How to improve AVF patency

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สถานการณ์

- NCD in Thailand (diabetes 8.9%-prediabetes?), obesity, fast food
- Nutrition ไทย หวาน เค็มจัด
- Renal failure- scarce renal transplanatation end up with AVF and PD
- Surgeon for access surgery - the bottle neck

How to achieve good patency in vascular access according to “phases of renal access creation”

1. Pre access
2. Access creation
3. Maturation
4. Late patency

Pre access

- Preserve renal function- NSAID
- Education-nutrition
- Vein preservation-dominant arm
- Arm exercise
- Early Referral
- Wait time-express way in virgin neck

Access creation

10-15% FAILURES

- Duplex Ultrasound: vein assessment (esp. obesity), central vein stenosis artery calcification
- Technique-microsurgical technique, Loupe
- Training – shortening learning curve
- Challenging groups-refer to experts

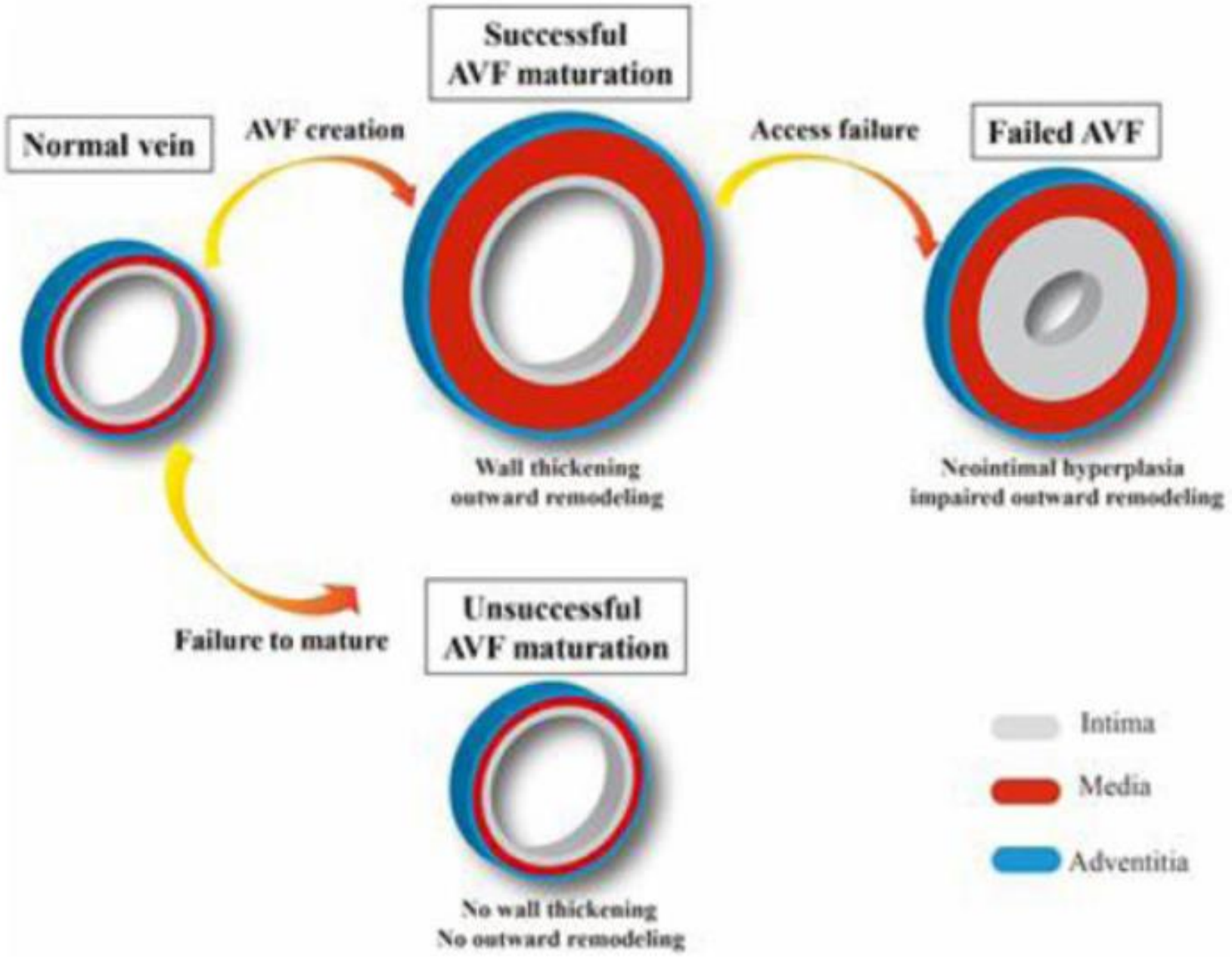
Maturation

20-25% Fail to mature (FTM)

- Atherosclerotic artery- poor inflow (ultrasound can detect)
- Stenosis: juxta-anastomotic stenosis, central vein stenosis: balloon assist maturation in the first 4 weeks

Late patency

- Dedicated team/centre
- Self care
- Cannulation practice: perfect
- Monitoring and Surveillance
- Managing v. aneurysms, central v stenosis
- Medications


Successful
AVF maturation
Normal vein
AVF creation
Access failure
Failed AVF
Wall thickening
outward remodeling
Neointimal hyperplasia
impaired outward remodeling
Failure to mature
Unsuccessful
AVF maturation
No wall thickening
No outward remodeling
Intima
Media
Adventitia

Late failure in the mature AVF

- In the setting of uremia and other systemic abnormalities, compounded with local injury as well as repeated needle puncture, even the mature AVF is predisposed to eventual failure. Neointimal hyperplasia worsens with time, typically leading to stenosis of the AVF venous limb.

1 Systemic abnormalities: ESRD patients have systemic abnormalities, such as uremia, systemic inflammation, endothelial dysfunction, lipid abnormalities, hyperparathyroidism, hyperphosphatemia and hypercalcemia. These abnormalities may predispose the vessel wall to inward remodeling and stenoses after AVF creation.

2. **Pre-existent vascular pathology:** The systemic abnormalities in ESRD patients induce accelerated atherosclerosis, vessel thickening, vascular calcification and stiffness

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REVIEW

Medical Adjuvant Treatment to Improve the Patency of Arteriovenous Fistulae and Grafts: A Systematic Review and Meta-analysis

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- The Cochrane Peripheral Vascular Diseases Group searched the for all randomised controlled trials (RCTs) investigating the effect of active drug versus placebo on patency. The primary outcome was fistula or graft patency rate.

Table 1. Type of AVF or graft used per study.

Adjuvant treatment	Type of AVF or graft	Study (first author
Aspirin	AVFs	Andrassy[13]
	AV shunt formation between the radial artery and the cephalic vein with a Teflon adapter and straight silastic arteriovenous-shunt material	Harter[19]
Dipyridamole	Prosthetic arteriovenous expanded PTFE grafts	Sreedhara[23]
Dipyridamole + aspirin	Prosthetic arteriovenous expanded PTFE grafts	Sreedhara[23]
Ticlopidine	AVFs	Fiskerstrand[16]
		Grontoft[17]
	Majority had native, distal arm AVFs with 16 artificial grafts, 9 with free vein grafts	Grontoft[18,a]
Warfarin	PTFE grafts	Crowther[14]
Fish oil	Synthetic AV grafts	Lok[8]
	PTFE grafts	Schmitz[9]
Clopidogrel	AVFs	Dember[6]
		Ghorbani[7]
Sulphinpyrazone	Mixture of AVFs, bovine grafts and 1 shunt	Michie[21,b]
PRT-201	AV grafts	Dwivedi[15]
	AVFs	Hye[20]
		Peden[22]

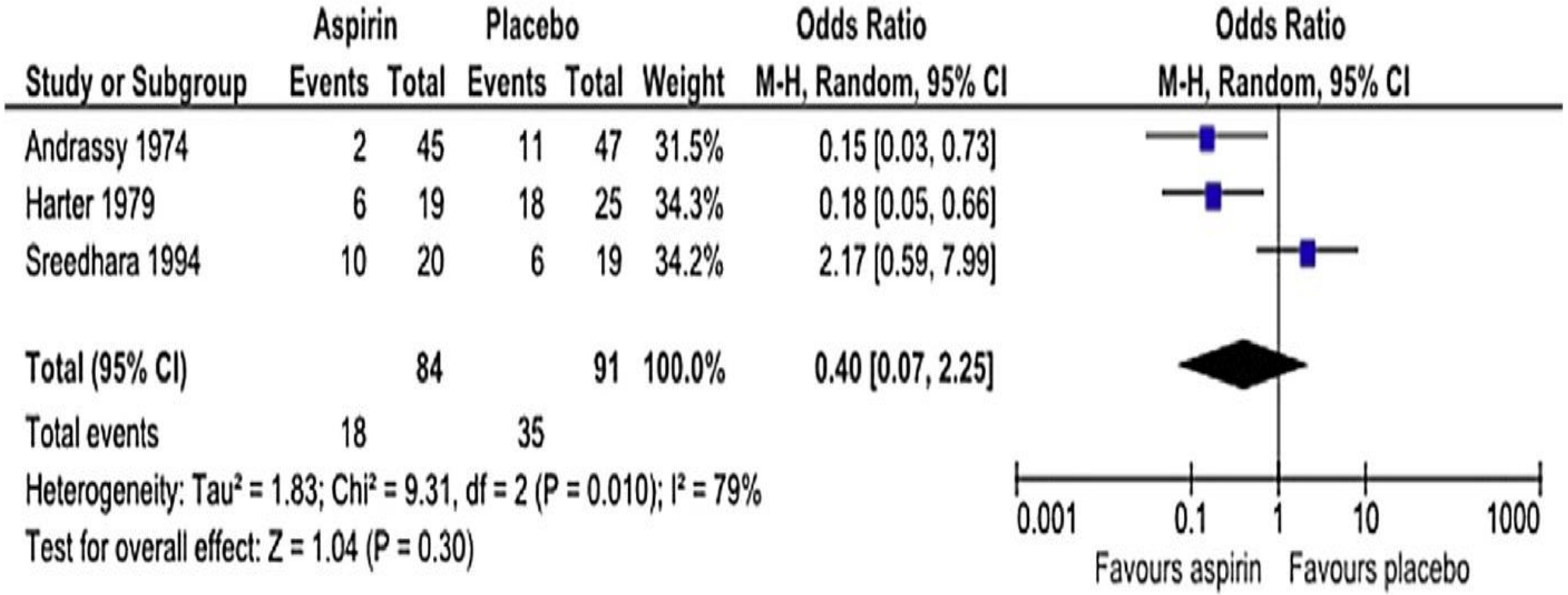


Figure 3. Forest plot of the meta-analysis of aspirin trials.

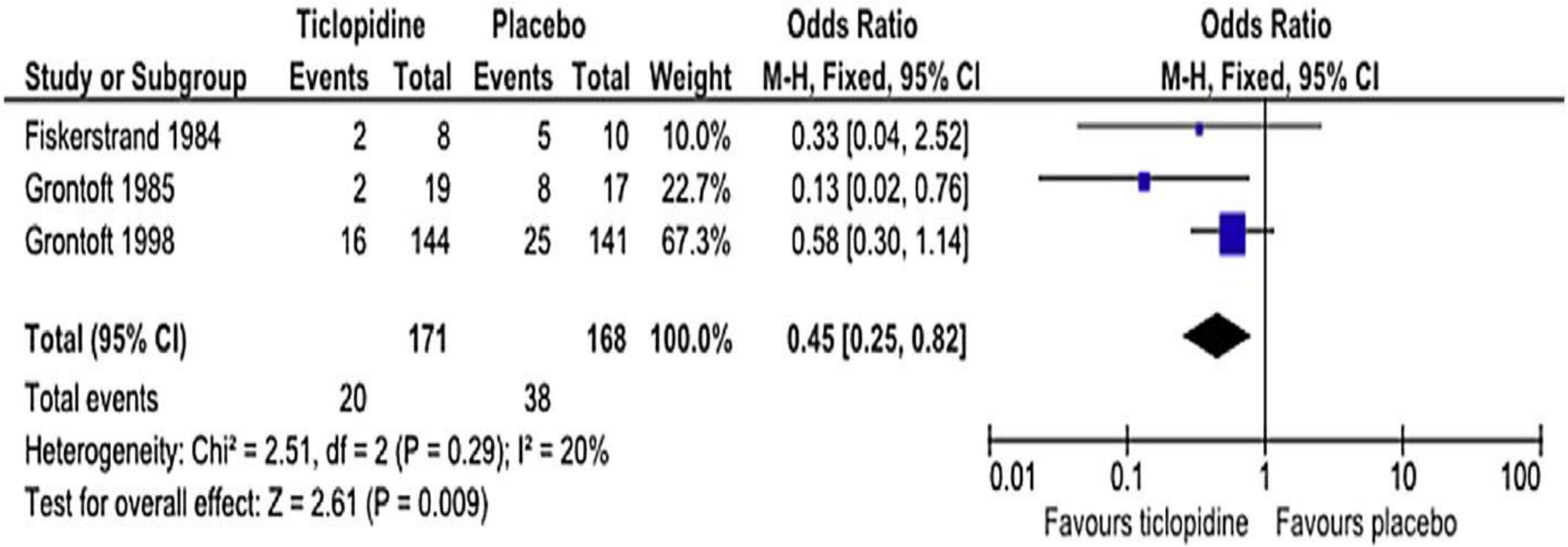


Figure 4. Forest plot of the meta-analysis of ticlopidine trials.

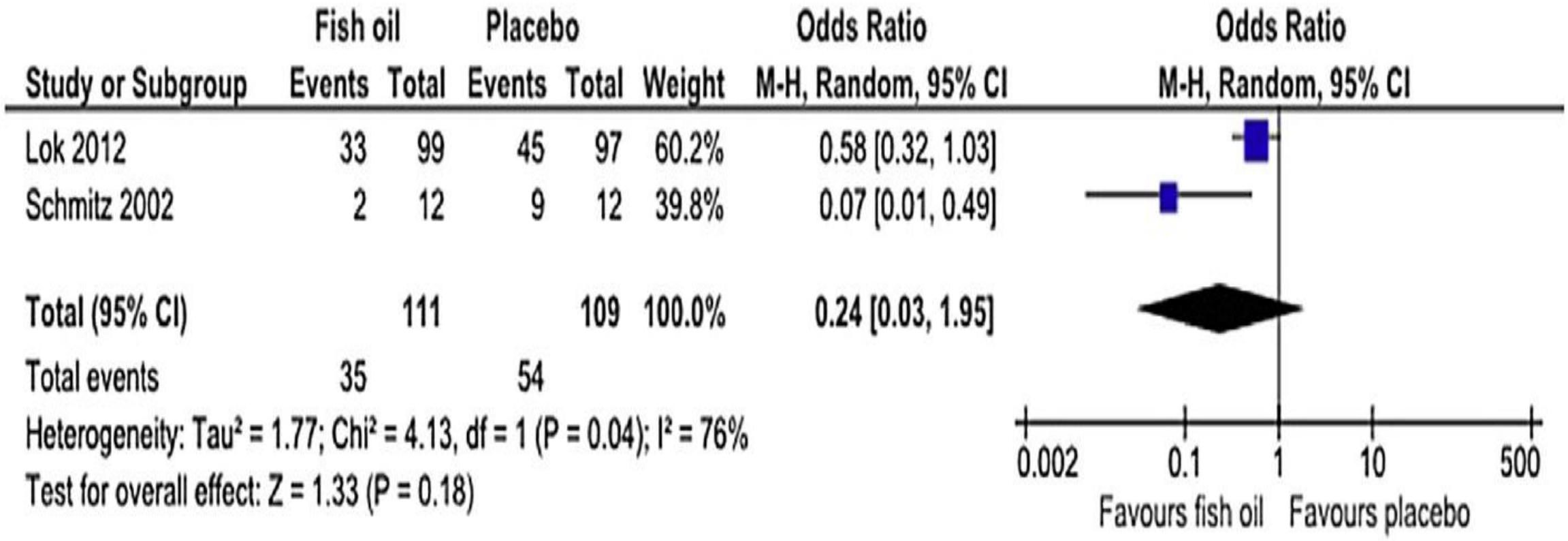
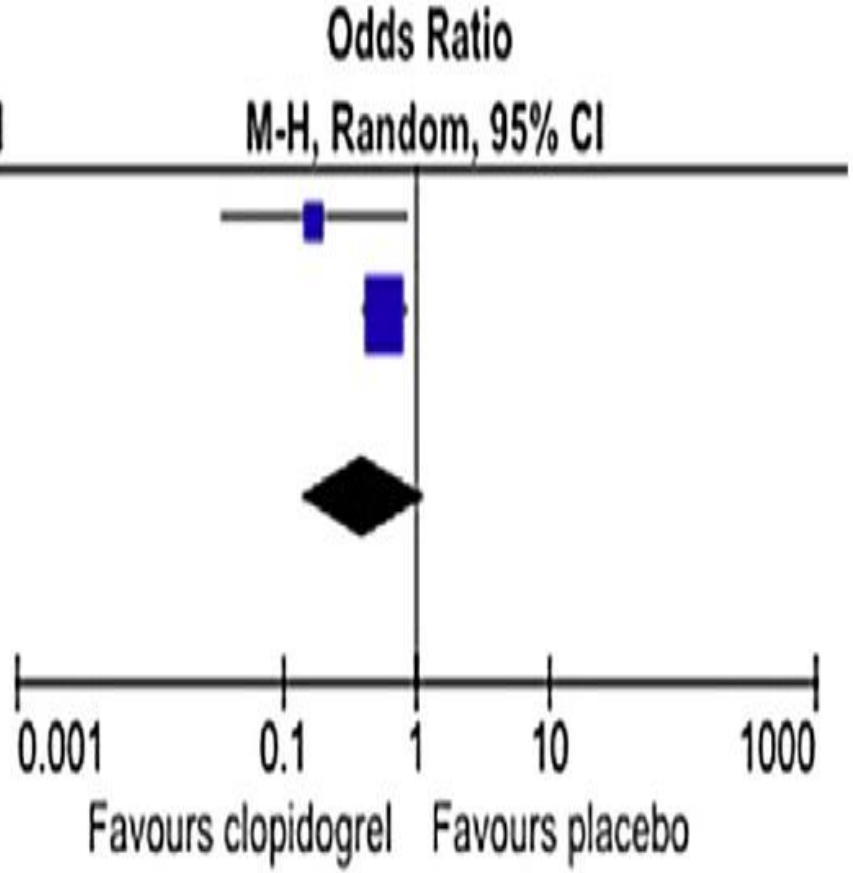


Figure 5. Forest plot of the meta-analysis of fish oil trials.

Study or Subgroup	Clopidogrel Events	Total	Placebo Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Ghorbani 2009 (1)	2	46	10	47	29.5%	0.17 [0.03, 0.82]
Dember 2008 (2)	53	436	84	430	70.5%	0.57 [0.39, 0.83]
Total (95% CI)		482		477	100.0%	0.40 [0.13, 1.19]
Total events	55		94			

Heterogeneity: $Tau^2 = 0.41$; $Chi^2 = 2.18$, df = 1 (P = 0.14); $I^2 = 54\%$

Test for overall effect: Z = 1.65 (P = 0.10)



Role of Cilostazol in Vascular Access Surgery

Novel therapies to reduce neointimal hyperplasia

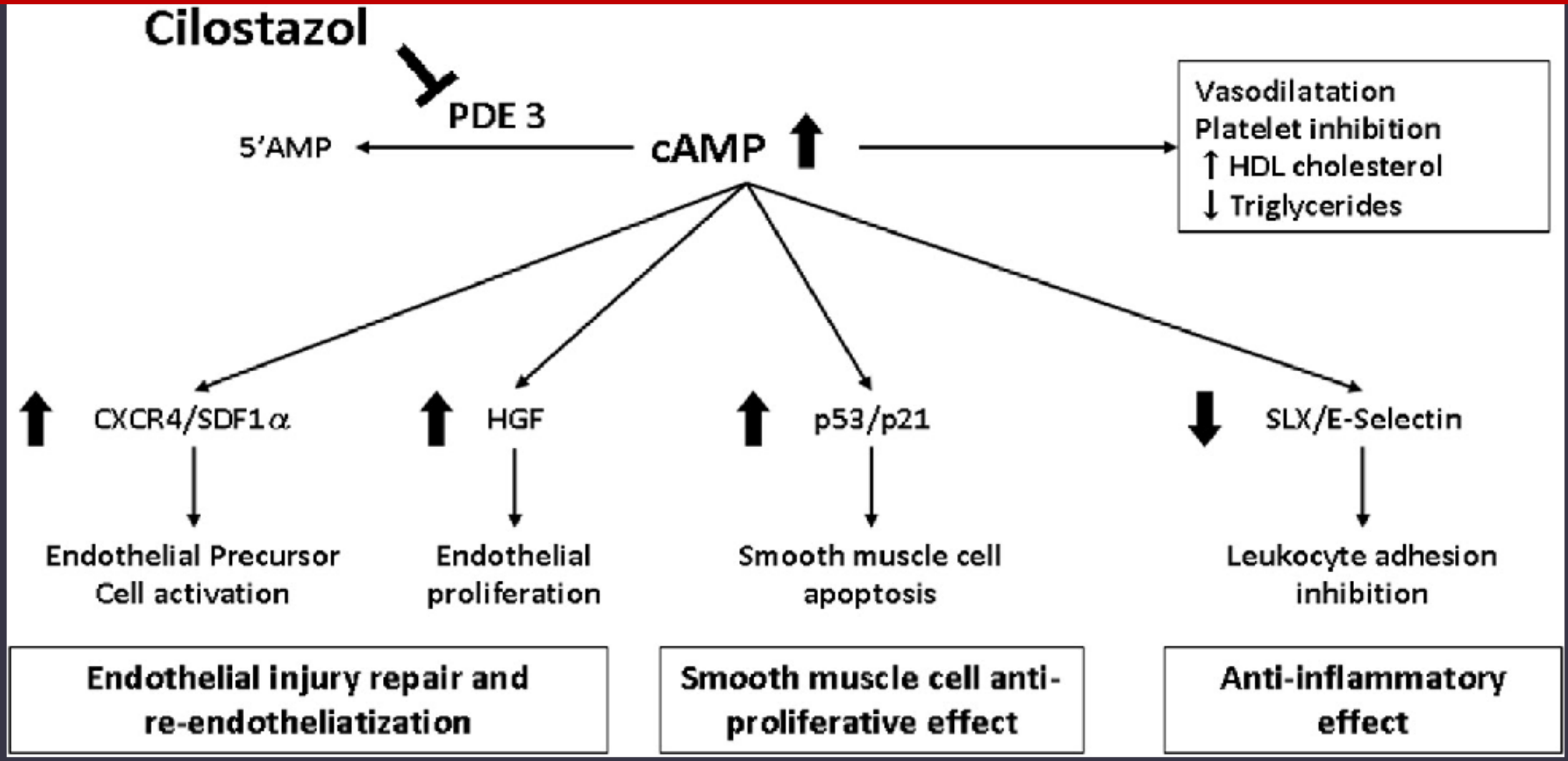
Table 5. Novel therapies to reduce neointimal hyperplasia

Agent	Potential therapeutic benefit(s)	Clinical outcomes reported
Cilostazol	Anti-platelet effect	Improved patency of angioplasty in haemodialysis patients with 100 mg Cilostazol.
	Inhibition of VSMC proliferation Inhibition of neointimal hyperplasia	Reduced restenosis following coronary angioplasty.
Statins	Anti-platelet effect Inhibition of VSMC proliferation	Improved AVF patency in retrospective analysis (71.5 versus 39.1%). Improved infrainguinal bypass graft patency in 2× retrospective analyses.
	Enhanced endothelial function	
Allogenic endothelial cell implants	Enhanced endothelial function	Safety of technique demonstrated. No clinical outcomes as yet.
NO	Enhance endothelial function	Minimal benefit on restenosis following coronary angioplasty, with high incidence side effects.
MAP kinase inhibitors	Inhibit VSMC proliferation	Experimental models only.

Reducing neointimal hyperplasia via VSMC inhibition and restoration of endothelial integrity

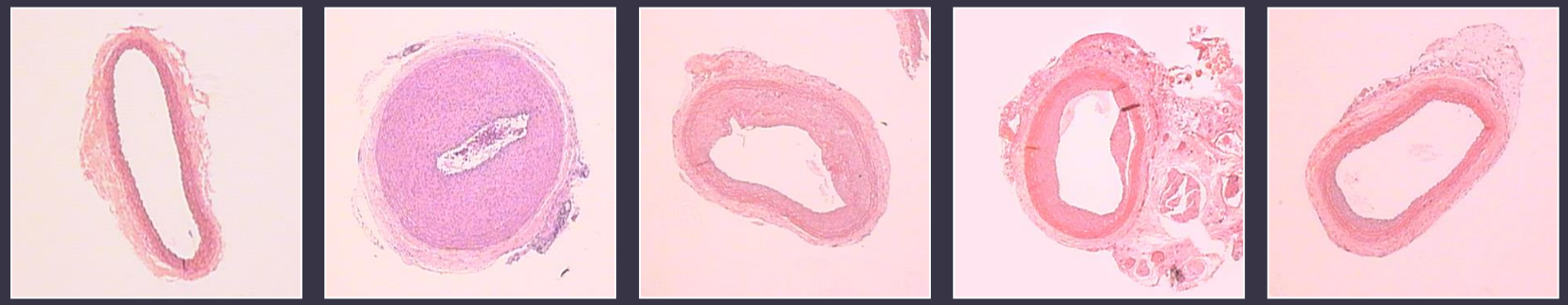
Jackson AJ., et al. Nephro Dial Transplant 2012:27 (5):20

What about the roles of Cilostazol ??

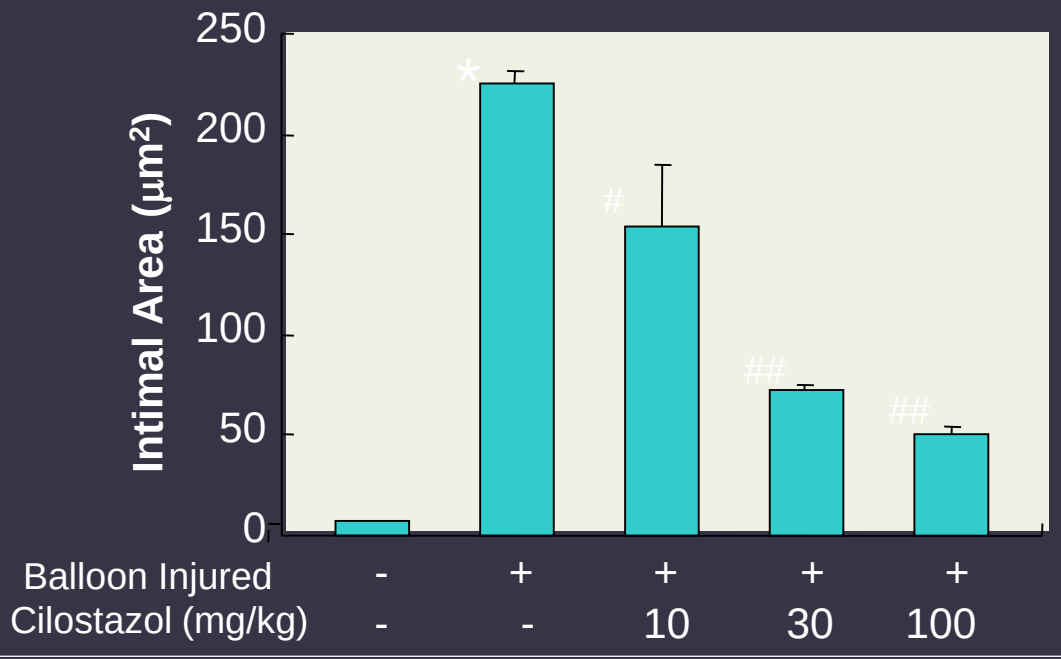


Ann Vasc Surg 2017; 41: 300–3

Effects on Neointimal Formation Rat Carotid Artery



A B C D E



A. Control
B. Balloon Injured
C. Cilostazol 10 mg/kg
D. Cilostazol 30 mg/kg
E. Cilostazol 100 mg/kg

Cilostazol inhibited high glucose-induced VSMC proliferation.

*p < 0.01 vs control
#p < 0.05, ##p < 0.01 vs balloon injured.

Lee IK et al. Hypertension. 2005 Apr;45(4):552-6

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Cilostazol May Improve Maturation Rates and Durability of Vascular Access for Hemodialysis

Todd E. Russell, MD[1], Gregory C. Kasper, MD[1], Andrew J. Seiwert, MD, FACS[1], Anthony J. Comerota, MD, FACS, FACC[1,2], and Fedor Lurie, MD, PhD[1,2]

Abstract

Cilostazol is effective in controlling pathophysiological pathways similar or identical to those involved in nonmaturation and failure of the arteriovenous access. This case–control study examined whether cilostazol would improve maturation rates and durability of vascular access for hemodialysis. The treatment group included 33 patients who received cilostazol for ≥30 days prior to creation of a dialysis access and continued with cilostazol therapy for ≥60 days after surgery. The matched (gender, age, race, diabetes, and the year of surgery) control group included 116 patients who underwent the same procedure but did not receive cilostazol prior to and at least 3 months after surgery. Primary outcomes were maturation and, for those that matured, time of functioning access, defined as the time from the first use to irreparable failure of the access. Secondary outcomes were time to maturation, complications, and time to first complication. Study group patients were 3.8 times more likely to experience fistula maturation compared to the controls (88% vs 66%, RR = 3.8, 95% confidence interval: 1.3-11.6, $P = .016$). Fewer patients in the study group had complications (76% vs 92%, $P = .025$), and the time from construction of the fistula to the first complication was longer (345.6 ± 441 days vs 198.3 ± 185.0 days, $P = .025$). Time to maturation was similar in both groups (119.3 ± 62.9 days vs 100.2 ± 61.7 days, $P = .2$). However, once matured, time to failure was significantly longer in the treatment group (903.7 ± 543.6 vs 381.6 ± 317.2 days, $P = .001$). Multivariate analysis confirmed that the likelihood of maturation was significantly higher in the treatment group patients. These results suggest that dialysis access patients may benefit from preoperative and postoperative cilostazol therapy. If confirmed by a randomized trial, this treatment will have a major beneficial impact on patients dependent on a well-functioning access for their hemodialysis.

Cilostazol Improves Maturation Rates and Durability of Vascular Accesss for Hemodialysis

- Case-controlled study
- Cilostazol can improve maturation rates and durability of vascular access for hemodialysis
- 33 patients who received cilostazol for >30 days before the creation of a dialysis access and continued with cilostazol therapy for >60 days after surgery

Russell T., et al. Journal of Vascular Surgery;2016:6

Cilostazol Improves Maturation Rates and Durability of Vascular Access for Hemodialysis

	Cilostazol (n=33)	Control (n=116)	Univariate analysis	Multivariate analysis
Fistula matured	88%	66%	OR=3.8, 95% CI: 1.3-11.6, P=0.016	OR=4.4, 95% CI: 1.2-16.9, P=0.03
Time to the first complication (days)	345.6±441	198.3±185	P=0.025	OR=9.3, 95% CI: 2.3-38.5
Time to failure (days)	903.7±543.6	381.6±317.2	P=0.001	OR=4.0, 95% CI: 1.3-12.1

Russell T., et al. Journal of Vascular Surgery;2016:6

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Thank you for your attention