BIOLOGY OF ARTERIOVENOUS (AV) FISTULA FAILURE

JOURNAL CLUB

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INTRODUCTION

- The increasing number of patients with end-stage renal disease now undergoing hemodialysis needs maintenance of an adequate vascular access function. A patent arterio-venous fistula (AVF) is related to better prognosis and quality of life for these patients.
- It is currently estimated that between 23%-46% of all AV fistulae have problems with early failure or failure to mature.

THE THREE BASIC TYPES OF AVF:

- ✓ Radial-cephalic
- ✓ Brachial-cephalic
- ✓ Brachial-basilic transposition
- ✓ Arterio-venous graft

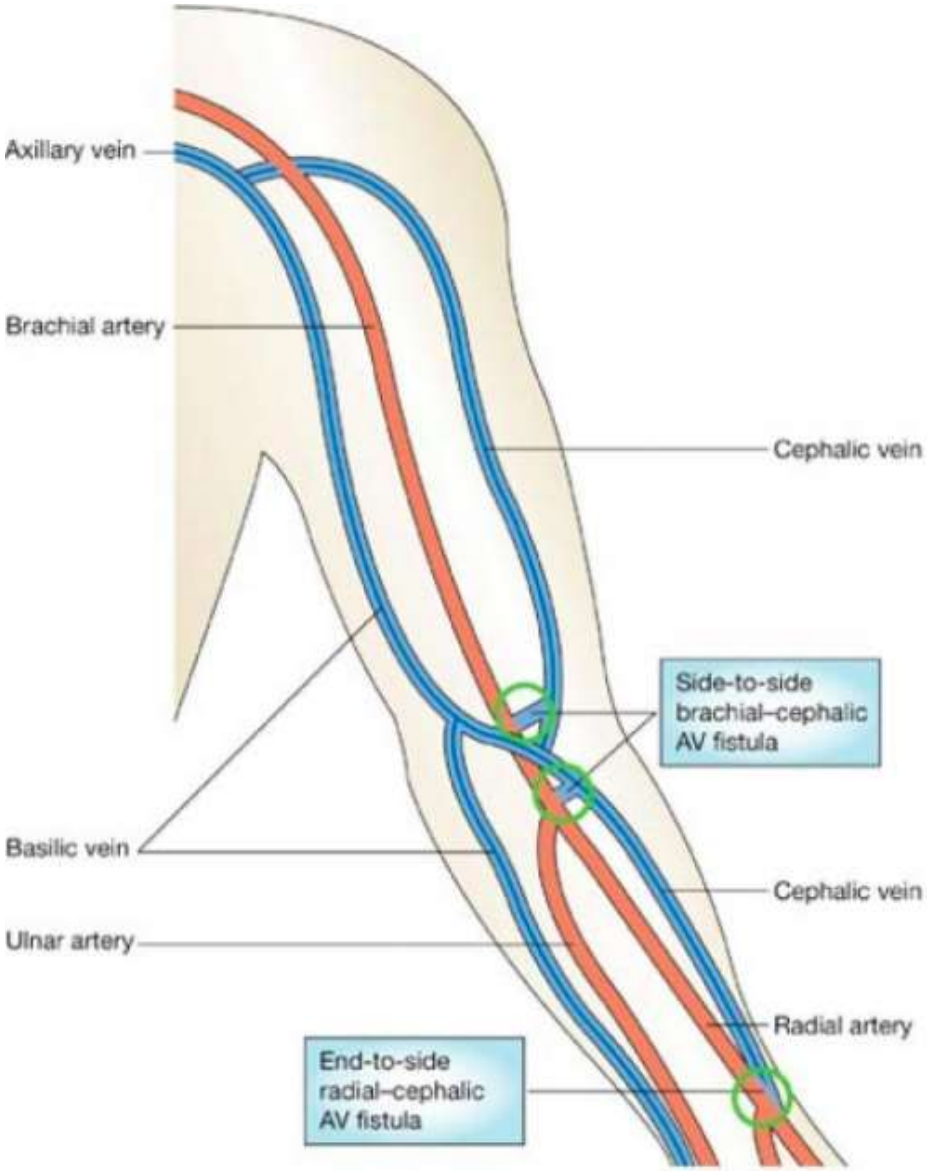
- The arterio-venous anastomosis can be achieved in different ways:

✓ Side to side

✓ End to side

✓ Side to end

✓ End to end


Axillary vein
Brachial artery
Cephalic vein
Side-to-side
brachial–cephalic
AV fistula
Basilic vein
Cephalic vein
Ulnar artery
Radial artery
End-to-side
radial–cephalic
AV fistula

ADEQUATE ARTERIOVERNOUS FISTULA

Defined as an AV fistula:

- that has a flow of greater than 600 ml/min
- diameter of greater than 0.6 cm
- approximately 0.6 cm from the skin surface

CLINICAL PROBLEM WITH ARTERIOVENOUS FISTULA

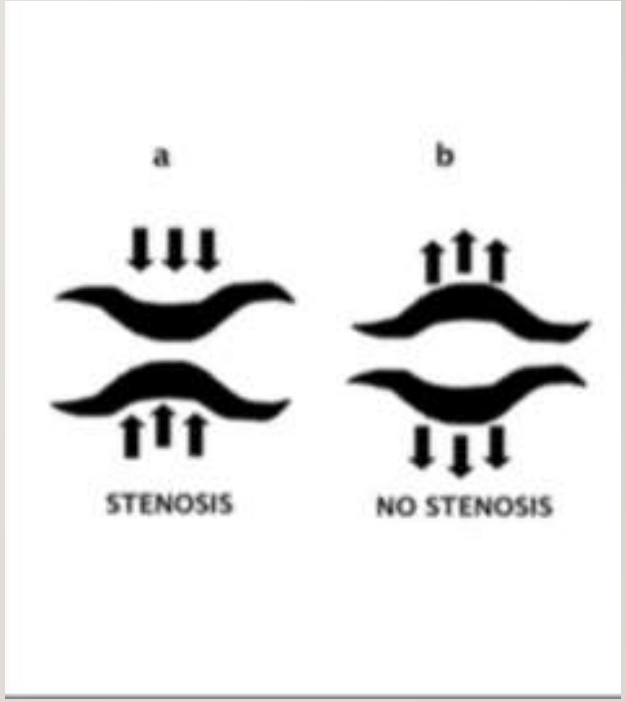
- It has a significant problem with early and late failures
- Early: never matures for adequate dialysis, or failed within 3 months of starting dialysis
- Both early and late failures are characterized by stenosis

PATHOLOGY INVOLVED IN FISTULA STENOSIS

1. Neointimal hyperplasia: - involves smooth muscle cells, myofibroblast and endothelial cells within the microvessels.

2. Adverse vascular remodelling: - involves vasoconstriction and inability to dilate adequately.

3. Combination of both



NORMAL PHYSIOLOGY OF AV FISTULA MATURATION

Wall shear stress

- shear stress is frictional force exerted by blood on vessel wall. The magnitude of shear stress is directly linked to blood flow.

- increase in shear stress results in endothelial quiescence (inactivated), and release of anti-inflammatory ,anticoagulant mediators as well as nitric oxide and reactive oxygen species.

- These result in vasodilatation and reduction on neointimal hyperplasia (beneficial vascular remodelling)

- Pattern of shear stress also plays a role. Oscillatory shear stress (in comparison to normal laminar flow) results in proinflammatory state and increased cellular proliferation.

PATHOGENESIS OF AV FISTULA FAILURE

1. DEMOGRAPHIC AND CLINICAL FACTORS:

- Increasing age
- Female gender
- Diabetes
- Presence of coronary and peripheral vascular disease
- Caucasian

- Skill of the operating surgeon: vessel handling, kinking, torsion, and vessel injury.
- Vessel quality and /or baseline genetic predisposition.

UPSTREAM EVENTS

- High level of laminar shear stress promotes vascular dilatation and lack on neointimal hyperplasia
- In contrast low level of LAMINAR shear stress (oscillatory) shear stress reduce vascular dilatation and promotes neointimal hyperplasia
- In AV fistula failure, there is ”bad” haemodynamic profile following surgery.
- Surgical injuries also play a role: insertion of dialysis needle, angioplasty can exacerbate the stenotic lesion.

DOWNSTREAM EVENTS

- In theory, neointimal hyperplasia is a result of migration of smooth muscle cells and myofibroblast from the media to the intima. The process is mediated by various mediators such as :insulin-like growth factor 1, ICAM-1,MMP-9.
- Inhibition of the mediators can improve AV fistula survival through local application of cell, gene, or drug-based therapy
- Eg: Use of drug-eluting stent reduce in-stent coronary restenosis.

CLINICAL TRIAL CONCEPT

- There has been a lot of interest in the use of currently available agents that has potential to block smooth muscle proliferation, and thrombosis.
- Dipyridamole and fish oil were both shown to prevent stenosis.
- Use of Plavix, Sirolimus, Rosiglitazone
- Gelfoam wraps which are loaded with endothelial cells, which is placed around AVF at time of surgery: release mediator which promotes vasodilatation and inhibit neointimal hyperplasia.
- Perivascular wrap with antiproliferative agent: Paclitaxel-loaded wrap.
- Local perivascular delivery through endovascular balloon: injecting the antiproliferative agents into the adventitia of stenotic part through microsyringe.

REFERENCE

- *www.sin-italy.org/jnonline – www.jnephrol.com*
- European Society of Radiology

- THANK YOU.