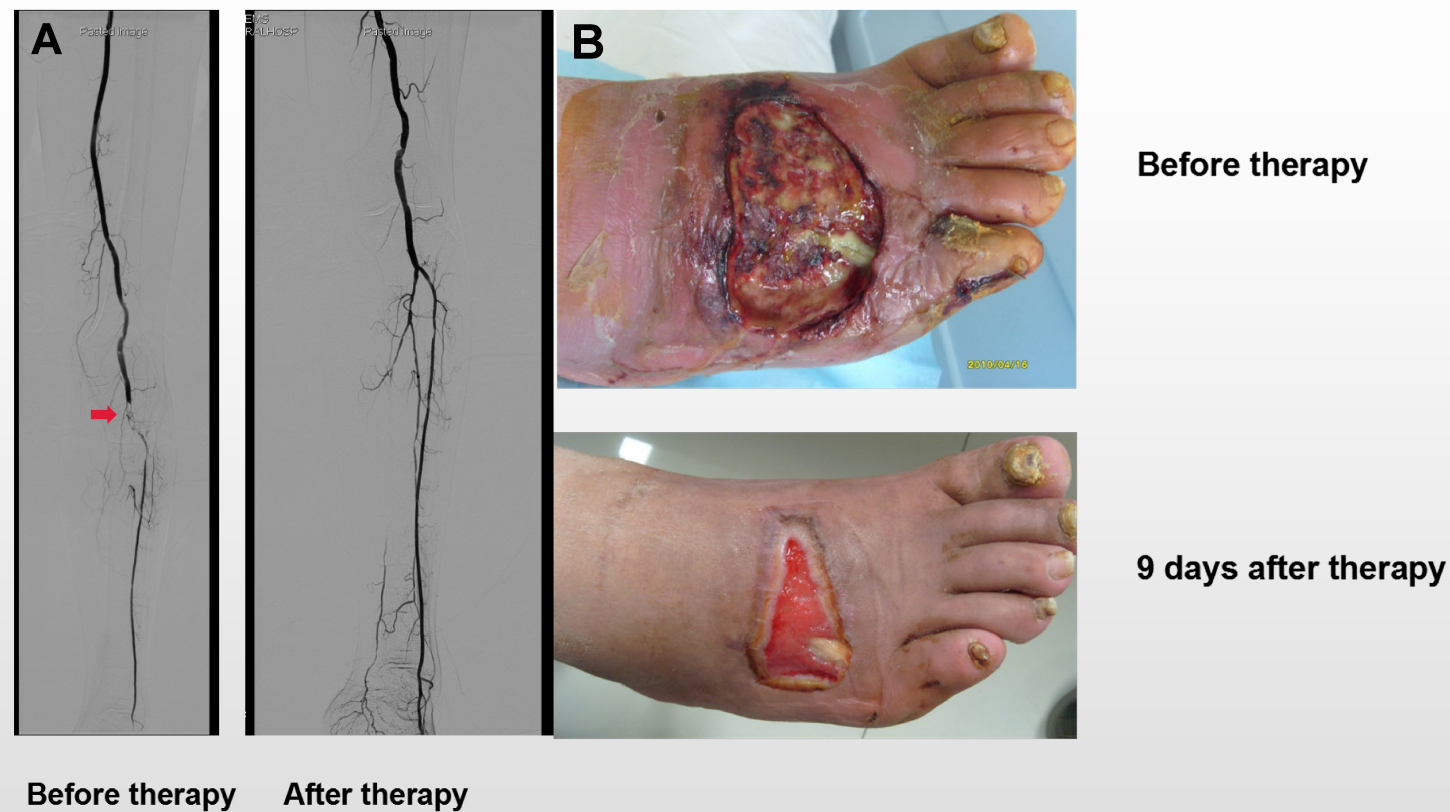
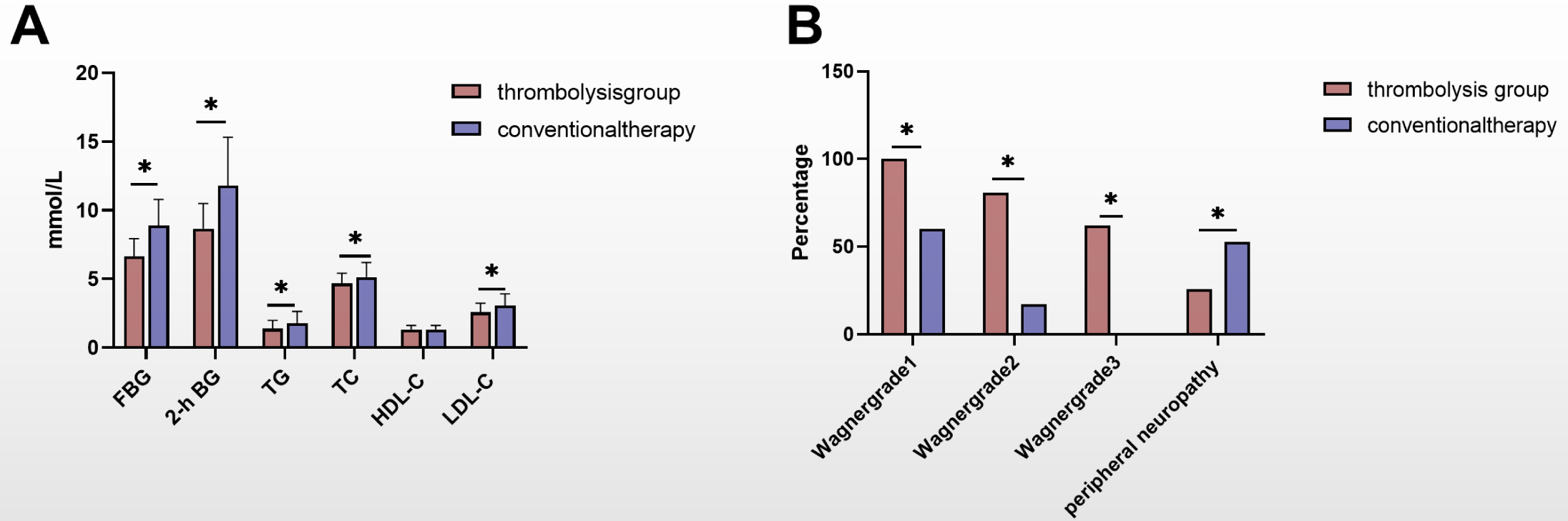


Supplementary Figure 1: The picture for continuous intra-femoral urokinase injection approach

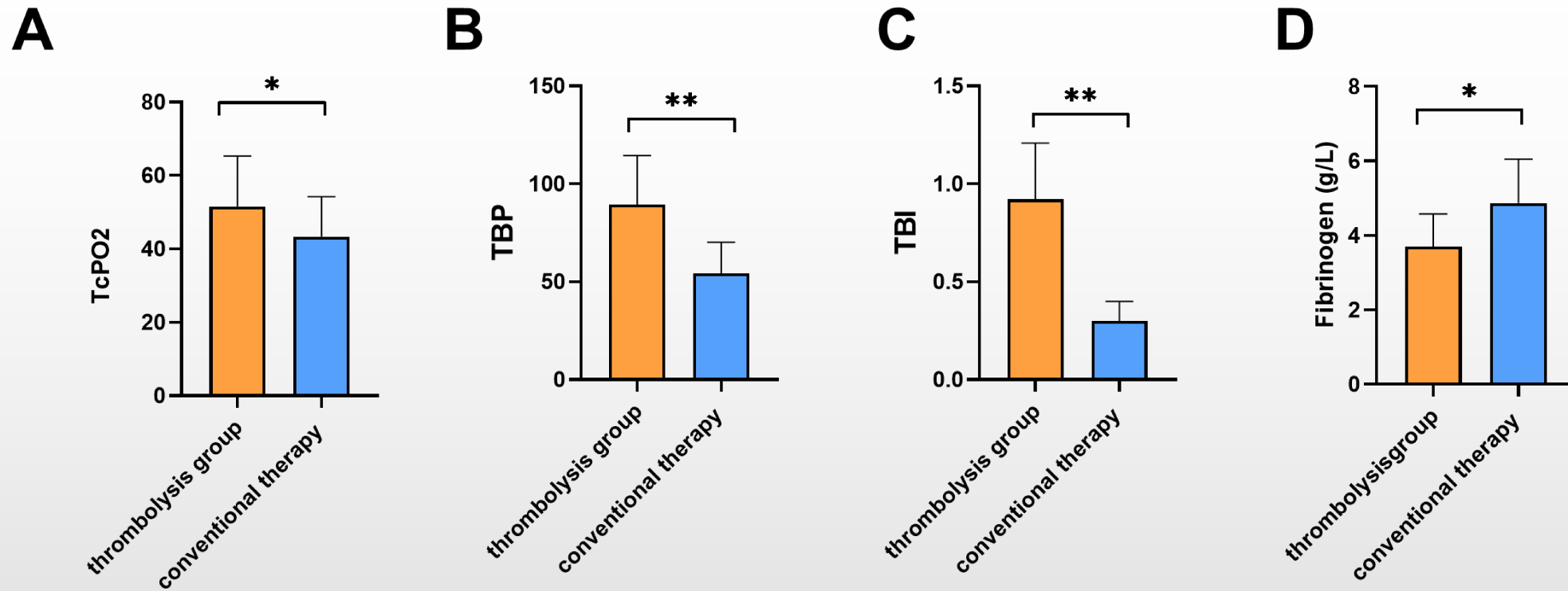


Supplementary Figure 2: The representative images for lower artery angiography and ulcer healing conditions

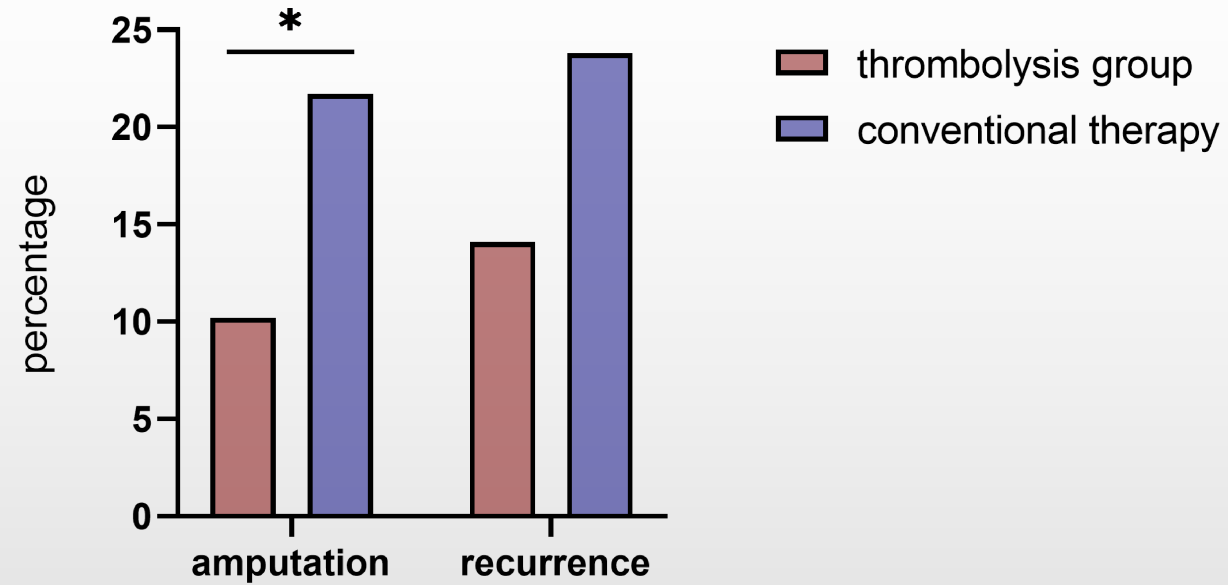
(A) The representative images for lower artery angiography before and after intra-femoral thrombolysis therapy (just conducted in 2 patients before and after thrombolysis). Solid arrow indicates the occlusion of the distal popliteal artery. (B) The representative ulcer healing conditions before and 9 days after intra-femoral thrombolysis therapy



Supplementary Figure 3. The glycolipid metabolic profiles at the first month after interventions



Supplementary Figure 4. The foot ulcers healing, blood supply at the first month after interventions



Supplementary Figure 5. The incidence of amputation and recurrence during the long term follow-up study

Supplementary Table 1—Cox regression analysis of demographic and clinical variables associated with ulcer closure

	Univariate analysis		Multivariate analysis	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Treatments	0.38 (0.26-0.57)	<0.001	0.003 (0.001-0.011)	<0.001
Age (y)	0.29 (0.16-0.54)	<0.001	0.236 (0.10-0.55)	0.001
Diabetes duration (y)	0.30 (0.14-0.65)	0.002	0.004 (0.001-0.016)	<0.001
HbA1c level	0.43 (0.28-0.66)	<0.001	0.21 (0.073-0.61)	0.004
Ulcer size, cm ²	0.46 (0.29-0.71)	<0.001	0.094 (0.026-0.34)	<0.001
Ulcer duration, mo	0.96 (0.66-1.38)	0.807	0.56 (0.35-0.88)	0.012

Supplementary Table 2—Summary of Adverse Events

	thrombolysis therapy(n=98)	conventional therapy(n=97)
Peripheral Swelling	0(0.0%)	1(1.0%)
Pyrexia	0(0.0%)	0(0.0%)
Wound infection	0(0.0%)	3(3.0%)
Decubitus ulcer	0(0.0%)	0(0.0%)
Pruritus	0(0.0%)	0(0.0%)
Hemorrhagic stroke	0(0.0%)	0(0.0%)
Pulmonary infarction	0(0.0%)	0(0.0%)
Allergic reaction	0(0.0%)	0(0.0%)
Oozing blood	2(2.0%)	1(1.0%)
Catheter defluxion	0(0.0%)	0(0.0%)

Supplementary Table 3—Incidence of cardiovascular events during follow-up study

Events	thrombolysis therapy(n=98)	conventional therapy(n=97)
Cardiovascular events	47 (48.0%)	58 (59.8%)
cardiovascular death	9 (9.2%)	18 (18.6%)
coronary heart disease events	23 (23.5%)	25 (25.8%)
total stroke	15 (15.3%)	15 (15.5%)
coronary and carotid revascularization	0	0
Total mortality	21 (21.4%)	31 (32.0%)

Only first event for each patient counted in each row. Data are number (%).

Supplementary Table 4—The mean health related quality of life scores from DFS-SF subscales questionnaire

	thrombolysis therapy(n=20)	conventional therapy(n=20)
DFS-SF scale : mean (SD)		
Leisure	40.5 (14.5)	37.5 (17.2)
Physical health	65.3 (20.2)	53.3 (13.2)
Dependence or daily life	57.5 (22.4)	52.0 (19.8)
Negative emotions	50.3 (13.7)	42.4 (18.3)
Being worried about ulcers or feet	43.0 (17.3)	37.7 (16.2)
Being bothered by ulcer care	58.7 (15.0)	45.2 (19.3)