not sure I was giving it the time and attention that it deserved'.

And with so much going on at GSK he does not miss his personal research either. His lab at UCL was the first to show that nitric oxide controls vascular tone in humans and they identified a novel pathway that regulates nitric oxide synthesis. The group did a collaborative piece of work using a big general practice database which showed that risk of myocardial infarction is elevated