Vascular UPDATE

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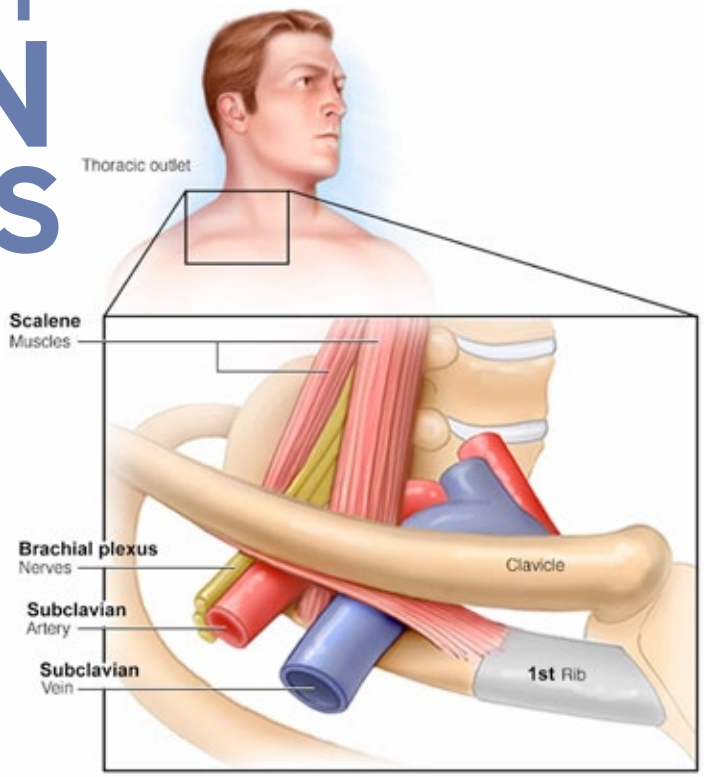
UPPER EXTREMITY DEEP VEIN THROMBOSIS



The incidence of deep vein thrombosis (DVT) is 1 per 1000 person per year. UEDVT accounts for about 4-10%. The subclavian & axillary vein are most frequently affected. UEDVT may be primary or secondary.

Primary causes of UEDVT

1. Paget-Schroetter syndrome:
Also known as as effort-related thrombosis, this predominantly affects young active, healthy men (more than women). Most patients have an underlying structural anatomical anomaly in the anterior triangle of the thoracic outlet. leading to impingement of the proximal subclavian vein. Repetitive movement of the arm causes intimal fibrosis and activation of coagulation cascade and effort related venous thrombosis

2. Thrombophilia:
Patient with inherited or acquired thrombophilia can uncommonly present with spontaneous UEDVT.

Secondary causes of UEDVT

1. Central venous catheters/ports (CVC):
The risk of developing a CVC related thrombosis ranges between 5-28% and is the most common cause of UEDVT. Risk factors associated with higher risk include:

- Associated malignancy
- Subclavian vein access
- Difficult placement or tortuous anatomy
- Catheter tip placed proximal to atrio-caval junction
- Larger lumen catheters
- Inserting a new catheter into same vein that was previously thrombosed or used for a prior CVC

2. Cancer
Cancer is a secondary cause of UEDVT due to induced prothrombotic states, or vein compression or infiltration by cancer or metastases. Approximately ¼ of patients diagnosed with idiopathic UEDVT are subsequently found to have an underlying cancer within a year of diagnosis of DVT.

Other secondary causes for UEDVT are:

3. Pacemaker & Defibrillator leads
4. Haemodialysis Arteriovenous Access catheters, fistulas and grafts
5. Surgery/immobilisation of upper limb
6. Pregnancy & OC use (uncommon cause of UEDVT)

Clinical Symptoms

A large proportion of patients with UEDVT are asymptomatic (30-60%).

Symptomatic patients have varying degrees of severity that parallel the degree of venous obstruction and acuity of onset of obstruction.

Typical symptoms are unilateral limb pain swelling and fatigue (Fig 1). Symptomatic pulmonary emboli occurs in 2-9% (compared to 15-29% in Lower extremity DVT) Patients with superior vena cava (SVC) thrombotic occlusion present with facial and chest wall plethora/swelling and Urschel's sign (shoulder and chest wall varicosities) (Fig 2).

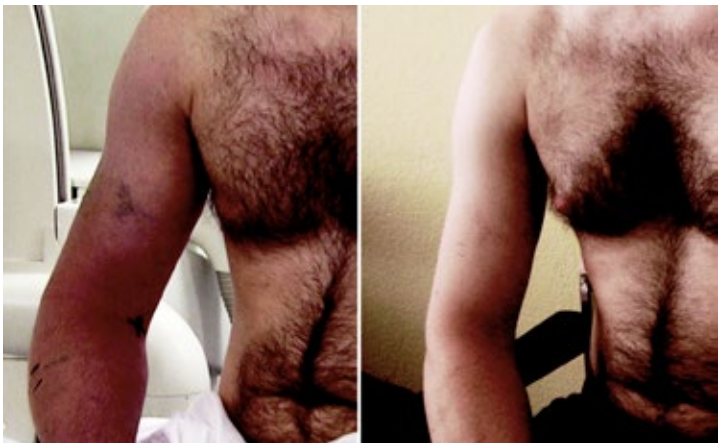


Fig 1

Diagnosis

Compression ultrasonography has a sensitivity of 97% and specificity of 96%, particularly in the distal upper extremity veins. The proximal axillary and subclavian veins are not easy to compress and the brachiocephalic & SVC are difficult to visualise due to their location and surrounding structures. The absence of phasic flow on respiration may indicate a proximal stenosis/occlusion. In poorly visualized cases, or where concomitant pathology is suspected, contrast CT (or MR) venography can be useful.

Management

The mainstay of managing most patients with UEDVT is anticoagulation. The guidelines follow the treatment recommendations for LEDVT. Anticoagulation is for a minimum of 3 months. Extended anticoagulation is recommended for:

- Cancer associated UEDVT: LMWH until cure or remission achieved
- CVC associated UEDVT if catheter can't be removed: anticoagulation to be continued as long as catheter remains

Paget Shroetter syndrome management

Most patients with this condition are young and healthy, and are offered anticoagulation combined with catheter directed thrombolysis (CDT) or pharmacomechanical thrombolysis. This is followed by surgical correction of the VTOS and surgical or endovascular (angioplasty/stenting) correction of the underlying venous stenosis.

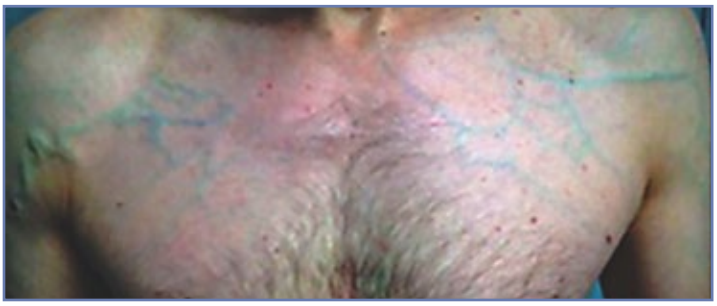


Fig 2: In patients who develop superior vena cava (SVC) thrombotic occlusion they usually present with facial and chest wall plethora/ swelling and Urschel's sign (shoulder and chest wall varicosities).

Surgical decompression of the VTOS includes excision of any cervical ribs, anterior 2/3rd of 1st rib, subclavius muscle and costoclavicular ligament division and venolysis of subclavian vein.

Poor surgical risk patients are anticoagulated.

CVC UEDVT management

The CVC is removed if no longer required and patient anticoagulated for 3 months. If the CVC is still required, but is occluded, thrombolytics are infused into catheter to attempt to re-establish patency. If the CVC is patent and is still needed, continue anticoagulation for duration of the CVC use.

Pacemaker & defibrillator leads UEDVT management

Anticoagulation for 3-6 months.

How soon should carotid endarterectomy be undertaken following a TIA, Stroke or successful thrombolysis?

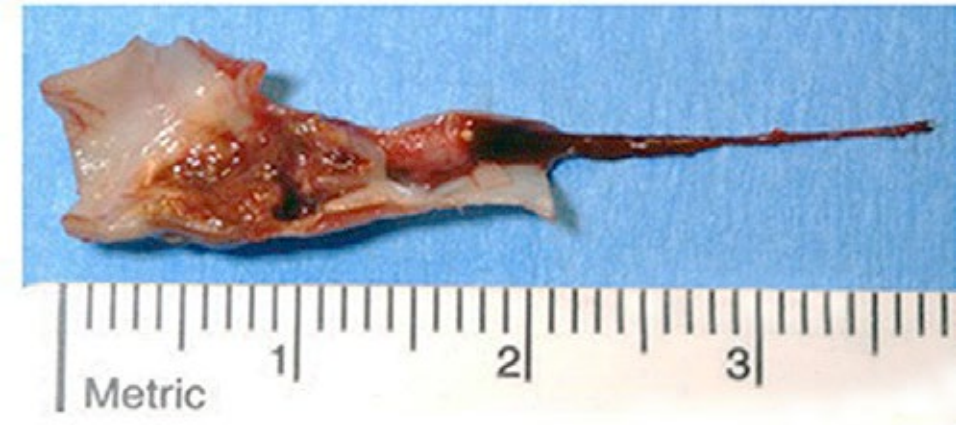


Fig 1: The typical appearance of the carotid artery resulting in acute stroke or TIA

Most carotid TIAs or strokes are associated with plaque rupture with or without super-imposed thrombus (Fig 1). The chances of a recurrent event are high (approaching 20% by 14 days and as high as 5-8% in the first 48 hours) Fig 2. The traditional approach of delaying carotid surgery for 6 weeks following a stroke was abandoned years ago and international guidelines now recommend an intervention within the first 14 days. Analysis of the classical trials of carotid surgery from the 1990s indicates that any real benefit for surgery is lost if surgery is delayed beyond 12 weeks, particularly in females.

Several studies have drawn attention to the considerable risks of operating within the first 48 hours of the event when the lesion is particularly unstable. The period between 3 and 7 days seems to be the ideal time to schedule the surgery unless the patient is neurologically unstable (crescendo TIAs or stroke in evolution). Under such circumstances, the operation needs to be performed as an emergency in spite of the fact that peri-operative stroke rates are very high.

Whilst waiting for surgery the modern approach is to place patients on due anti-platelet therapy including clopidogrel as well as statins and careful blood pressure control. This has been shown to significantly reduce the risk of recurrent events.

Patients with a good result from acute thrombolysis for stroke can safely undergo carotid endarterectomy once 48 hrs have elapsed.

Patients with suspected TIAs or minor strokes must be referred timeously for appropriate investigation as the first 48 hours is the highest risk period for recurrent events.

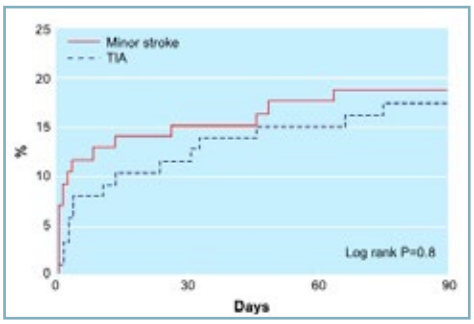
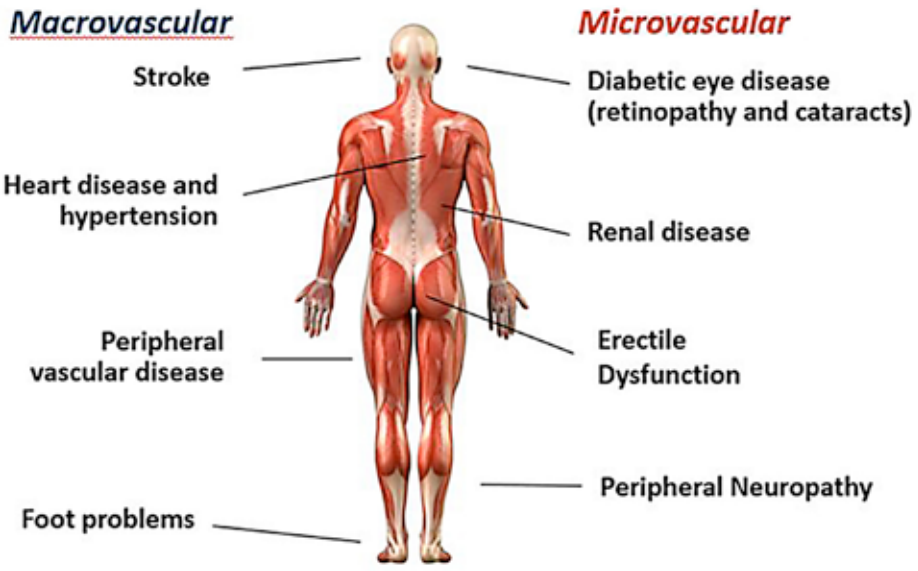


Fig 2: Risk of stroke following tia or minor stroke

HOW DOES DIABETES CAUSE VASCULAR DISEASE?

Diabetes is a potent risk factor for the development of atherosclerosis and affects both the macro and microvascular arterial beds. The risk of CAD and stroke is increased 2-4 times in patients with diabetes and up to 40% of long standing diabetics develop significant peripheral arterial disease. Diabetes is the leading cause of adult onset blindness, renal failure and is the commonest cause of non-traumatic amputations.

A number of molecular mechanisms are responsible for the accelerated atherosclerosis in diabetic patients (Fig 1).



1. Endothelial dysfunction

Insulin regulates the production of the vasoconstrictor endothelin-1 and the vasodilator nitric oxide (NO) in the endothelium through enzymatic pathways that interact with serum glucose levels. Insulin increases NO production by activating endothelial NO synthase. Insulin resistance is therefore prothrombotic and proatherogenic by enhancing vasoconstriction and inflammation at the endothelial level.

2. Plaque instability

In addition to increasing cardiovascular atherosclerotic plaque burden, insulin deficiency decreases smooth muscle actin and collagen content and increases plaque necrosis, causing decreased plaque stability.

3. Skeletal muscle hemodynamics

Insulin increases the blood flow to skeletal muscles by NO-mediated vasodilation and capillary recruitment. This interaction between insulin and limb skeletal muscles is impaired in diabetics because of deficiency or resistance. This leads to the gradual decrease in limb skeletal muscle perfusion.

4. Advanced glycation end products (AGEs)

AGEs are the products of nonenzymatic reactions (glycation) between glucose molecules and proteins, lipids, and nucleic acid. Chronically elevated serum glucose concentration and oxidative stress result in an increase in circulating AGEs. Cell receptors for AGEs trigger inflammation and apoptosis in the endothelium and thus play an important role in plaque formation and atherosclerosis. In addition, glycation of low density lipoprotein enhances its uptake by macrophages and endothelium, resulting in the formation of foam cells and subsequent advanced atherosclerosis.

5. Oxidative stress

Hyperglycemia results in an increase in tissue levels of reactive oxygen species (ROS). This, in turn, results in activation of protein kinase C pathway, increased formation of AGEs, NO depletion, and increased production of angiotensin II, resulting in vasoconstriction and atherosclerotic plaque development. More importantly, ROS enhance proinflammatory gene expression and subsequent endothelial apoptosis and thrombosis. ROS have been considered central in the progression of diabetic vascular complications and are therefore considered potential targets for future pharmacologic interventions.

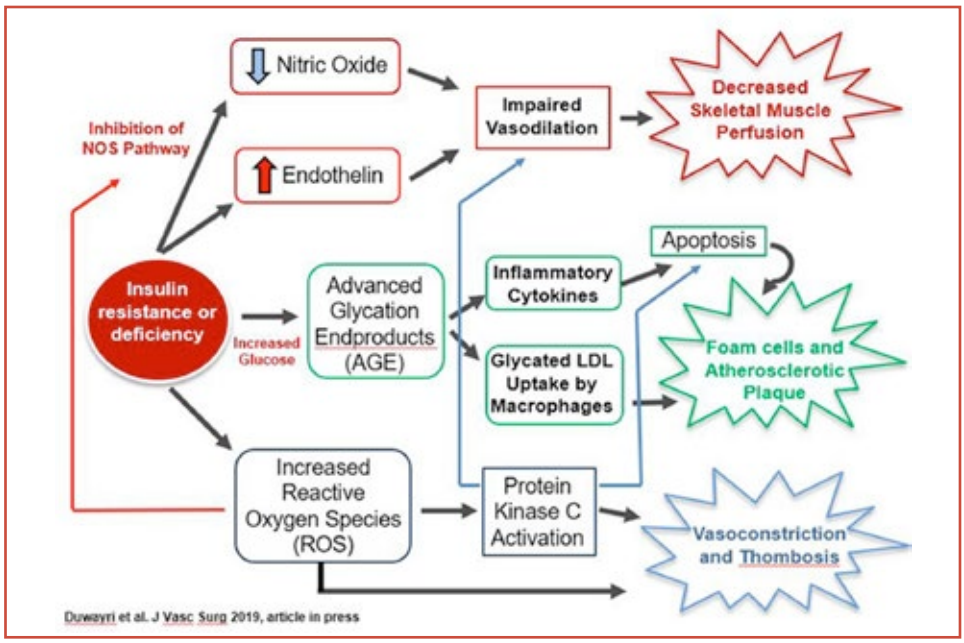


Fig 1

WHAT'S NEW at Matley&Partners

Ella, Bernie, James and Nicky celebrated the birth of **Sarah Ruby Maree** who arrived on Monday 9 September 2019.

ENDOVASCULAR ANEURYSM REPAIR: 2019 AND BEYOND

Since EVAR arrived in South Africa 20 years ago, it has evolved steadily. Over that time, it has become the first choice of treatment option for management of Abdominal Aortic Aneurysm (AAA). As the stent-grafts have improved and evolved, more patients are treatable using EVAR. The alternative option – open repair – is still required for some patients, however, as not all AAA are suitable for EVAR.

Currently, standard EVAR is suited to patients who have a true infra-renal AAA, with suitable, non-aneurysmal iliac arteries. There are several factors which may make patients unsuitable for EVAR, thus making open repair the only option for these patients.

Sometimes Vascular Surgeons may carry out an EVAR on a patient who has an AAA where the anatomy of the AAA falls outside the IFU (Instructions for Use) of the device. When this is done, there is an increased risk of failure, which may lead to the need for secondary interventions or even rupture of the AAA.

As a result of the clear need for Endovascular solutions for patients whose AAA fall outside the IFU of existing devices, the manufacturers have produced several new additional devices for Vascular Surgeons to use to treat these difficult AAA cases.

Iliac Branch Devices (Fig 1) are stent-grafts which have a built-in bifurcation to allow stent-grafting into the internal and external Iliac

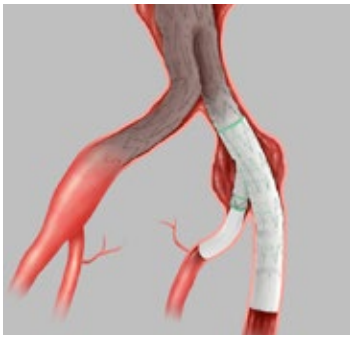


Fig 1

vessels, while maintaining flow to those vessels. This allows treatment of common iliac aneurysms which previously required open surgical repair. The availability of IBD has enabled us to manage 5-10% more AAA with stent-grafts.

FEVAR (Fenestrated EVAR) (Fig 2) is the technique of managing supra-renal AAA with stent-grafts. Flow must be maintained to the visceral and renal vessels in these patients. FEVAR requires a custom-made stent-graft with holes cut into the fabric which are cannulated to allow placement of a small covered stent into those renal and visceral vessels while still allowing

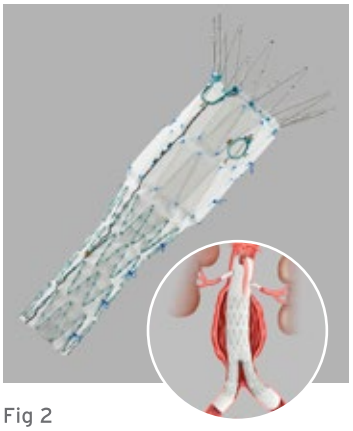
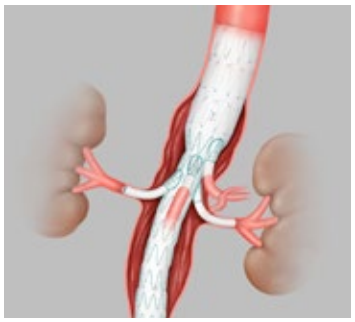


Fig 2

the stent-graft to seal on the aortic wall. The fenestrated device is custom made for each individual patient using data obtained from CT scans of the AAA. The device can only be used for that specific patient, costs approximately R300 000.00, and takes 6 weeks to deliver after being ordered! "Off the shelf" solutions to this problem are currently under development, and will hopefully ease this stumbling block.

True thoraco-abdominal AAA can be treated with **Branched EVAR (BEVAR)**. (Fig 3 and 4)) Once again, a custom-made device with pre-installed branches is deployed within the Aorta, and the branches are then cannulated to allow deployment of a bridging stent-graft from



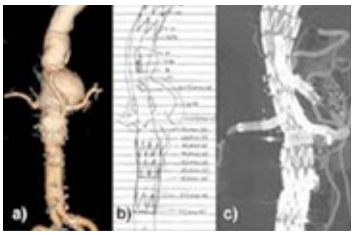


Fig 3&4

the main device into the renal and visceral vessels, thus maintaining vital organ perfusion after the BEVAR has been completed. Branched and fenestrated technologies have now also been extended to the thoracic aorta. Ascending Aortic Aneurysms and arch aneurysms can now be treated by endovascular means (Fig 5), thus removing the need for heart bypass and circulatory arrest with their attendant complications. The operative risk for intrathoracic aortic aneurysm repair is considerable, so these technological advances are likely to be harnessed to the benefit of patients as soon as the devices are presented in an "off the shelf" form. Currently they are custom made, as for the BEVAR And FEVAR devices for thoraco-abdominal AAA repair.

The future direction in Aortic Aneurysm management will be to develop devices which will enable more and more aneurysms which are currently unsuited to stent-graft repair to be repaired by endovascular means. The increased utilisation of these devices will lead to an inevitable decrease in the costs of the devices, which will – in turn – make them more accessible for use. Endovascular solutions to problems after EVAR, FEVAR and BEVAR will also be developed: the problem of endoleak after stent-graft repair can be extremely challenging, and new devices and products to assist clinicians in managing endoleak will come to market.

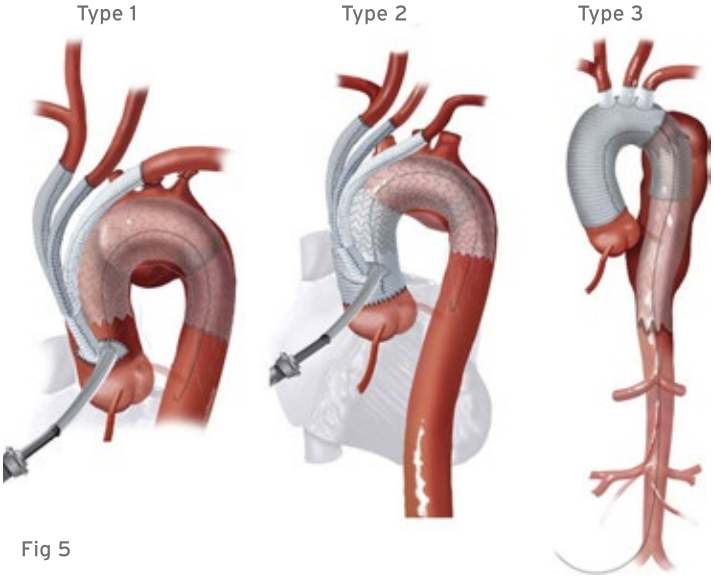


Fig 5