Challenges of Endovascular Therapy in Patients with Critical Limb Ischemia

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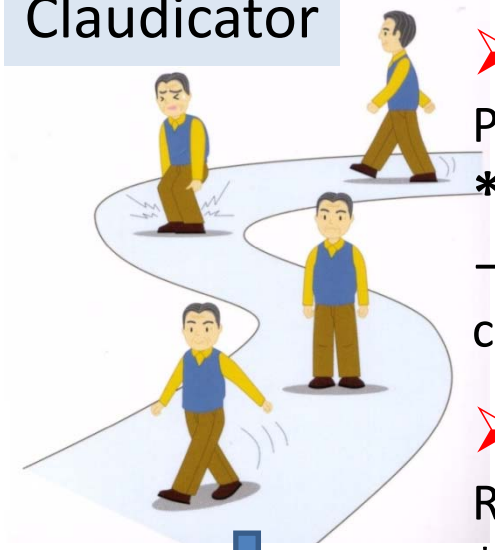
Treatment Strategy for Patients with peripheral artery disease (PAD)

Claudicator



Stable angina pectoris (SAP)

Optimal therapy

➢**Claudicator**

Pharmacotherapy+supervised exercise

*Suspected proximal lesion

→Revascularization is advised before conservative therapy.

➢**Critical limb ischemia (CLI)**

Revascularization

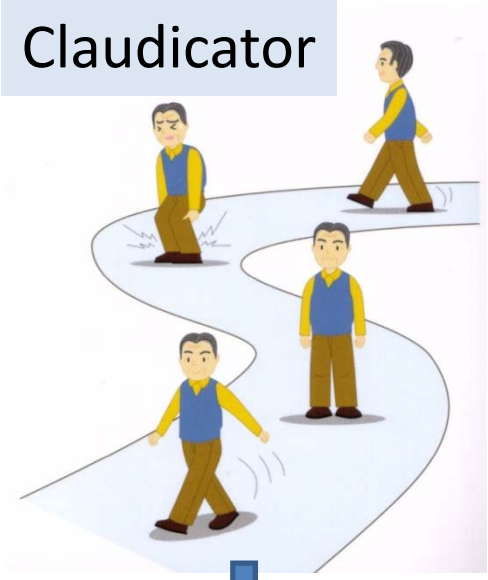
*No other pharmacotherapy can be recommended for treatment of CLI [TASC II recommendation 28].

CLI

Acute coronary syndrome (ACS)

Epidemiology of patients with PAD (peripheral arterial disease, claudicator)

Claudicator



Stable angina pectoris (SAP)

5-year outcome in the patient with intermittent claudication (IC)

Limb morbidity

- Stable claudication 70-80%
- Worsening claudication 10-20%
- Critical limb ischemia 5-10%

CV morbidity and mortality

- Mortality 10-15%
  75%: CV causes
  25%: Non CV

➢**5-year clinical course of leg** in IC Pt is surprisingly stable in most cases. Major amputation is a relatively rare outcome of claudication, with only **1% to 3.3%** of patients with IC needing major amputation over 5 years

➢5-year mortality in Pts with IC is 10-15% and mostly secondary to cardiovascular (CV) disease

TASC II

Epidemiology of patients with PAD (peripheral arterial disease, critical limb ischemia)

1-year outcome in the Pt with CLI

Limb morbidity and mortality

- Alive with two limbs 45%
- Amputation 30%
- Mortality 25%

➢Clinical course of limb and prognosis in Pt with critical limb ischemia are extremely poor. Approximately half these patients die or undergo major amputation within one year

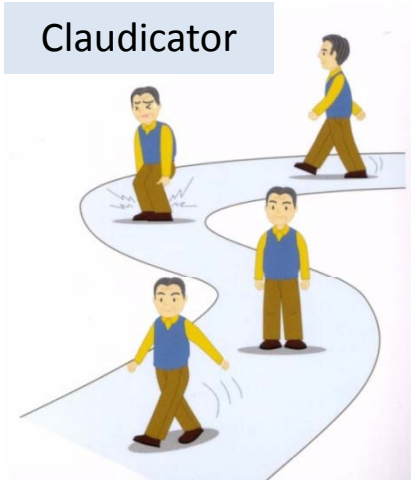
➢Surprisingly, more than half the patients with below-knee major amputation for ischemic disease had absolutely no symptoms of leg ischemia as recently as 6 months before

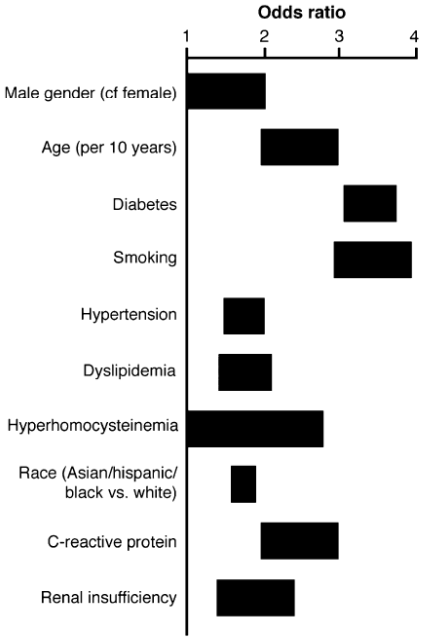
Acute coronary syndrome (ACS)

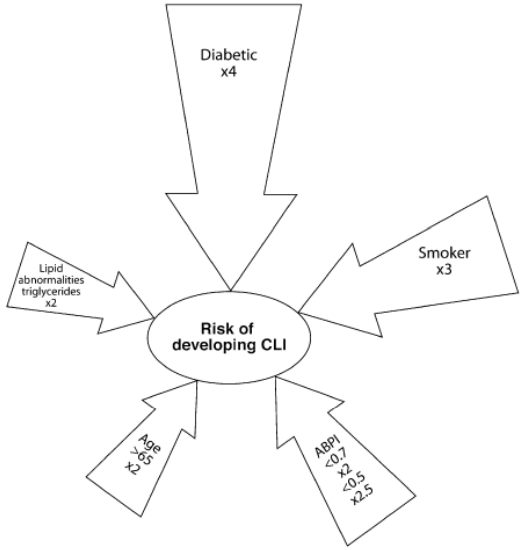
TASC II

Clinical course of patients with PAD

Claudicator







CLI

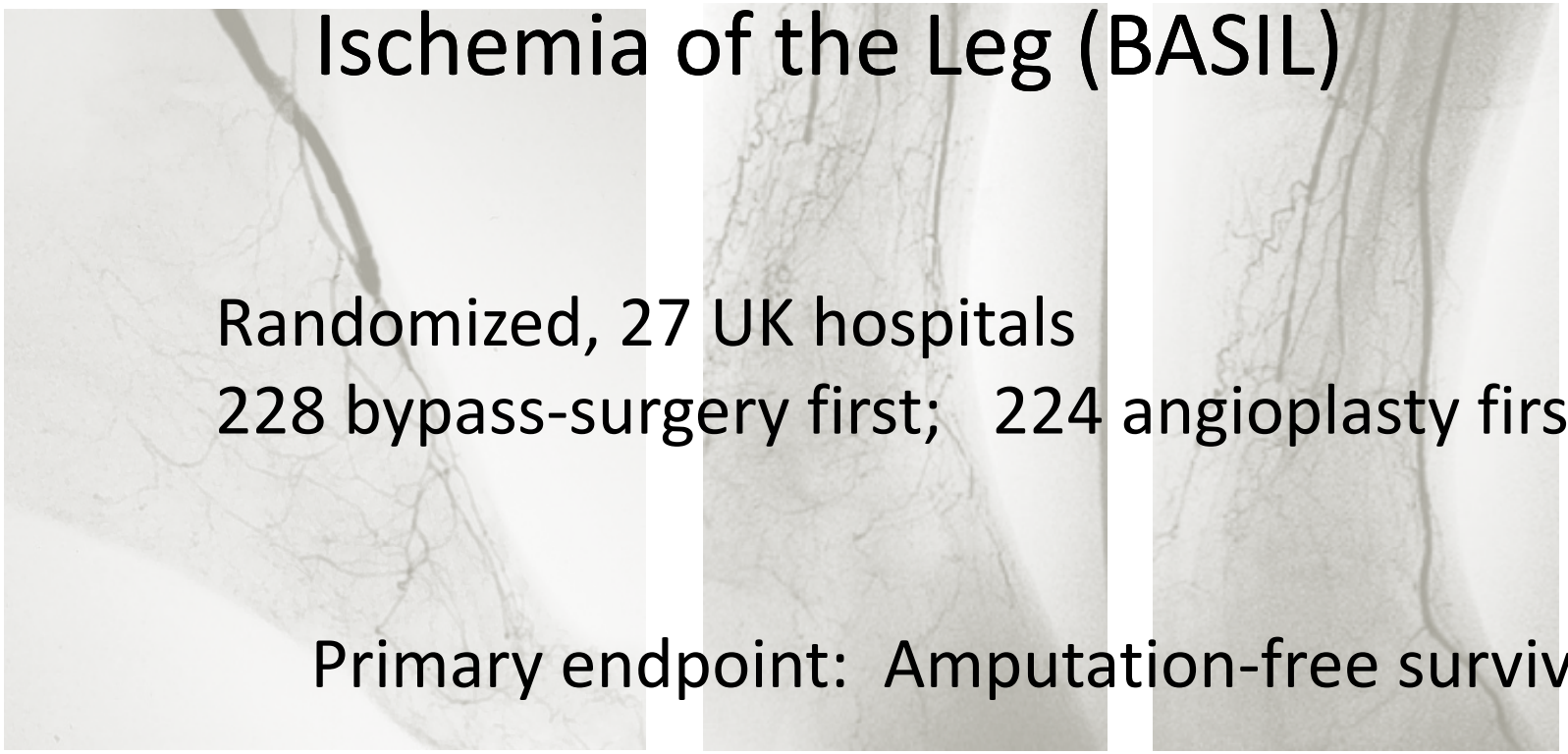
Normal subjects → **PAD** → **CLI** → **Amputation・death**

CLI is an important clinical issue in pts with PAD because of the high risk of amputation and death if optimal revascularization is not possible

TASC II

Surgery vs. Endovascular Therapy (EVT)

Bypass vs. Angioplasty in Severe Ischemia of the Leg (BASIL)



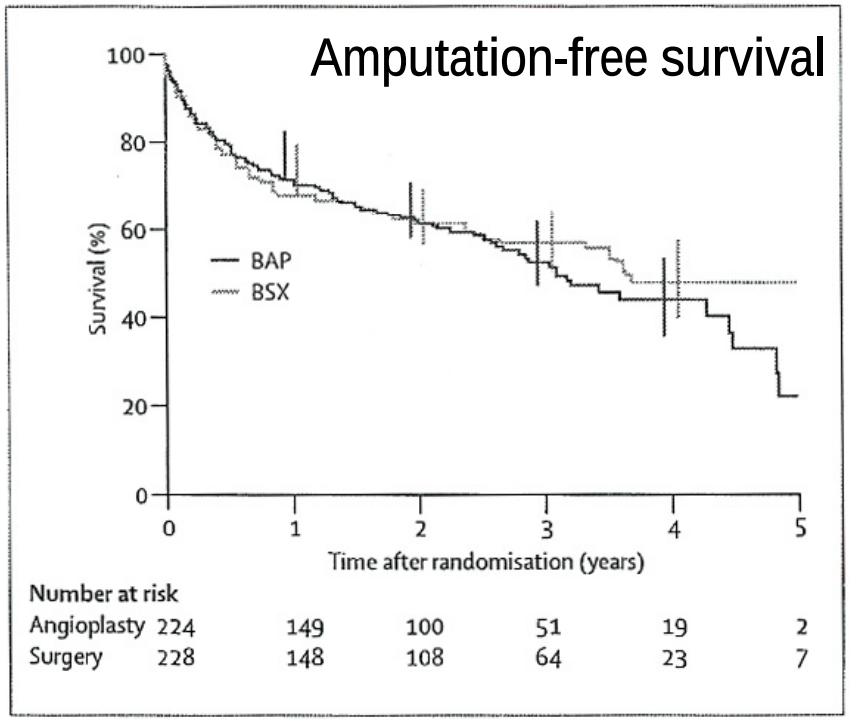
Randomized, 27 UK hospitals
228 bypass-surgery first; 224 angioplasty first

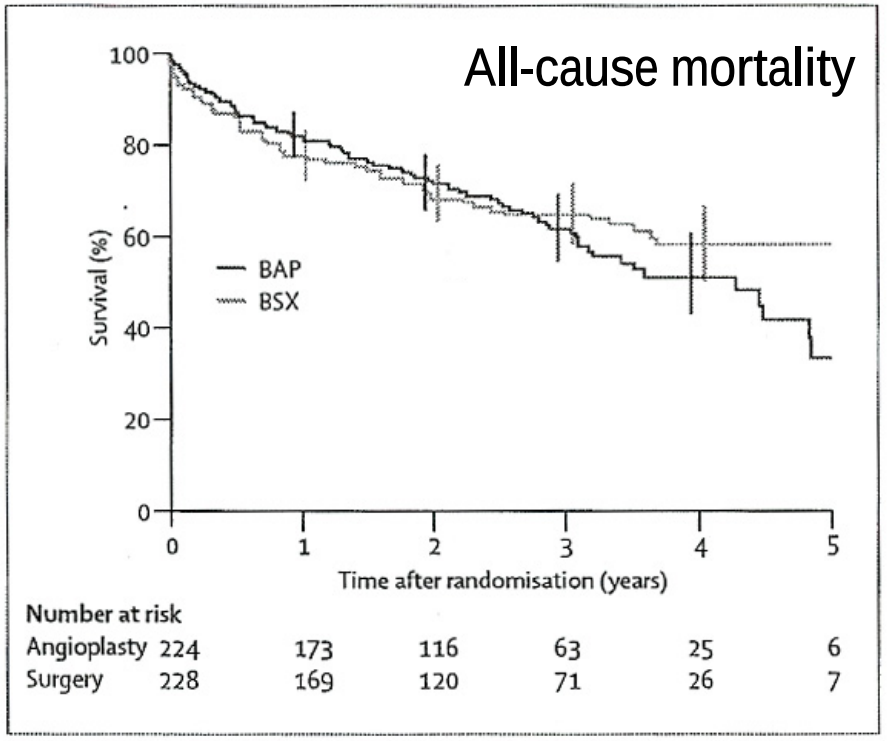
Primary endpoint: Amputation-free survival

Lancet. 2005;36: 1925-34.

Surgery vs. Endovascular Therapy (EVT)

Bypass vs. Angioplasty in Severe Ischemia of the Leg (BASIL)



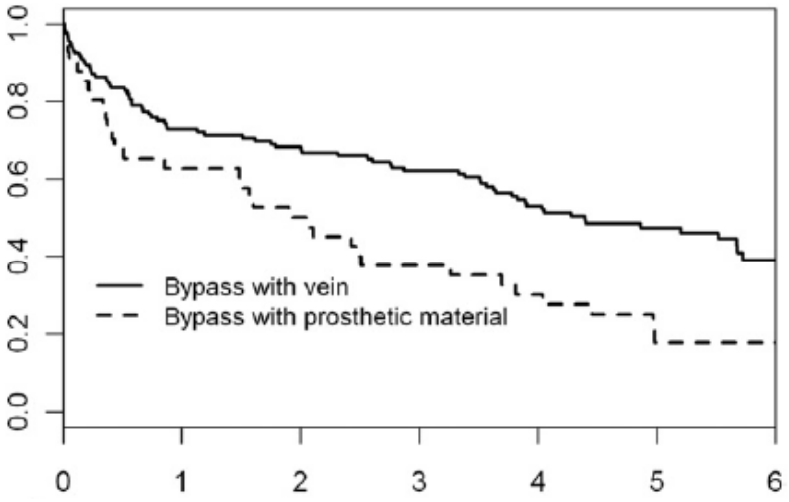


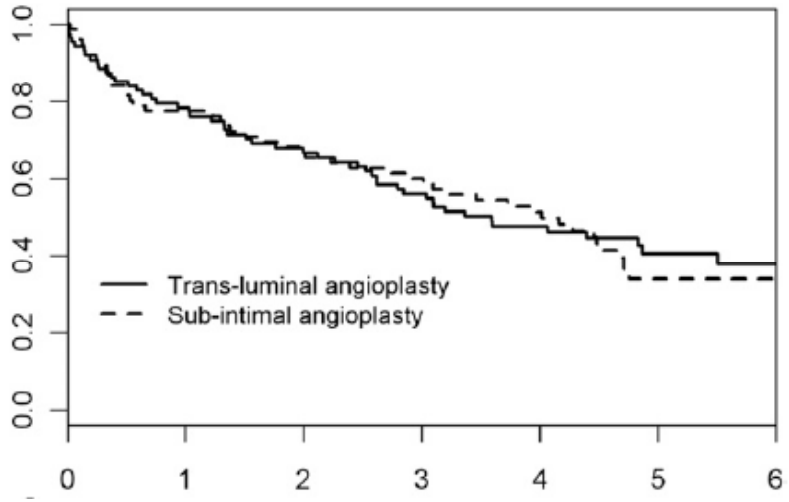
Lancet. 2005;36: 1925-34.

Bypass vs. Angioplasty in Severe Ischemia of the Leg (BASIL)

- Analysis of amputation-free and overall survival by treatment received -

AFS (amputation-free survival) for patients undergoing bypass therapy (SVG vs. PTFE) and angioplasty (Sub vs. Intra)



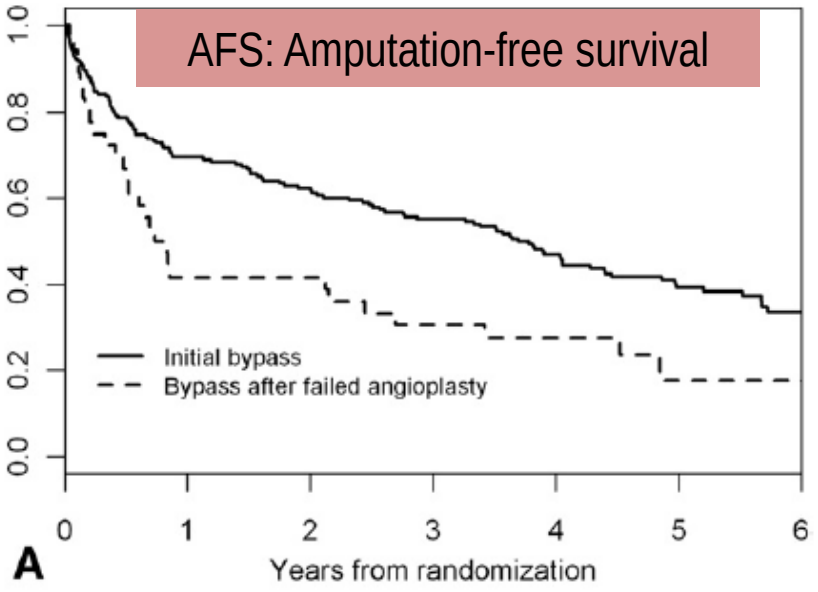


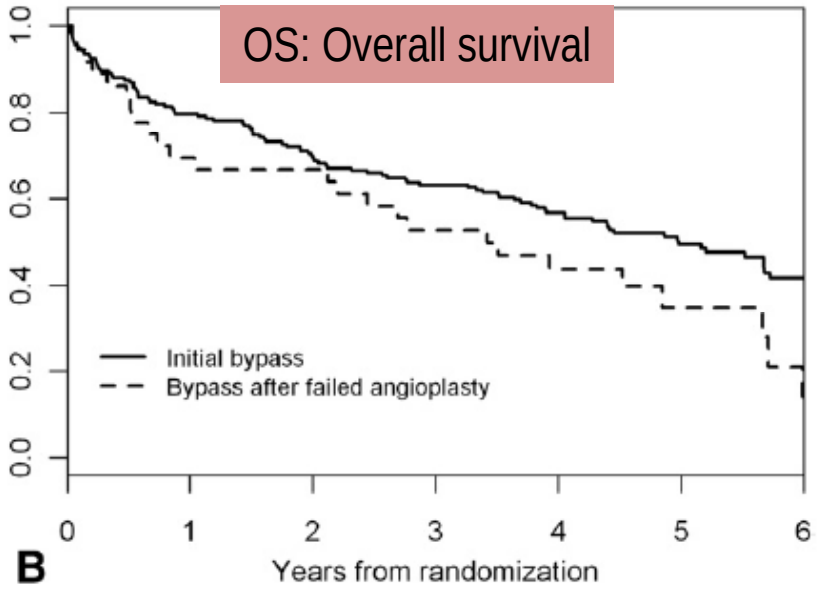
AFS: Bypass (SVG) > Angioplasty (Sub=Intra)> Bypass (PTFE)

J Vasc Surg 2010; 51:18S-31S

Bypass vs. Angioplasty in Severe Ischemia of the Leg (BASIL)

- Analysis of amputation-free and overall survival by treatment received -





Results of BSX after failed BAP

The 37 patients who underwent BSX after first attempted failed angioplasty had a poorer AFS (*P .006, log-rank test) and a somewhat* poorer OS (*P .06, log-rank test) than the 184 patients* who underwent BSX as their first treatment

J Vasc Surg 2010; 51:18S-31S

Bypass vs. Angioplasty in Severe Ischemia of the Leg (BASIL)

- Analysis of amputation free and overall survival by treatment received -

➢BAP patients underwent treatment of the SFA alone (38%) or combined with the popliteal artery (42%) and **crural arteries (20%)**. CLI due to **isolated BTK lesion** was present in only **6.8% of cases.**

* Because they will not survive to reap the long term benefits of surgery. In addition, the result of prosthetic bypass shows poor durability in infra-inguinal lesions.

J Vasc Surg 2010; 51:18S-31S

Infrapopliteal Percutaneous Transluminal Angioplasty Versus Bypass Surgery as First-Line Strategies in Critical Leg Ischemia

A Propensity Score Analysis

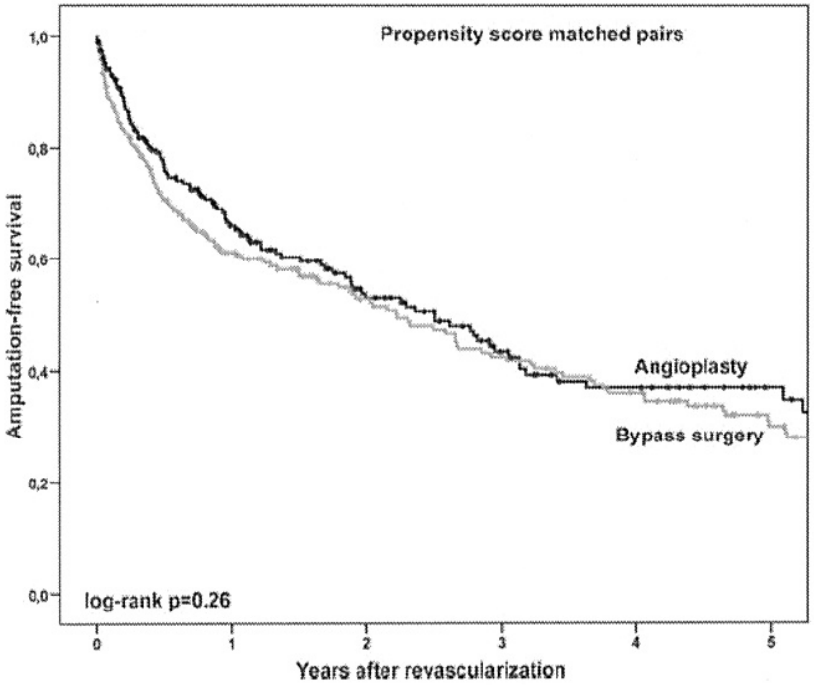
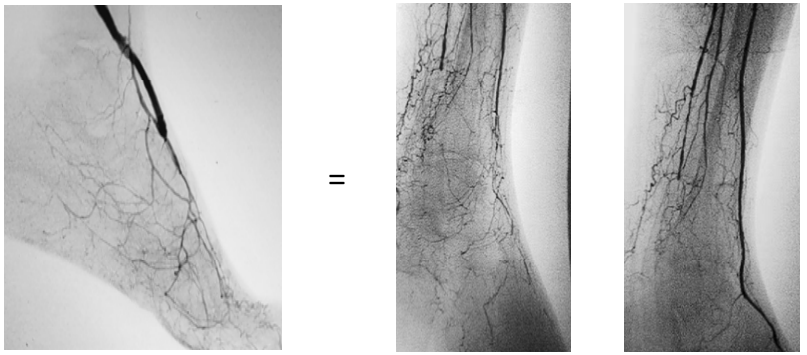


FIGURE 1. Amputation-free survival after infrapopliteal PTA and bypass surgery for CLI in the overall population and in 208 propensity-score–matched pairs.



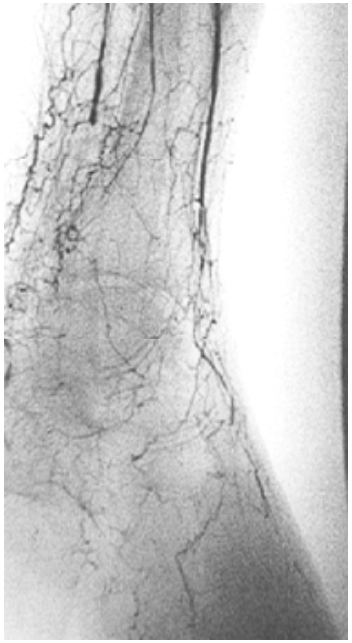
In propensity-score-matched pairs, PTA and bypass surgery (BSX) achieved similar 5-year amputation-free survival

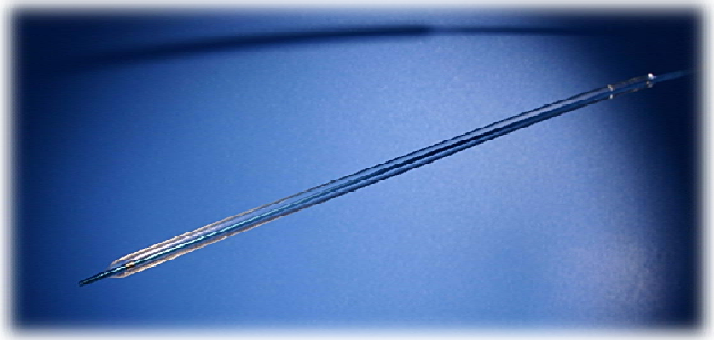
(BSX: 29.9% vs.PTA: 36.9%, p=0.26)

Ann Surg 2010;252:765-773

Next step･･･

For evaluating the actual efficacy of BTK angioplasty





We examined long-term clinical outcomes after EVT with angioplasty for CLI patients presenting with pure isolated below-the-knee (BTK) lesion

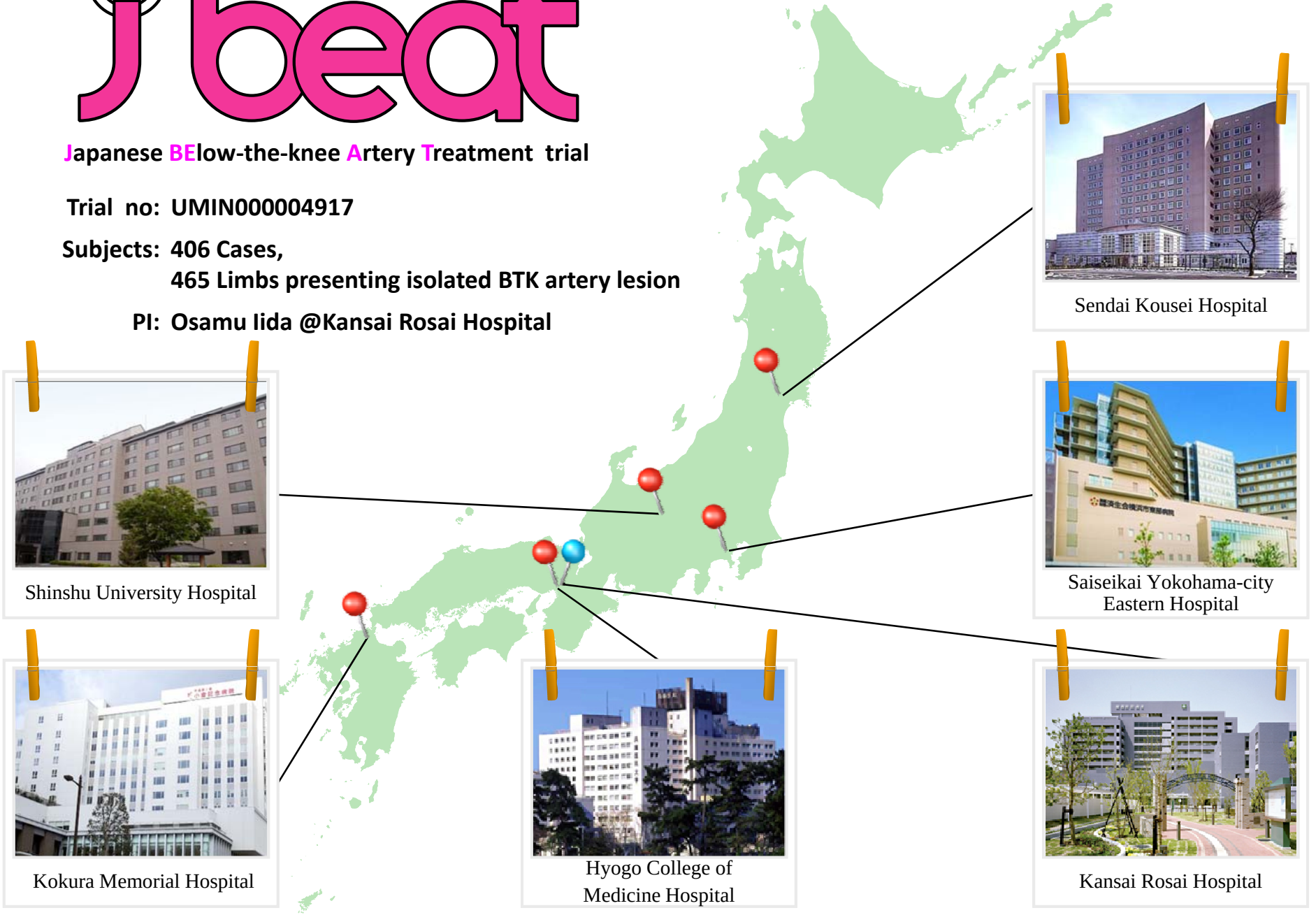
j beat

Japanese **BE**low-the-knee **A**rtery **T**reatment trial

Trial no: UMIN000004917

Subjects: 406 Cases,
465 Limbs presenting isolated BTK artery lesion

PI: Osamu Iida @Kansai Rosai Hospital



Sendai Kousei Hospital

Shinshu University Hospital

Saiseikai Yokohama-city
Eastern Hospital

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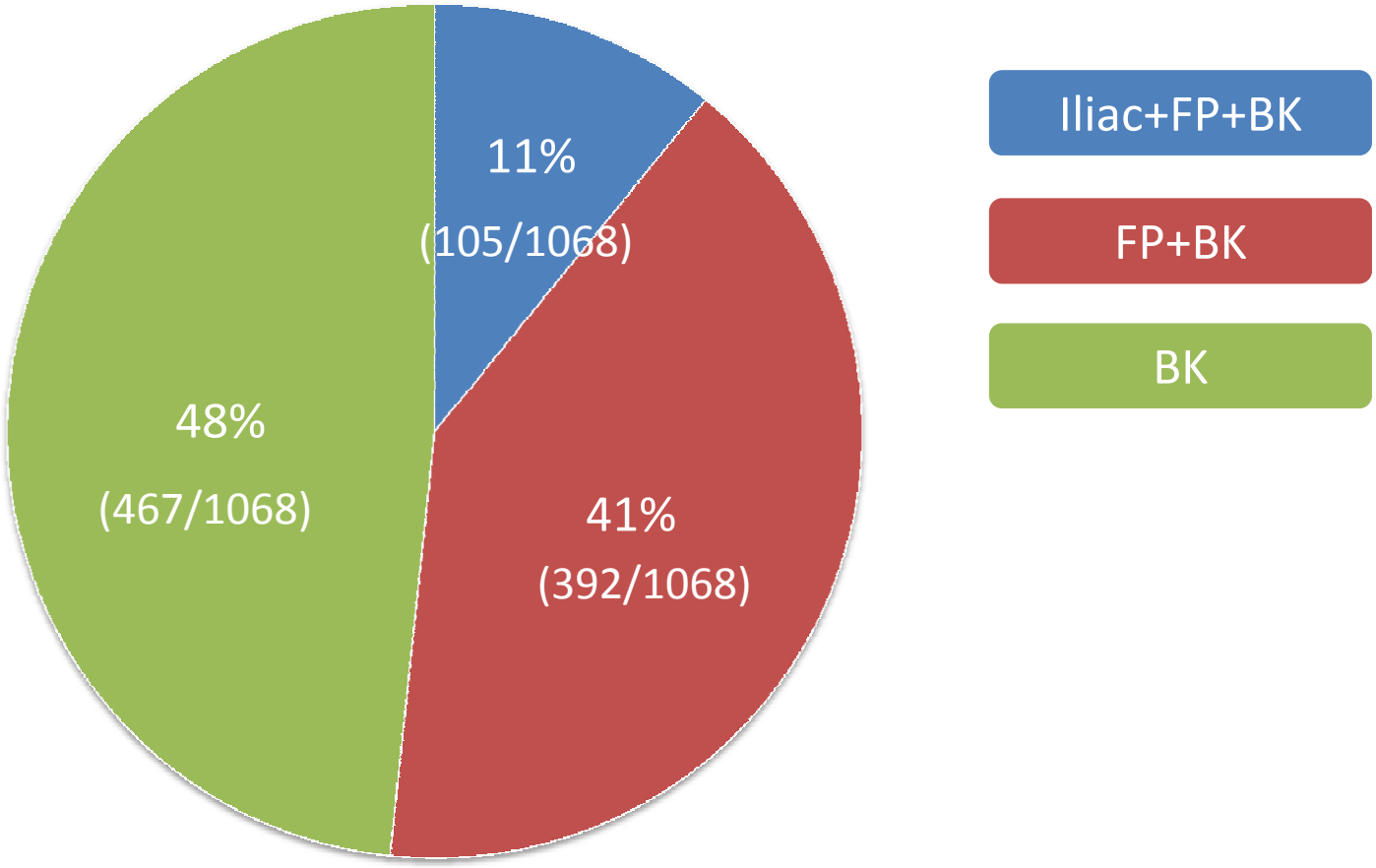
Distribution of culprit lesions

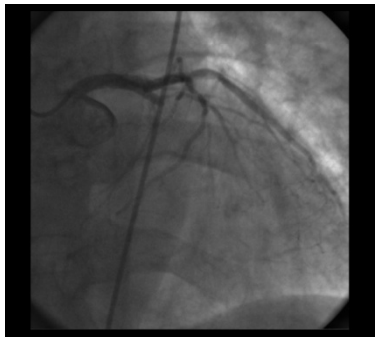
N=900 patients, 1068 limbs (2004-2010) in 6 CVC



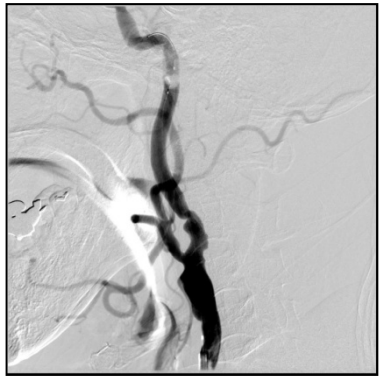
In approximately half the patients, critical limb ischemia was due to an isolated below-the-knee lesion

Patient characteristics in the J-BEAT trial

Patients status	
Age	71±11
Male gender	67% (274)
BMI (body mass index)	22±3
BMI<18	14% (57)
Non-ambulatory status	43% (175)
Risk factors	
Hypertension	77% (314)
Hyperlipidemia	29% (117)
Diabetes mellitus	**69% (280)**
Current smoking	30% (121)
End stage renal disease on dialysis	**60% (242)**
Cardiovascular disease	
CAD (Coronary Artery Disease)	**52% (210)**
CVD (Cerebrovascular disease)	**29% (118)**



52% CAD in CLI Pts



29% CVD in CLI Pts

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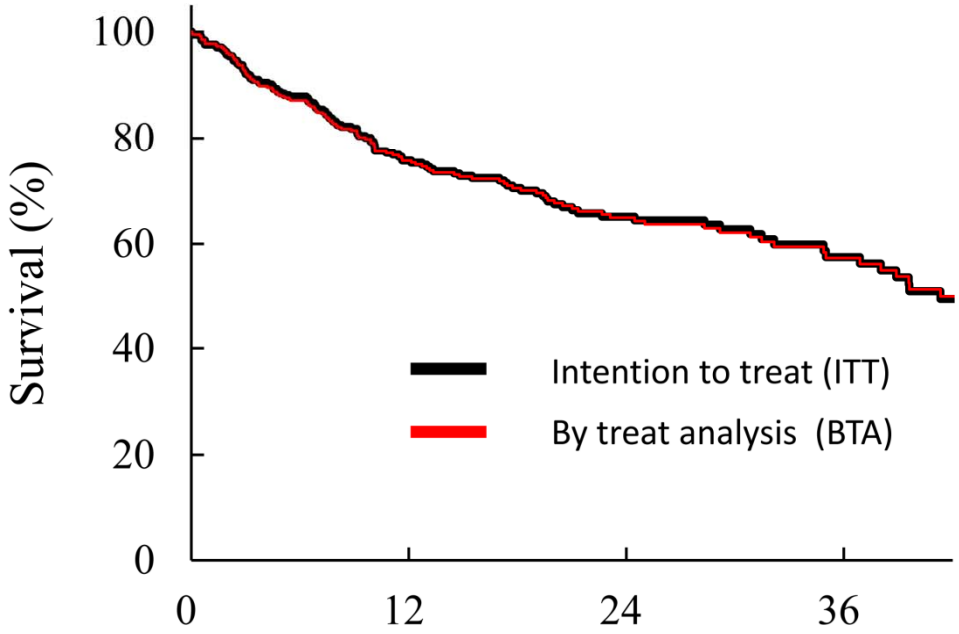
Patient (Survival)



Months		0	12	24	36
at risk	ITT	406	208	103	51
	BTA	377	195	96	47
%	ITT	100	75.7	64.9	57.3
	BTA	100	75.6	65.1	57.5
SE	ITT	.000	.023	.029	.035
	BTA	.000	.024	.030	.037

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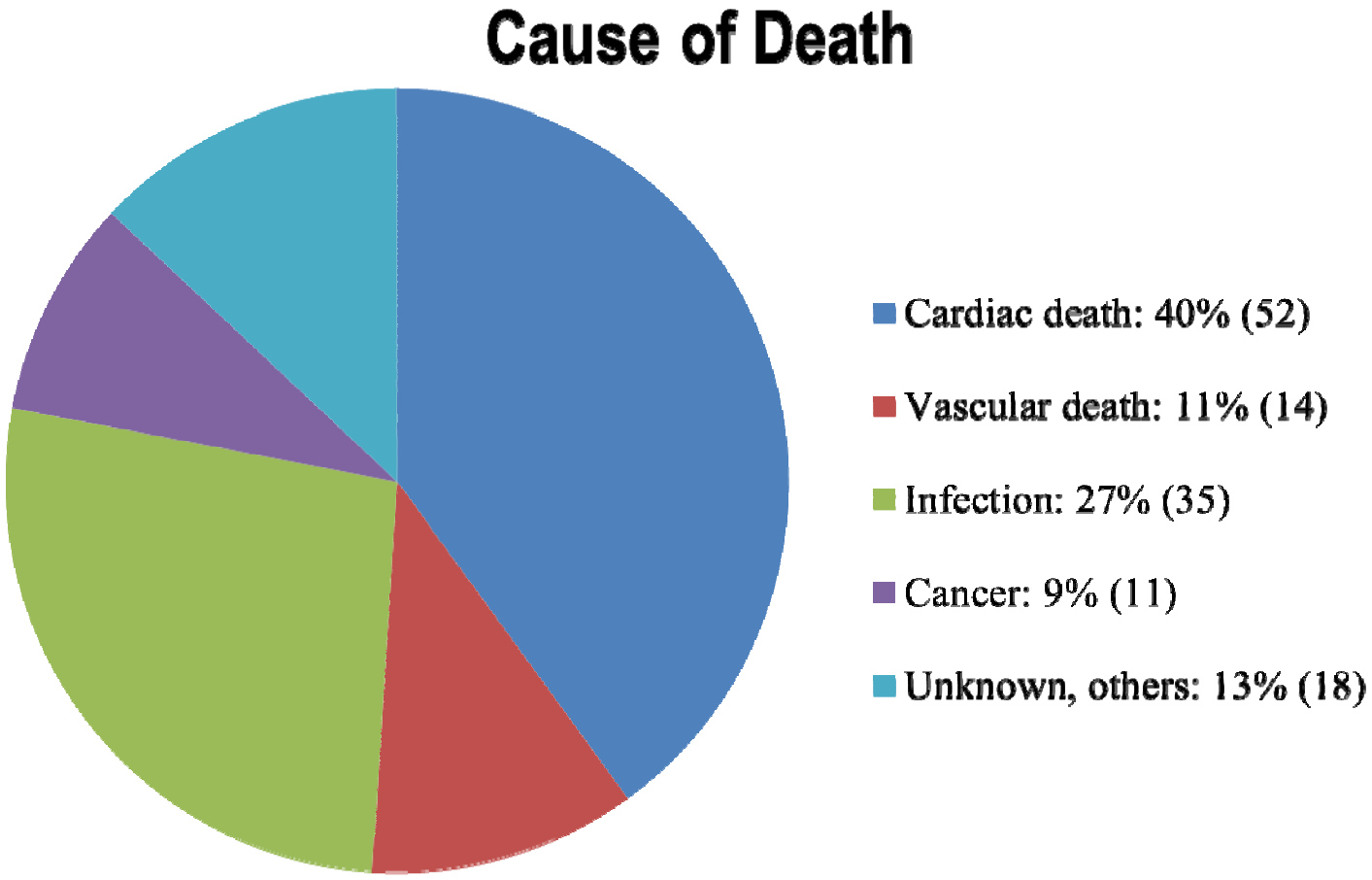
Cause of Death
Cardiac death: 40% (52)
Vascular death: 11% (14)
Infection: 27% (35)
Cancer: 9% (11)
Unknown, others: 13% (18)

Patient Mortality

Predictors of mortality by multivariate analysis

	95% CI	Hazard ratio	P-value
BMI<18	1.278-5.541	2.661	0.0089
Alb (mg/dL)	0.554-1.652	0.957	0.8738
Non-ambulatory	1.090-3.230	1.877	0.0230
ESRD on dialysis	0.799-2.777	1.490	0.2092
Hb (g/dL)	0.817-1.143	0.966	0.6906
HR>80	0.862-2.514	1.472	0.1564
EF<45 %	1.829-7.438	3.688	0.0003
CVD	0.983-2.954	1.704	0.0575
Rutheford classification	0.720-1.837	1.15	0.5590
ABI<0.6	0.939-3.172	1.726	0.0790
CRP>3	0.886-3.203	1.684	0.1118
Vessel calcification	0.500-1.859	0.964	0.9134

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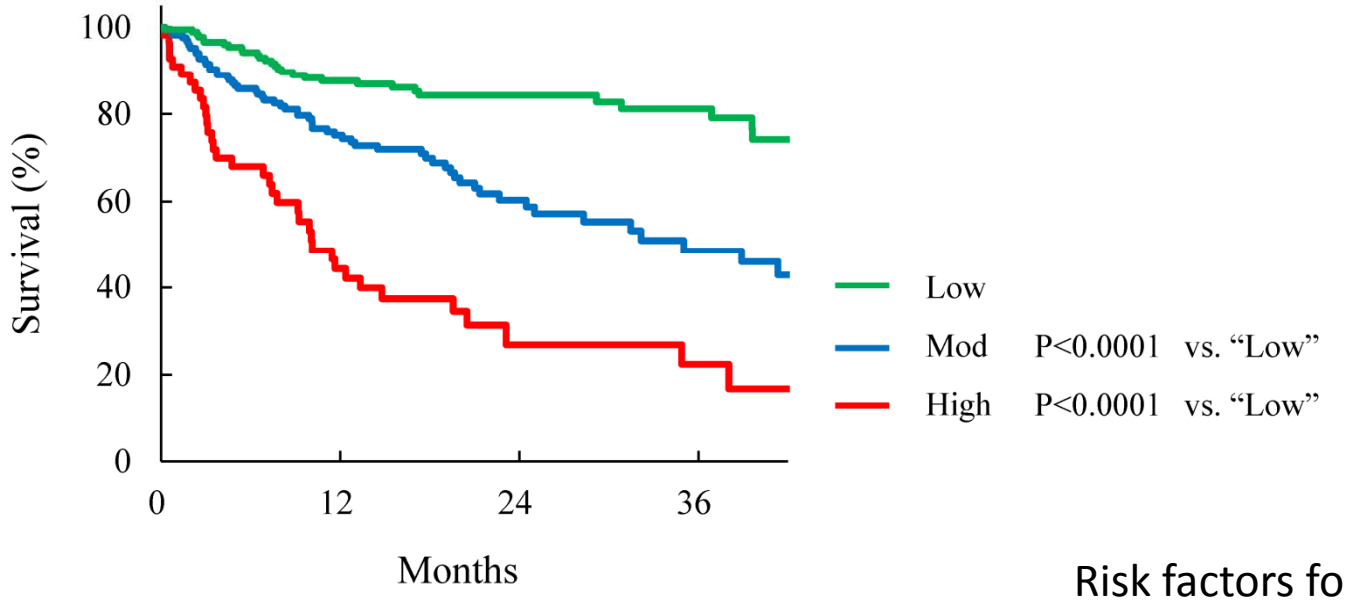
Patient mortality according to number of risk factors based on multivariate logistic analysis



Months		0	12	24	36
at risk	Low	181	120	73	40
	Moderate	170	96	38	19
	High	55	20	6	5
%	Low	100	87.6	84.3	81.1
	Moderate	100	75.1	60.3	48.6
	High	100	44.3	26.9	22.4
SE	Low	.000	.026	.030	.036
	Moderate	.000	.035	.046	.058
	High	.000	.071	.074	.074

Risk factors for survival
BMI<18, EF<45,Non-ambulatory
* Number of risk factors: 0 (low-risk, n=181), 1 (moderate-risk, n=170) and 2-3 (high-risk, n=55)

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Lower limb and lesion characteristics in J-BEAT (n=465)

Lower limb status	
Rutherford classification	5.0±0.6
Rurtherford 5, 6	**79% (369/465)**
ABPI before angioplasty	0.78±0.25
SPP (skin perfusion pressure) before procedure	34±17
SPP (skin perfusion pressure) after procedure	49±19
White blood cell count/ CRP (C-reactive protein)	7600±3100/2.6±4.0
Vessel calcification	64% (297)
Diseased artery after angioplasty	
ATA (anterior tibial artery)	39% (183)
PTA (posterior tibial artery)	60% (277)
PA (Peroneal artery)	44% (206)
Number of below-the-knee run-offs after angioplasty	1.6±0.8
More than 1 vessel run-off after angioplasty	52% (243)
Repeat revascularization	29% (135)

79% (369/465) of Pts had non-healing ulcer

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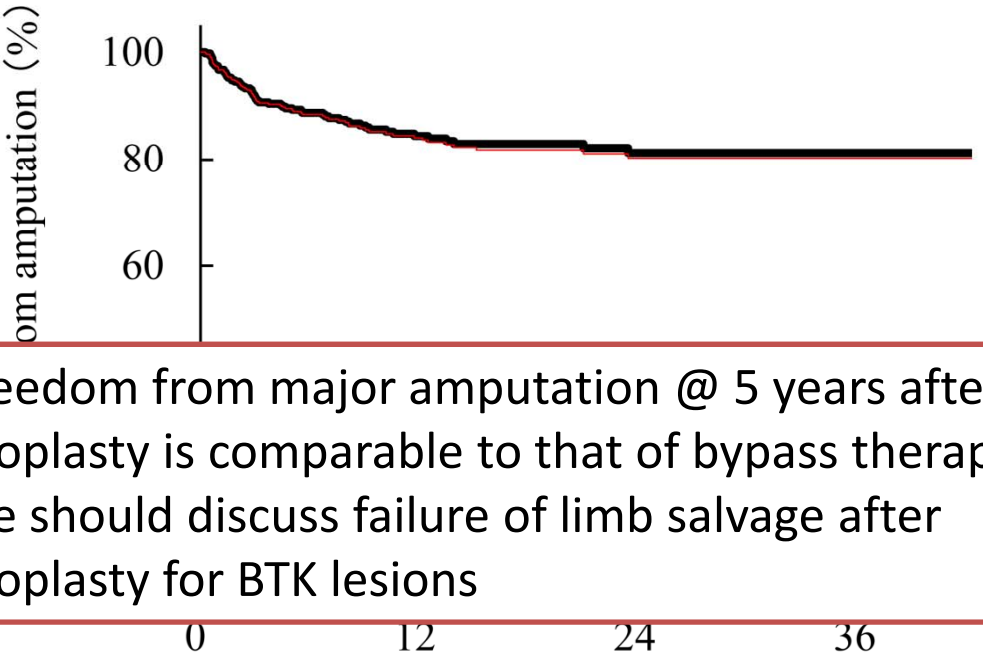
Freedom from major amputation



✓Freedom from major amputation @ 5 years after angioplasty is comparable to that of bypass therapy

✓We should discuss failure of limb salvage after angioplasty for BTK lesions

Months			0	12	24	36
at risk	ITT		465	203	88	44
	BTA		437	190	82	41
%	ITT		100	84.1	80.3	80.3
	BTA		100	84.4	81.3	81.3
SE	ITT		.000	.019	.023	.023
	BTA		.000	.019	.024	.024

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Lower limb

Predictor of major amputation by multivariate analysis

	95% CI	Hazard ratio
Rutherford 6	1.228-4.387	2.321
Non-ambulatory	0.827-2.648	1.480
Presence of diabetes mellitus	1.100-4.792	2.296
Alb (g/dL)	0.513-1.513	0.088
CRP>5	1.251-5.341	2.585
Age<60	1.427-5.294	2.749
White blood cell (WBC) count	0.937-1.136	1.032

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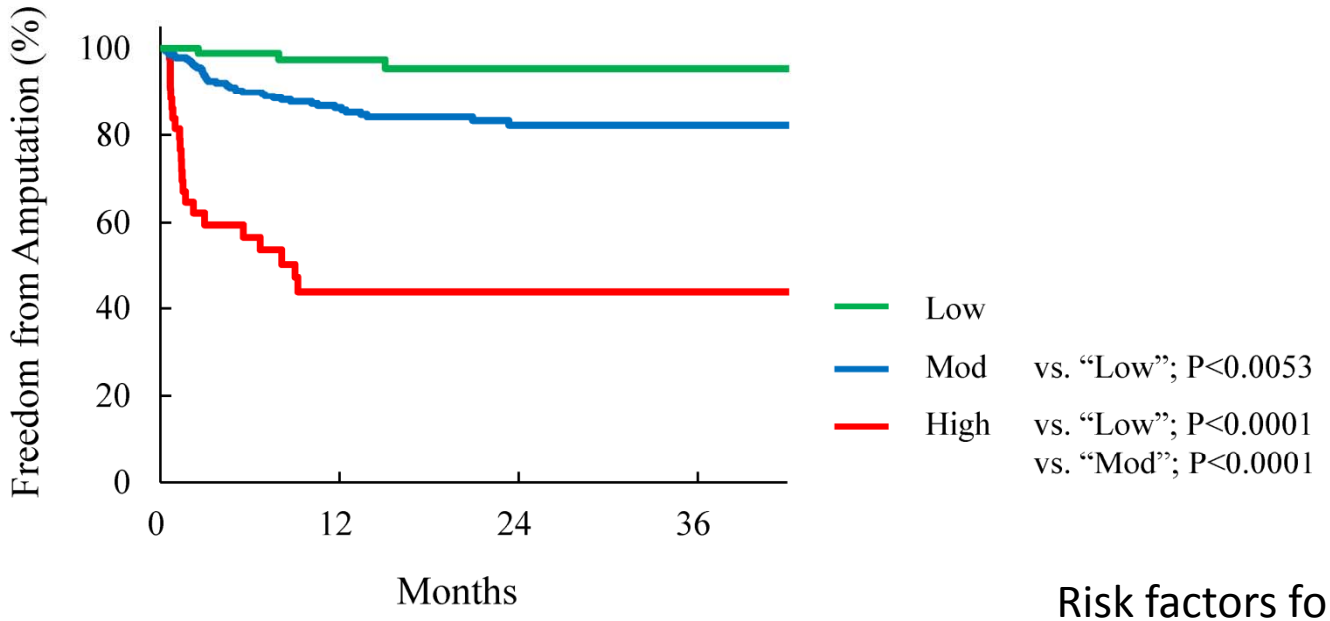
Freedom from amputation according to number of risk factors based on multivariate logistic analysis



Months		0	12	24	36
at risk	Low	93	54	25	15
	Moderate	327	171	71	37
	High	45	11	7	2
%	Low	100	97.4	95.4	95.4
	Moderate	100	86.2	82.2	82.2
	High	100	43.7	43.7	43.7
SE	Low	.000	.018	.027	.027
	Moderate	.000	.021	.026	.026
	High	.000	.083	.083	.083

Risk factors for major amputation
Rutherford 6, Presence of DM, Age<60, CRP>5
* Number of risk factors: 0 (low-risk, n=93), 1-2 (moderate-risk, n=327) and 3-4 (high-risk, n=45)

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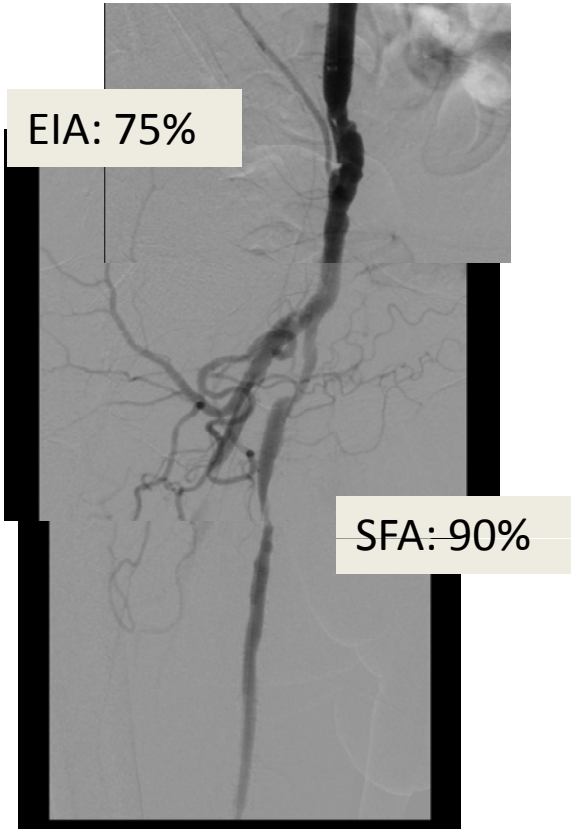
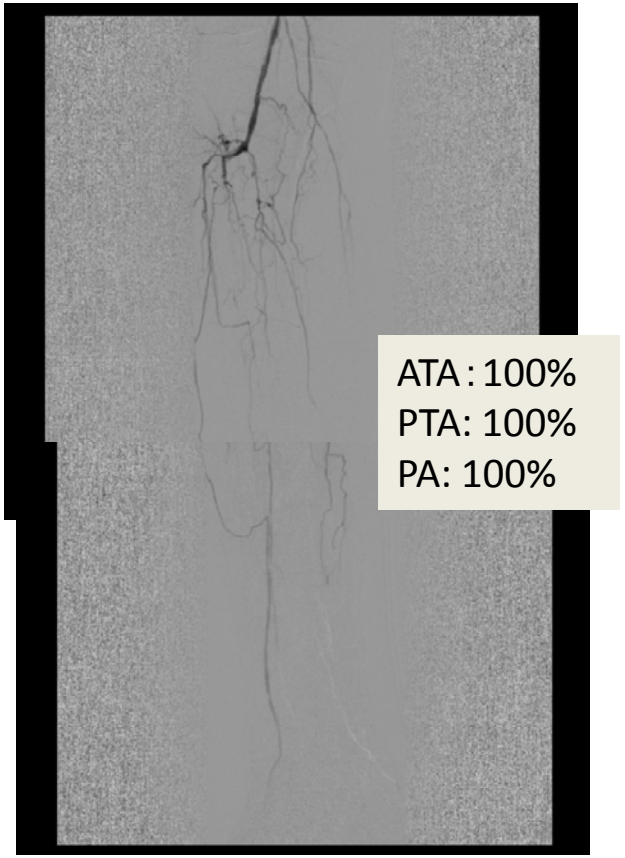
75 y/o Male (Rutherford 6)

ESRD on dialysis
DM
PAD for Ao-bi FA bypass

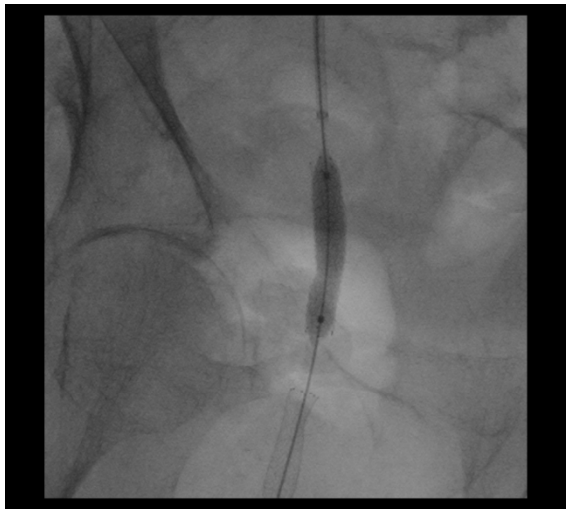
WBC: 17700
CRP: 11.5
Enterococcus faecalis

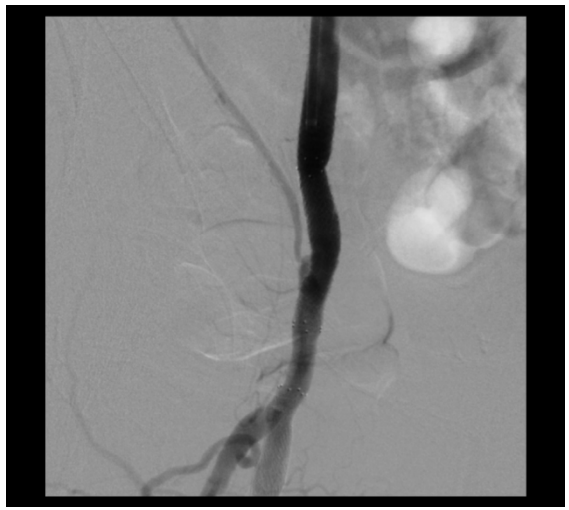
75 y/o Male (Rutherford 6)

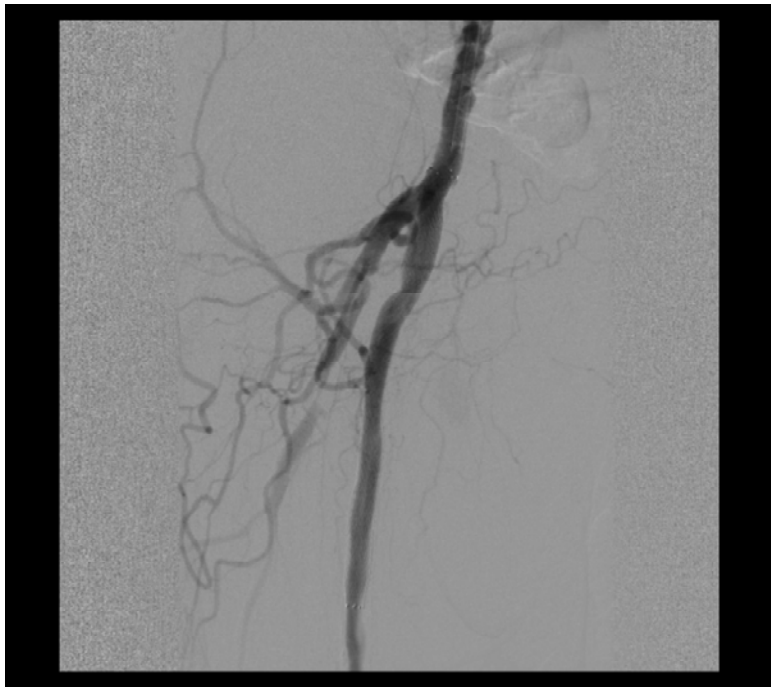




75 y Male (Rutherford 6)

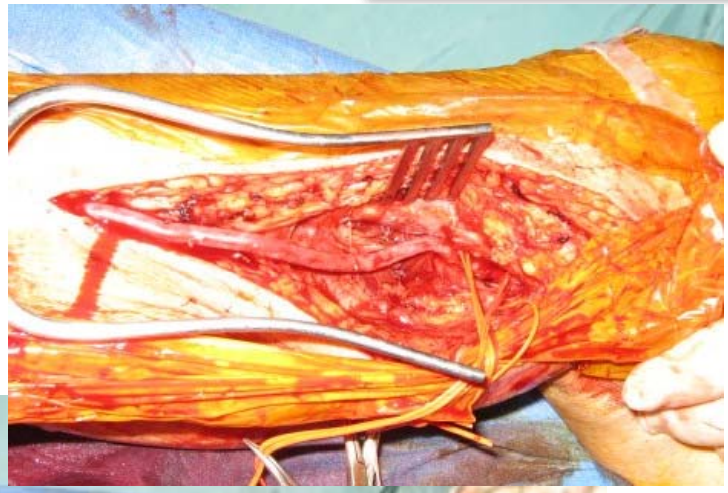


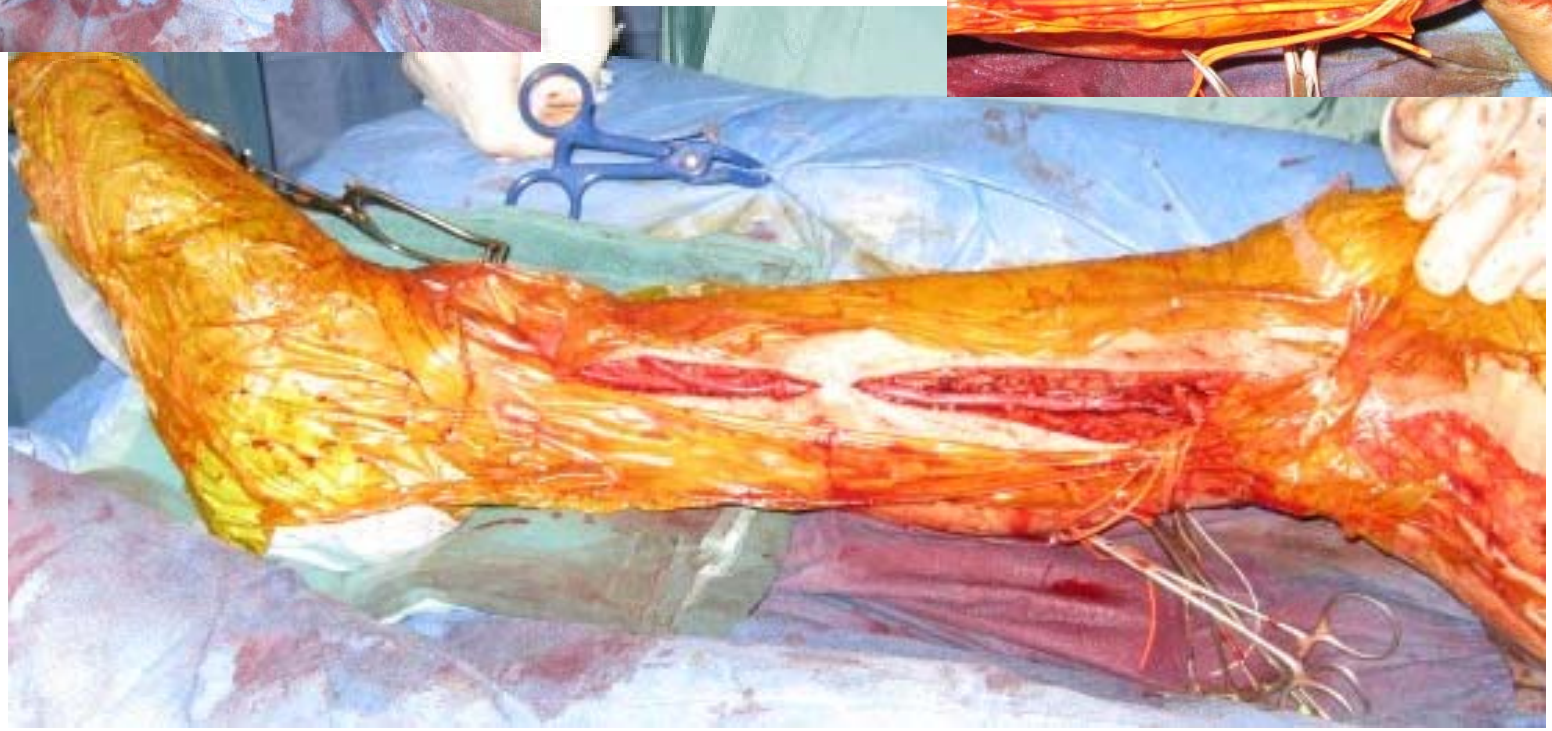




EIA 75%→ 0% (SMART 10 × 40mm)
SFA90% → 0% (SMART 8 × 100mm)

Distal bypass (BTK Pop a- DPA)





Distal bypass (BTK Pop a-DPA)

After hybrid therapy

Challenges of Endovascular Therapy in Patients with Critical Limb Ischemia

➢J-BEAT survival score

1) BMI < 18, 2) Non-ambulatory status, 3) Ejection fraction < 45%

✓The survival rate was lower in the higher risk groups (1- and 5-year rates: low risk, 87% and 58%; intermediate risk, 74% and 36%; and high risk, 49% and 12%, respectively; *P*<0.001).

➢J-BEAT amputation score

1) Rutherford 6, 2) DM, 3)CRP>5, 4) age<60 yrs

✓The rate of limb salvage was lower in the higher score groups (1 and 3 years: low risk, 93% and 88%; intermediate risk, 73% and 73%; and high risk, 44% and 44%, respectively; *P*<0.001).

Iida O, et al. Eur J Vasc Endovasc Surg. 2012;43:313-21.