Amputation-free survival between endovascular therapy and bypass surgery in CLI patients:
interim analysis of the CRITISCH registry*

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Clinic for Vascular Surgery

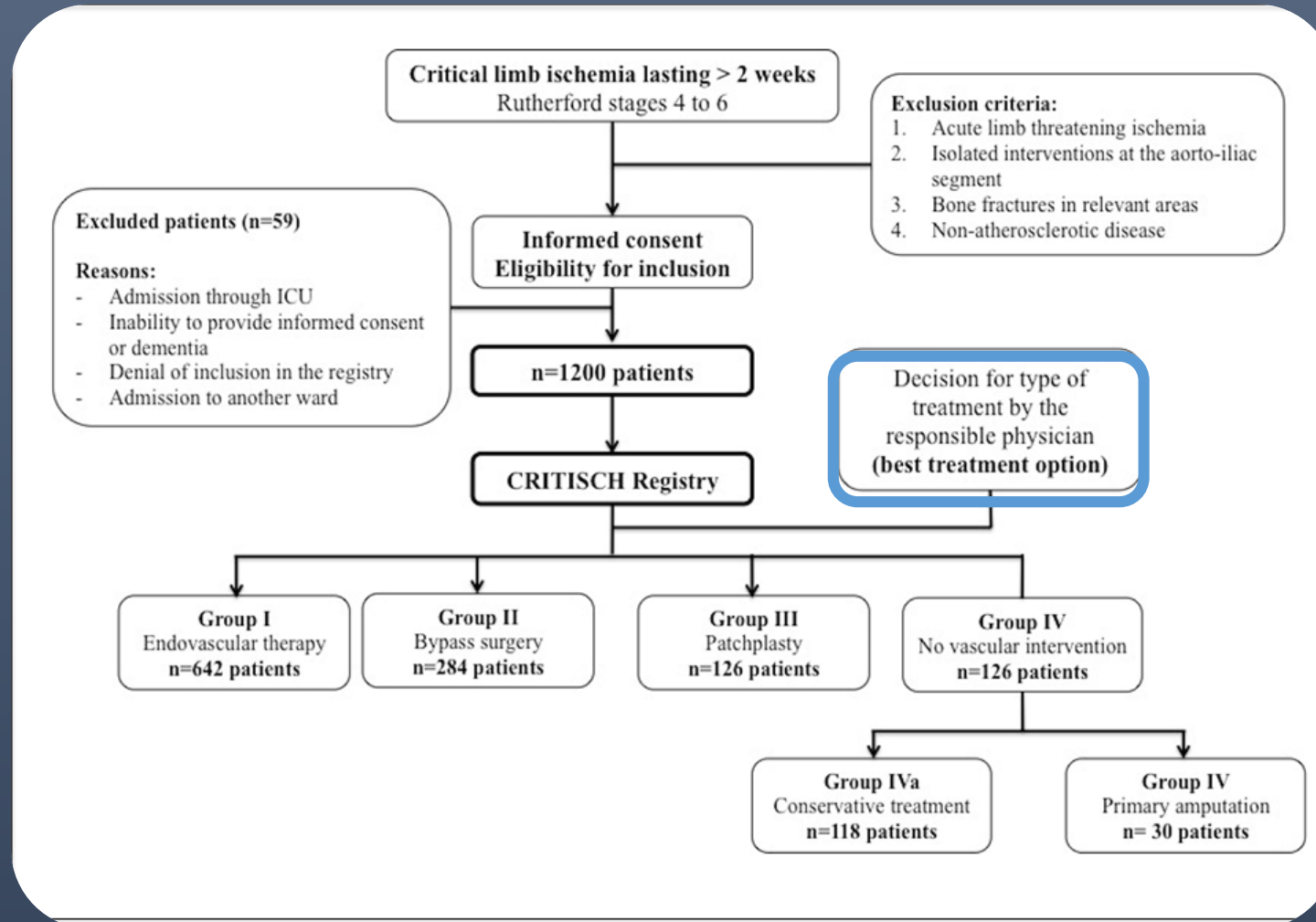St. Franziskus Hospital Muenster GmbH

Overview

Multicentre prospective interdisciplinary registry

Sponsors
DGG, DIGG

Recruitment time
20
months
01/2013-09/2014

27
vascular centers of excellence

1200
consecutive CLI patients
(Rutherford 4-6)

First-line treatments
- Endovascular
- Bypass surgery
- CFA patchplasty
- No vascular intervention
  - Conservative
  - Major amputation

Study design

In-hospital results
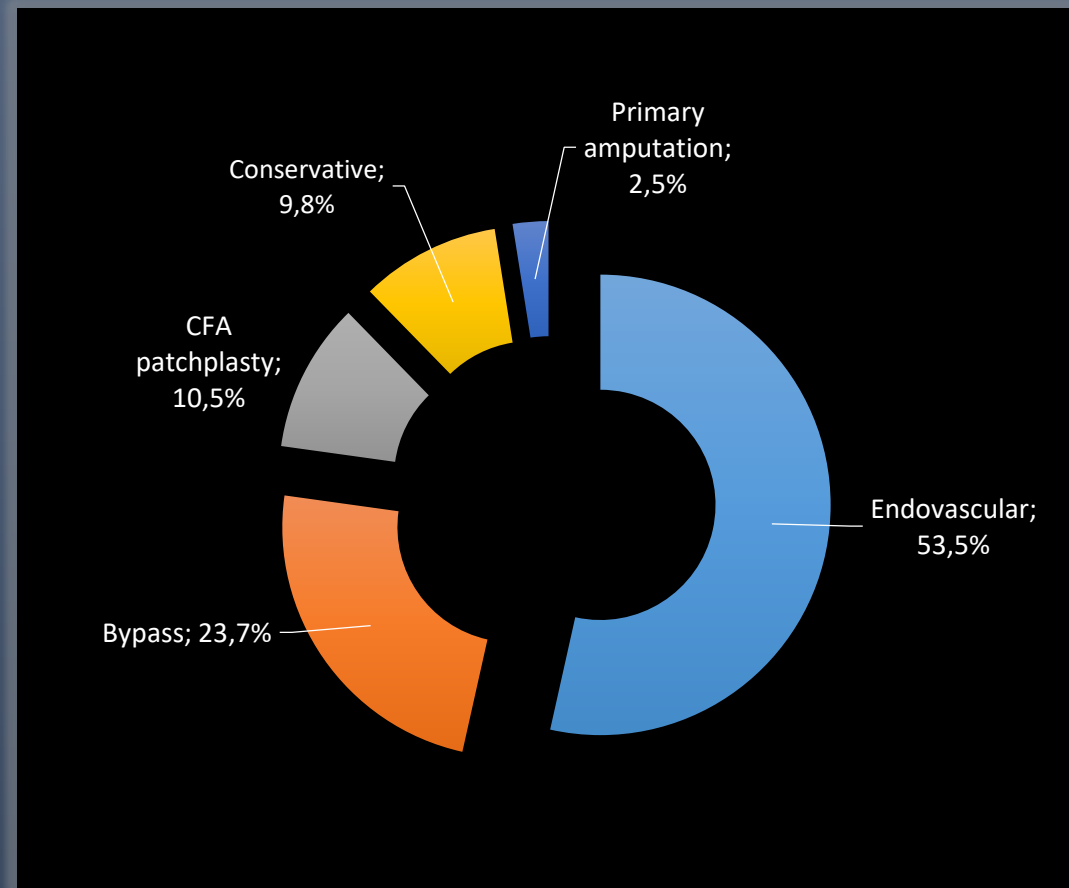
Risk factors for death and/or amputation	Odds Ratio
Coronary artery disease	2.96
Acute coronary syndrome < 6 months	3.67
ESRD (Dialysis or GFR<15)	3.31
Chronic kidney disease (Stage 3-4)	6.34
Bypass surgery	3.34

Chart labels: Primary amputation; 2,5% — Conservative; 9,8% — CFA patchplasty; 10,5% — Endovascular; 53,5% — Bypass; 23,7%

Bisdas T, Borowski M, Torsello G for the CRITISCH collaborators. Current practice of first-line treatments strategies in patients with critical limb ischemia. J Vasc Surg 2015;62:965-73

Interim analysis

- Preplanned power analysis

- 250 events (major amputation / death)

- No randomisation

- Cox-regression analysis

- Non-inferiority: 1-sided Wald-test
  - HR<1.33
  - α=0.58% (2.5% level of significance)
  - 80% power

Patients' characteristics

	Endovascular n=642	Bypass surgery n=284	P-value
Median age (years)	**75**	73	< 0.001
Males	405 (63%)	192 (68%)	0.206
Coronary artery disease	298 (46%)	118 (42%)	0.174
Previous myocardial infarction < 6 months	25 (4%)	17 (6%)	0.172
Renal insufficiency (60<eGFR<15)	**251 (39%)**	86 (30%)	< 0.001
Dialysis (eGFR<15)	**65 (10%)**	13 (5%)	0.006
Diabetes mellitus	310 (48%)	136 (48%)	0.943
Obesity	93 (14%)	40 (14%)	0.919
Previous vascular intervention/operation	251 (39%)	**139 (49%)**	0.006
Statins	359 (56%)	176 (62%)	0.097
TASC C/D	423 (66%)	**265 (93%)**	< 0.001
> 1 run-off vessels	469 (73%)	**253 (89%)**	< 0.001

Procedures

	Femoral vessels (n=347)		Popliteal vessels (n=272)		Tibial vessels (n=368)		Previous bypass (n=26)	
Group I Endovascular (N=642)	PTA only	125 (36.0%)	PTA only	104 (38.2%)	PTA only	259 (70.4%)	PTA only	8 (30.8%)
	PTA + Stent	141 (40.6%)	PTA + Stent	90 (33.1%)	PTA + Stent	24 (6.5%)	PTA + Stent	3 (11.5%)
	DCB	63 (18.2%)	DCB	53 (19.5%)	DCB	36 (9.8%)	DCB	2 (7.7%)
	DCS	6 (1.7%)	DCS	2 (0.7%)	DCS	12 (3.3%)	DCS	2 (7.7%)
	Other	38 (11.0%)	Other	32 (11.8%)	Other	22 (6.0%)	Other	12 (46.2%)
	Failed to cross	19 (5.5%)	Failed to cross	17 (6.3%)	Failed to cross	33 (9.0%)	Failed to cross	1 (3.8%)
Group II Bypass surgery (N=284)	Leg vein							151 (53.2%)
	Arm vein							11 (3.9%)
	Combined leg and arm vein							3 (1.1%)
	Dacron							32 (11.3%)
	PTFE							71 (25%)
	Other							22 (7.7%)

Selection criteria
Bypass surgery versus endovascular therapy

Selection criteria for bypass surgery	Odds Ratio (95% CI)
eGFR > 60 mL/min/1.73 m^2	2.00 (1.47 to 2.73)
At least 1 Run-off vessel	4.18 (2.73 to 6.40)
TASC II C/D lesions	8.99 (5.44 to 14.87)
Previous vascular intervention	1.4 (1.03 to 1.89)

Amputation-free suvival

FIGURE 1 Relation Between Treatment Strategy and AFS

Amputation-free survival

The rates were estimated by the Kaplan-Meier method and were only drawn if the standard error was <10%. AFS = amputation-free survival.
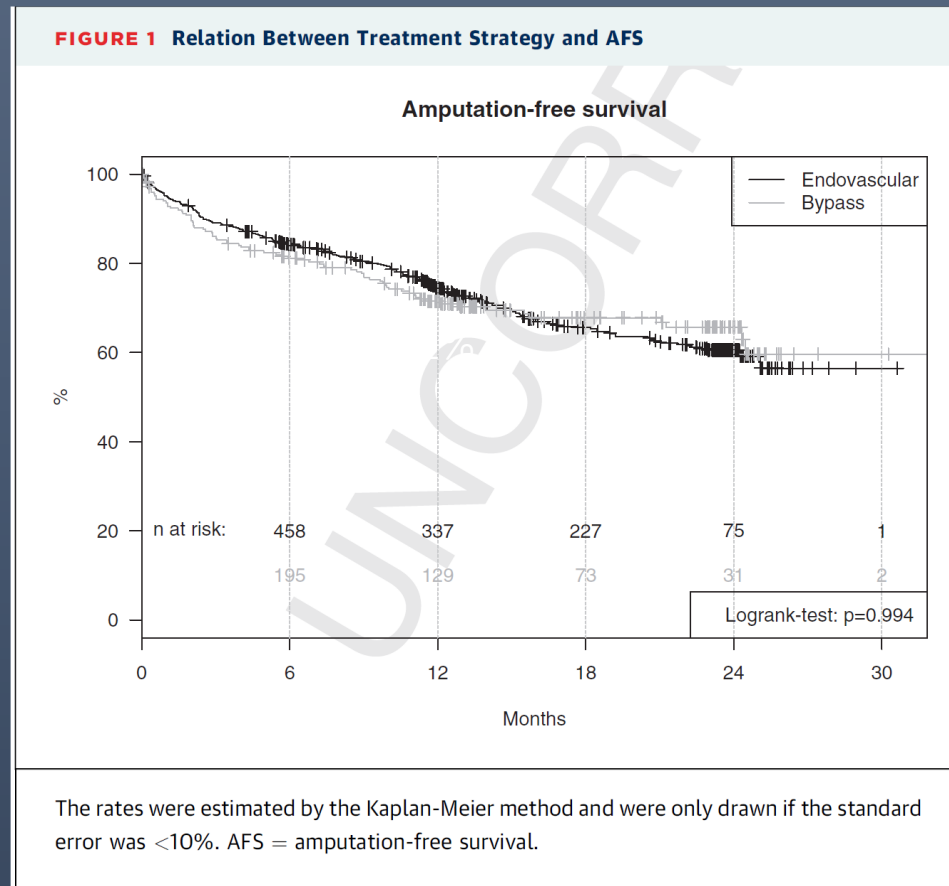
Cox regression analysis
HR: 0.91, 95%CI: 0.75-1.19

Wald test:
P=0.0029 < α=0.0058
1-sided (1- α)-CI=**1.29** < prespecified
HR:1.33

Statistical significant
non-inferiority of endovascular
versus bypass surgery
(at 2.5% level of significance)

Bisdas et al. JACC Cardiovasc Interv. 2016 Dec 26;9(24):2557-2565

Risk factors for amputation/death

TABLE 3 Amputation-Free Survival

	HR	95% CI	p Value
Endovascular vs. bypass	0.91	(0.70–1.19)	0.492
Age (x vs. x − 1)			
Modified PREVENT III risk score	1.12	(1.03–1.20)	0.004
Male vs. female			
Diabetes vs. no diabetes	1.25	(0.98–1.59)	0.074
eGFR <60 vs. eGFR ≥60 ml/min	1.44	(1.09–1.89)	0.010
Obesity vs. no obesity			
Angina vs. no angina			
PMI vs. no PMI			
TASC C/D/not applicable vs. A/B			
0 vs. 1 or more run-off vessels			
Rutherford 5 vs. Rutherford 4	0.80	(0.54–1.18)	0.253
Rutherford 6 vs. Rutherford 4	1.37	(0.90–2.08)	0.147
PVI vs. no PVI			
No statin vs. statin	1.24	(0.98–1.58)	0.078

Hazard ratios (HR) of AFS with 95% confidence intervals (CI) were obtained by multivariate Cox regression; to prevent overfitting, model building was carried out by all-subset variable selection based on the Akaike Information Criterion, so not all variables were included into the final model.

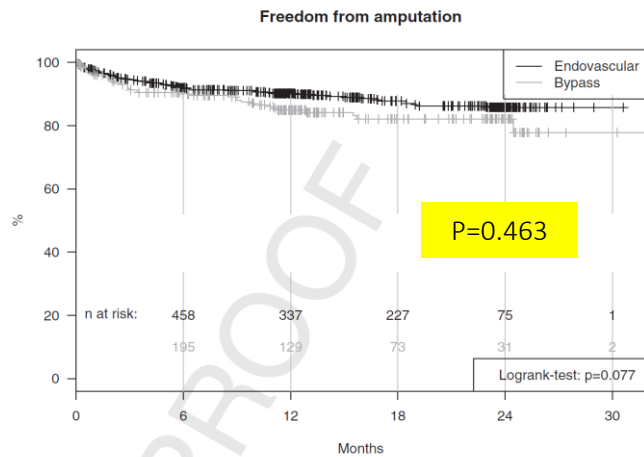PMI = previous myocardial infarction; other abbreviations as in Table 1.

Frailty

CKD

No statins

Secondary endpoints

FIGURE 2 Relation Between Treatment Strategy and Freedom From Amputation

Freedom from amputation

P=0.463

Logrank-test: p=0.077

The rates were estimated by the Kaplan-Meier method and were only drawn if the standard error was <10%.
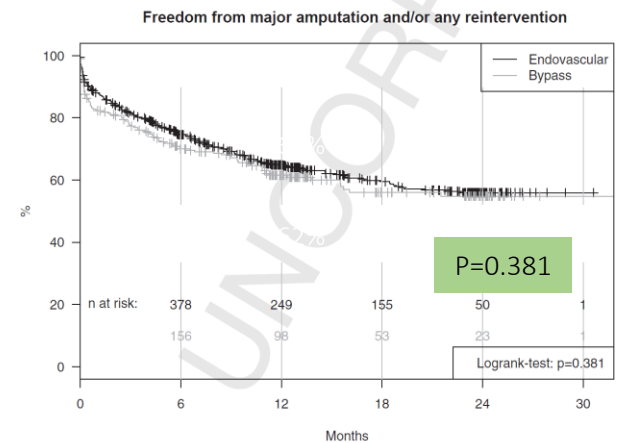
Freedom from amputation

FIGURE 3 Relation Between Treatment Strategy and Overall Survival
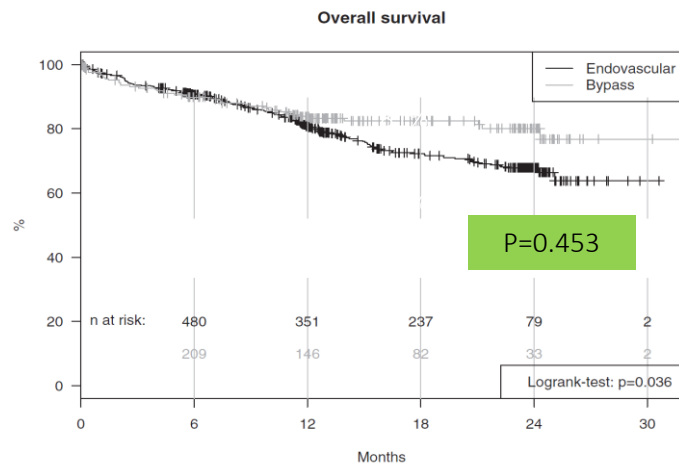
Overall survival

P=0.453

Logrank-test: p=0.036

The rates were estimated by the Kaplan-Meier method and were only drawn if the standard error was <10%.

Survival

FIGURE 4 Relation Between Treatment Strategy and Freedom From Major Amputation and/or Any Reintervention at the Index Limb

Freedom from major amputation and/or any reintervention

P=0.381

Logrank-test: p=0.381

The rates were estimated by the Kaplan-Meier method and were only drawn if the standard error was <10%.

Freedom from major amputation / any reintervention

Conclusions

- When physicians are free to individualize the therapy in CLI patients, endovascular therapy was non inferior to bypass surgery

- Future research should focus on comparison between endo and bypass in specific cohorts of patients

- CRITISCH registry showed that frail patients or patients with CKD are such specific cohorts requiring further analysis