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Effectiveness of Balloon Angioplasty and Stent Angioplasty: Wound Healing in Critically Limb Ischemic

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Abstract

Introduction. Critical limb ischemia (CLI) is a vascular disease that has a significant amputation and mortality risk with diabetes mellitus; the most significant risk factor in CLI is prevalent among Indonesian. Endovascular intervention (EVI) is preferred in treating CLI because it is non-invasive and effective. Balloon angioplasty and stent angioplasty are the most common method of EVI in Indonesia. This study aims to compare the effectiveness of balloon angioplasty and stent angioplasty on wound healing in CLI.

Method. A cross sectional study enrolled 90 subjects of CLI who underwent endovascular intervention using balloon angioplasty dan stent angioplasty from January 2013 to July 2017 in dr. Cipto Mangunkusumo General Hospital, Jakarta. The wound healing period between balloon angioplasty dan stent angioplasty analysed using an unpaired T-test.

Results. The wound healing period in balloon angioplasty and stent angioplasty distributed normally. The mean value of the wound healing period in balloon angioplasty and stent angioplasty is 84.8 ± 2.423 and 59.93 ± 2.423 days with a mean difference of 25 days. The difference in the wound healing period in both groups is statically significant.

Conclusion. *Stent angioplasty* is a better method than *balloon angioplasty* for wound healing in patients with CLI.

Keywords: Critical limb ischemia, endovascular intervention, wound healing

Introduction

Critical limb ischemia (CLI) is a condition characterized predominantly by resting pain and ischemic ulcer or gangrene. It has a high risk of amputation as well as a high mortality rate.¹ The incidence of peripheral artery disease (PAD), especially CLI, reached 500 – 1,000 new cases per one million-year in the United States. CLI prevalence has been increasing due to the high incidence of diabetes mellitus.² In Indonesia, diabetes mellitus incidence showed increasing number, i.e., 5.7% in 2017 to 6.9% in 2013.³ Purwanti (2013) stated that out of 1,785 diabetic patients, 21% of them had microvascular complication as PAD.⁴ In PAD, there is a progressive atherosclerosis process in arterial vessels, especially in the legs. Iliac, femoral, and popliteal arteries are the most common affected sites.⁵

The optimal treatment for CLI is the revascularization of the occluded arteries. Bypass surgery and endovascular intervention (EVI) are standard techniques used for CLI treatment.⁶ EVI considered superior to bypass surgery due to better limb salvage.⁷ In CLI, wound healing is the cause of low quality of life and high medical fare.⁸ Karawanda (2012) in his study stated that wound healing achieved in 80% of patients within 54 days and 97% in 145 days after EVI.⁹ Specifically, the two most common EVI techniques were balloon angioplasty (or percutaneous transluminal angioplasty [PTA]) and stent angioplasty, which has different wound healing duration.¹⁰ In the 1-year follow-up, patients treated with balloon angioplasty had a 67.9% cure rate and patients treated with stent angioplasty had a 73.6% cure rate.¹¹

Method

This study was a cross-sectional analytic design that compared the duration of wound healing in CLI patients treated by balloon angioplasty versus stent angioplasty. The study conducted at dr. Cipto Mangunkusumo General Hospital. Subjects were CLI patients treated by balloon angioplasty or stent angioplasty by the Vascular Surgery Division of dr. Cipto Mangunkusumo General Hospital on January 2013 – May 2017. Sampling enrolled by consecutive sampling methods based on medical records. Based on the calculation, the minimal sample was 88 subjects. Exclusion criteria were incomplete data on medical records. The Committee ethic of Faculty Medicine, Universitas Indonesia, approved this study.

Data collected from medical records including subjects' characteristic (age, gender, body mass index, smoking history), clinical data (amputation history, resting pain, ankle-brachial index, ulcer location), laboratory data (hemoglobin, hematocrit, white blood cells, platelet count, serum glutamic oxaloacetic transaminase, serum glutamic pyruvic transaminase, urea, creatinine, prothrombin time, activated partial thromboplastin time, cholesterol, triglyceride, fasting blood glucose, HbA1C), EVI method, duration of wound healing.

Statistical Package conducted the statistical analysis for the Social Sciences (SPSS) version 20.0 software. Hypothesis test was done by unpaired T-test, followed by the Mann-Whitney test.

The study approved by the Committee of Ethics, Faculty of Medicine, Universitas Indonesia No 1112/UN2.F1/ETIK/2017.

Results

Subjects' characteristics presented in Table 1. The mean age of subjects was 58 years old, and most of them were males. The most common location of CLI was a right leg, followed by the left leg and both legs. Essential characteristics were not significantly different between patients in the balloon angioplasty group and stent angiography group. The statistical difference found in blood glucose level, HbA1C, and body mass index data (Table 1).

Table 1. Subjects' characteristics

	Value (N = 90)	Balloon Angioplasty (n = 46)	Stent Angioplasty (n = 44)	P value
Age, mean (standard deviation)	58.7 ± 10.55	59.1	58.3	0.709
Gender, n (%)				
Males	46 (51.1)	20	26	0.139
Females	44 (48.9)	26	18	
Location, n (%)				
Right leg	38 (42.2)	23	15	0.097
Left leg	36 (40)	19	17	
Both legs	16 (17.8)	4	10	
Aortoiliac disease		0	2	
Affected vessels, n (%)				
Femoral artery	52 (46.8)			
Iliac artery	6 (5.4)			
Popliteal artery	24 (21.7)			
Anterior tibia artery	14 (12.6)			
Posterior tibia artery	12 (10.8)			
Peroneal artery	3 (2.7)			
Pre-intervention blood laboratory works				
Hemoglobin, mean (SD)	11.3 (7.6-14)	11.15	11.35	0.637
Hematocrit, mean (SD)	34 (23-42)	33.2	33.7	0.620
White blood cells, mean (SD)	11.215 (3000-115000)	12.100	10.560	0.191
Platelet, mean (SD)	233.500 (13000-726000)	230000	246000	0.248
SGOT, mean (SD)	34 (10-375)	32	41.5	0.131
SGPT, mean (SD)	25 (7-267)	25	25	0.326
Urea, mean (SD)	31 (11-193)	31.6	30.5	0.634
Creatinine, mean (SD)	0.9 (0.1-10.6)	0.9	0.8	0.451
PT, mean (SD)	1 (0.8-1.4)	0.9	1	0.609
aPTT, mean (SD)	1 (0.8-1.7)	1	1	0.648
Total cholesterol, mean (SD)	190 (59-310)	185	197.5	0.256
Triglyceride, mean (SD)	151.49 ± 25.93	151.5	151.5	0.997
Random blood glucose, mean (SD)	155.5 (26-350)	166	143	0.014*
HbA1C, mean (SD)	6.9 (5.2-8.8)	7	6.25	0.022*
Basic clinical conditions				
Smoking habit, n (%)		17	20	0.413
Diabetes mellitus, n (%)		33	20	0.011*
BMI, mean (SD)	53 (58.9)	23.87	23.39	0.598
Resting pain, n (%)	23.63 ± 4.35	158.5	161.2	0.057
Right ABI, mean (SD)	87 (96.7)	43	44	0.494
Left ABI, mean (SD)	0.85±0.2	0.87	0.84	0.479
	0.8 (0.3-1.2)	0.8	0.7	0.069

SGOT: serum glutamic oxaloacetic transaminase, SGPT: serum glutamic pyruvic transaminase, PT: prothrombin time, aPTT: activated partial thromboplastin time, ABI: ankle-brachial index, BMI: Body Mass Index

Table 2. The comparison of outcome between balloon angioplasty versus stent angioplasty

Outcome	Balloon angioplasty (n = 46)	Stent angioplasty (n = 44)	P value
Amputation	22	16	0.271
Resting pain			
– Resolved	4	3	
– Improving	40	41	0.348
– Unchanged	2	0	

In terms of postoperative outcomes, the average length of stay (LOS) of the We found that the data was not distributed regularly. The median duration of the procedures have done in 225 minutes, with the most prolonged duration of the operation is 450 minutes. Median of intraoperative blood loss was around 50 mL, with one patient loss his blood around 500 mL (see table 2).patients is 8.6 ± 1.6 days, with most of the patients feel mild pain in average visual analogue score 3.5 ± 1.1 on the first post-operative day. The average time needed to recover to daily activity was 7.3 ± 1.8 days.

Discussion

The mean age of the subjects in our study was 58 years old, and most of them were males (51.5%). The mean age in our study was relatively younger than other previous CLI intervention studies. A study by Kanolkar and Ephrem in India had a mean age of subjects of 65 years old,¹ and a study by Iida et al. in Japan had older mean age, i.e., 73 years old.¹⁸ Epidemiology records in other countries such as Australia, America, and Germany noted an increasing incidence of CLI in older individuals (75-80 years old).¹⁹ It concluded that CLI patients in Indonesia were younger. Different lifestyles could explain this difference in mean age among countries.

The most common site of CLI in our study was the femoral artery (46.8%), followed by popliteal artery (20.7%), anterior tibial artery (12.6%), and posterior tibial artery (10.8%). Other arteries, iliac, and peroneal artery, had a lower incidence. This finding differed from Khanolkar and Ephrem's study, which stated the infra-popliteal artery as the most common site of CLI.¹ The high prevalence in femoral and popliteal arteries might be caused by a chronic narrowing in diabetes mellitus or lousy lifestyle.²⁰ The incidence of diabetes mellitus in our subjects was quite high, which could explain the possible chronic vessel narrowing. The anatomical site in which the popliteal artery was compressed in joint articulation might also play a role.

We found a below-normal value of hemoglobin and hematocrit in our subjects; this could be caused by chronic inflammation state in CLI. CLI patients commonly associated with other chronic conditions (s), making it more possible to cause anemia. Recurrent infection and several operative procedures might also have affected the hemoglobin and hematocrit level. The study by Shah et al. was also showed anemia in CLI patients in England.²¹ Anemia might also be caused by malnutrition and duration stay in the hospital.²¹ The high leukocyte level in our subjects considered related to chronic inflammation as well. Several subjects had ulcer wounds, which was vulnerable to infection, therefore increasing the risk of leukocytosis.

SGOT and SGPT levels of our subjects were within normal limits. Until now, there was no literature stating the correlation between SGOT/SGPT levels with CLI. Our median of urea level was higher than normal (31 versus 20 mg/dL), but our median creatinine was within the standard limit (0.9 mg/dL). Increased urea, also described by Gary et al. study.²² This study also found that disruption was higher in iliac, femoral, and

popliteal arteries in patients with a high level of urea. The high level of urea was due to hemodynamic imbalance found in CLI patients, which would affect the renal urea excretion.²² Gary et al. found a difference in subjects with normal urea level and high urea level. Even though serum creatinine in this study was relatively within normal limits.²² There were several factors affecting creatinine levels, such as old age, congestive heart failure, malnutrition, and a catabolic state. PT and aPTT level was normal in our subjects. No previous studies stated any relation between PT and aPTT with CLI.²² But, coagulopathy was closely related to vessel occlusion, which could be evaluated using coagulation panel and fibrinolytic system.

The total cholesterol level in our study was 190 mg/dl, which was normal. Our mean triglyceride level was a little higher than the upper limit, i.e., 151.5 mg/dL. Cholesterol and triglyceride levels were known to be risk factors of CLI¹¹; cholesterol level more than 270 mg/dL had a higher chance of having intermittent claudication. High triglyceride also found in CLI patients.¹¹ High cholesterol and triglyceride mean a higher incidence of atherosclerosis, which potentially causing CLI. Our standard level of cholesterol and triglyceride probably caused by previous cholesterol-lowering therapy. The high level of random blood glucose and HbA1C in our subjects possibly related to our high incidence of diabetic patients. Diabetes was also the leading risk factor of CLI.¹¹ The other risk factor was a smoking habit, which found in 41% of our subjects.

Several characteristics were statistically significant between the two intervention groups, which might affect the final analysis. Those characteristics were a median of random blood glucose, HbA1C, and prevalence of diabetes mellitus. These findings might be due to by our sampling method that did not warrant randomization. Even though, in the clinical perspective, the difference was not significant. The median value of random blood glucose in both groups was within normal limits, and HbA1C value in both groups was in the high category. Therefore, we concluded that this difference might not affect our analysis.

The duration of wound healing was significantly between CLI patients treated with balloon angioplasty and stent angioplasty. The difference was 25 days (85 days in balloon angioplasty group versus 60 days in-stent angiography group). We considered this difference as significant clinically because it was nearly a month. We defined duration as wound healing, starting from patient admission until her/his ulcer healed. The most crucial factor of CLI wound healing was the revascularization strategy to bring back the perfusion to the distal part of occlusion.²³ Stent angiography, therefore, could be considered a better revascularization strategy than balloon angioplasty.

The better vessel patency could cause faster wound healing in-stent angiography compared to balloon angioplasty. A study by Reed et al. showed a higher rate of re-admission after balloon angioplasty compared to stent angioplasty, in which the patients had re-occurrence or worsening of claudication and resting pain.²⁴ Stent angioplasty in smaller vessels was still a controversy, considering the risk of thrombosis and intimal

hyperplasia. Another study also stated that stent placement into a vessel had good patency and no re-obstruction noted after 24 months of intervention.²⁰ Stent angioplasty could be used in small vessels if balloon angioplasty failed. The efficacy of stent angioplasty in sub-intimal recanalization and calcification was limited.²⁵ Furthermore, balloon angioplasty had lower durability due to the re-narrowing of vessels after the intervention. The minus side of stent angioplasty was the anatomical restriction and risk of stent fracture, which might cause re-stenosis and re-occlusion.²⁰ Risk factors of stent fracture were stent type, length, and number. Balloon angioplasty could be done for a vessel less than 2 mm in diameter, a type of vessel that cannot be done by stent angioplasty. Balloon angioplasty in the infra-popliteal artery also showed good results, with 75% limb salvage in 12 months.²⁵ Another study stated good limb salvage with balloon angioplasty in severe tibial disease. On the contrary, the stent in infra-popliteal had the risk of dissection and calcification due to imperfect stent expansion. Extensive stenting was also increasing the risk of reduced flow and thrombosis.²⁰

We found an insignificant difference in resting pain and amputation rates between the two groups. This finding was similar to previous studies. However, amputation incidence in our subjects was relatively high, i.e., 42%. Another study by Hedayati et al. showed their amputation rate was 6-7% in 12 months for CLI patients underwent endovascular intervention.²⁶ The gap between amputation rate might be caused by different geographic and epidemiologic profile. The previous study stated no major amputation after 12 months of intervention in aorto-iliac and femoro-popliteal disease.²⁰ Resting pain was improved almost in all subjects in that study. Improvement of resting pain was a direct effect of revascularization.

Conclusion

The duration of wound healing was significantly between CLI patients treated with balloon angioplasty and stent angioplasty by 25 days. Stent angiography resulted in shorter wound healing compared to balloon angioplasty. Stent angioplasty is a better method than balloon angioplasty for wound healing in patients with CLI.

Disclosure

The author(s) declare to have no conflict of interest to disclose

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