MINISTRY OF EDUCATION AND TRAINING MINISTRY OF DEFENCE
108 INSTITUTE OF CLINICAL MEDICAL AND PHARMACEUTICAL SCIENCES

HỒ MINH TUẤN

CLINICAL, LABORATORY AND IMAGING CHARACTERISTICS AND OUTCOMES OF UNDERGOING PERCUTANEOUS CORONARY INTERVETION IN PATIENTS WITH DE NOVO CHRONIC THREE CORONARY ARTERY DISEASE AND SYNTAX SCORE ≤ 22

Speciality: Cardiovascular Internal Medicine

Code: 62720141

ABSTRACT OF MEDICAL PHD THESIS

Hanoi – 2023

THE THESIS WAS DONE IN: 108 INSTITUTE OF CLINICAL MEDICAL AND PHARMACEUTICAL SCIENCES

Supervisor:

1. ...
2. ...

Reviewer:

1.
2.
3.

This thesis will be presented at Institute Council at: 108 Institute of Clinical Medical and Pharmaceutical Sciences
Day Month Year

The thesis can be found at:

1. National Library of Vietnam
2. Library of 108 Institute of Clinical Medical and Pharmaceutical Sciences
3. Central Institute for Medical Science Infomation and Technology

BACKGROUND

Cardiovascular disease is the leading cause of death in Viet Nam and over the world, in which coronary artery disease is very common, especially triple-coronary artery disease accounts for an increasingly high rate. Triple coronary artery disease has clinical characteristics, investigations and treatment modalities which are different from other groups of coronary artery disease. Triple coronary artery disease is defined as significant stenosis of vessel lumen at three epicardial coronary arteries. Despite optimal medical treatment, there is still a high rate of chronic triple coronary artery stenosis with angina and moderate to high risk exercise testing. Therefore, these patients need coronary revascularization to improve symptoms and prognosis.

The results of percutaneous coronary intervention in chronic coronary artery disease with Syntax ≤ 22 are different from the disease of one or two vessels and strongly related to clinical characteristics and investigations. Coronary artery revascularization in patients which have stenosis of three vessels with Syntax $\leq$ 22 by percutaneous intervention is either anatomical of coronary arteries revascularization or functional revascularization based on exercise test results. Clinicians in the world and Vietnam still have many questions related to treatment outcomes such as angina symptoms, cardiovascular events, and death.

Study objective:

1. Evaluation of clinical characteristics and investigations in patients with triple chronic coronary artery stenosis with Syntax ≤ 22 undergoing percutaneous coronary intervention.

2. Evaluation of intervention results in patients with chronic triple coronary artery stenosis with Syntax ≤ 22 at 12 months.

New contributions of the thesis:

The study has shown the safety and effectiveness of PCI in patients with three chronic coronary artery lesions with Syntax score ≤ 22 related to improve anginal symptoms and composite cardiovascular events. Therefore, this may be another reperfusion method for this group of patients besides coronary artery bypass graft surgery. This thesis also shows that diabetes increases the risk of composite cardiovascular events, and patients who are using oral anticoagulants or chronic anemia have an increased risk of bleeding.

Dissertation layout:

This thesis consists of 129 pages (excluding appendices and references). Introduction: 02 pages. Overview: 39 pages. Subjects and research methods: 26 pages. Research results: 37 pages, Discussion: 35 pages. Conclusion and recommendations: 03 pages. The thesis has 55 tables, 4 charts, 19 drawings, 200 references, including 11 Vietnamese documents, 189 English documents.

CHAPTER 1.
OVERVIEW

1.2. Approach to diagnose chronic coronary syndrome

1.2.2. Investigations for diagnosing chronic coronary syndrome

1.2.2.1. Resting investigations

ECG: three vessels stenosis of left main disease usually has ST depression at multiple leads and ST elevation at avR

Echocardiography: approximately half of patients have regional wall motion abnormalities and LVEF < 50%

1.2.2.2. Exercise investigations

Dobutamine echocardiography: Stress echocardiography is valuable in localizing and identifying the ischemic myocardial zone corresponding to the diseased coronary arteries and provides prognostic information. Dobutamine echocardiography is performed according to the recommendations of the American Society of Echocardiography: dobutamine was initiated at 5 mg/kg/min and increased every 3 minutes to 10, 20, 30, and 40 mg/kg/min. If target heart rate is not reached, atropine can be added. Dobutamine ultrasound is a safety method. Dobutamine echocardiography in patients with chronic three coronary arteries stenosis has a high sensitivity of 94% and specificity is not different from other myocardial perfusion imaging methods.

1.3. Management of chronic three coronary artery stenosis

1.3.1. Medication

Antiplatelet agents before and after coronary stenting: aspirin and/or clopidogrel. Anti-anginal drug group consists of beta-blockers, calcium channel blockers, nitrates, and ivabradine which individualized in each patient according to the European Heart Association and American Heart Association guidelines.

1.3.2. Percutaneous coronary intervention

PCI treatment of chronic three-vessel coronary artery disease with Syntax ≤ 22: ESC in 2018: PCI indication: group I, evidence level A. Indication ACC/AHA/SCAI 2017: high appropriate indication with 7 or 8 points.

1.5. Studies in Viet Nam and abroad

1.5.1. Studies in Viet Nam

Currently, there are not many studies on PCI in chronic three-vessel coronary artery disease in Vietnam. But in clinical practice, chronic three-vessel coronary artery disease (PCI) is very common, and the results of follow-up and safety of the procedure are still controversial.

1.5.2. Studies over the world

Over the past 10 years, studies of chronic three-vessel coronary artery disease have shown that for patients with a Syntax score ≤ 22, PCI has a better or non-inferior outcome than CABG. The PCI studies with chronic three-vessel CAD were conducted with endpoints of cardiovascular events as well as angina improvement, the first was the 10-year follow-up MASS II study. However, some other studies have shown variable results in improving angina symptoms as well as cardiovascular events.

Edward L. H. et al conducted study with 11294 patients which had chronic multi vessel coronary artery disease undergoing PCI, in which 3499 patients were completely reperfused (residual Syntax= 0) and 7795 patients had incomplete reperfusion (residual Syntax > 0). After 12 months the rate of MI was 5.4% in the complete reperfusion group; and 6.7% in the incomplete reperfusion group, respectively. Study from Vasim. F. et al recruited 299 patients with three-vessels stenosis and Syntax score ≤ 22, 5 years after PCI, residual Syntax score >8 correlate with increase risk of death. Sunitha A. et al had studied 135 patients with three-vessel stenosis who underwent percutaneous intervention, there was no difference in composite cardiovascular events between the complete reperfusion group (residual Syntax = 0) and no complete (Syntax residual > 0), but there

was a difference in cardiovascular events in the group with residual Syntax > 8.

Because of different results in terms of composite cardiovascular events, angina pectoris of the above PCI studies with three chronic coronary artery disease. Therefore, we carried out this study to elucidate the PCI method for chronic three-vessel coronary artery disease with Syntax score ≤ 22 on outcomes of angina, composite cardiovascular events and bleeding complications in Vietnamese patients. And the relationship between angina, composite cardiovascular events with subclinical features and residual Syntax > 0, residual Syntax > 8.

CHAPTER 2.
METHODS AND MATERIALS

2.1. Subject of study

2.1.1. Inclusion criteria

Clinical criteria

- Above 18 yrs
- Stable angina with at least 1 month optimal medical treatment
- Non-invasive stress test with dobutamine: posistive with moderate or high risk

Invasive angiography criteria

- Lesion of three-vessels and stenosis ≥ 70% through quantitative coronary angiography (QCA).
- Syntax score ≤ 22

2.1.2. Exclusion criteria

- Index acute coronary syndrome

- Prior CABG
- Prior PCI
- Chronic total occlusion lesion
- LVEF < 40%, severe valvular heart disease
- CKD with eGFR < 30ml/min
- Pregnant patient

2.1.3. Sample size of study

Including 177 patients with three chronic coronary artery stenosis who received PCI stenting and then followed up with medical treatment for 12 months. Study was conducted at Tam Duc Heart Hospital, from January 2017 to July 2021. Patients were diagnosed with coronary artery disease and received medical treatment for at least 1 month, followed by a positive dobutamine ultrasound which moderate or high risk. After invasive coronary angiography, patients who met the inclusion criteria and did not have exclusion criteria were have a consultation with cardiac surgeon then these patients underwent intervention and coronary stent.

2.2. STUDY METHOD

2.2.1. Study design

Prospective study, cross-sectional observation and longitudinal follow-up after PCI for 12 months, with appropriate sampling.

2.2.2. Study facilities and equipment

2.2.3.Study institution

Studied patients were treated before the intervention, followed up after the intervention, and periodically re-examined at Tam Duc Heart Hospital. Follow-up examination: 30 days, 3 months, 6 months, 12

months. Echocardiography in interventional cardiology department and clinic. Hs-Troponin T, biochemistry, and hematology were done at the laboratory.

2.2.4. Study process

Clinical and laboratory features were recorded through a uniform medical record for all patients.

Medical treatment for at least 1 month: Aspirin: 75 - 165 mg/day or Clopidogrel: 75 mg/day. Antianginal drugs: according to ESC and ACC/AHA guidelines were individualized based on BP, heart rate, LVEF.

Dobutamine echocardiography after at least 1 month of medical treatment: Evaluation of myocardial ischemia zone. Patients with a positive dobutamine echocardiography with moderate or high risk are indicated for invasive coronary angiography.

Process of percutaneous coronary intervention procedure

- Preoperative tests. Consent to the procedure and consent for participating in the study. Document consultation for coronary angiography and interventional.
- The patient was fasted for at least 6 hours before the procedure. Transfer to the catheterization room after being qualified for the procedure and coronary angiography.
- Monitor pulse, BP, capillary oxygen saturation, heart rate. Instrument Kit, anesthesia method: local anesthetic with 2% lidocaine, approach methods: radial or femoral artery.
- JL, JR or Tig/5F catheter for coronary angiography and 3-way stopcock. Insert the catheter into the coronary artery, Nitroglycerine 100-200 μg directly into the coronary artery and take the coronary artery image according to conventional imaging protocol.

- Analysis of coronary artery images and quantitative analysis (QCA).
- Syntax score calculation: website: http://www.syntaxscore.com, has 3 levels: low (0-22), medium (23-32) and high (≥ 33).
- Select intervention patients with Syntax score: 0-22. Heart team disscussion for revascularization method: decision is stenting.
- Select the vessel corresponding to the myocardial ischemia zone according to the results of dobutamine echo. All lesion of the LM and/or LAD segment 1 will have stent implantation. Anticoagulation: Unfractionated heparin: 70-100 units/kg IV before PCI to achieve ACT: 250-350 seconds and repeat 1000-1500 units (or 1/2 dose) IV every hour if PCI process took more than 1 hour.
- Engage interventional catheter and conduct intervention procedure.

Intervention for non-LM lesion

Advance a 0.014" floppy guidewire through the lesion. Lesion preparation (with non-compliant balloons have 1:1 ratio with coronary artery diameter, if the non-compliant balloons do not go through lesion, use a compliant balloon first) or cutting balloon or Rotablator. Implant a drug-eluting stent. Post-dilatation the stent with a non-compliant balloon. Check again with at least 2 angles projector.

Intervention for LM lesion

Assessment for classification of coronary artery lesions according to Medina classification. Angle between LAD and LCX. Wiring into LAD and LCX. IVUS for assessment of lesion characteristics and coronary artery diameter before stenting.

+ 2 stents strategy: dilatation with non-compliant balloon which have 1:1 ratio to the diameter of the coronary artery (LAD or LCX branch), if the non-compliant balloon does not cross, use a compliant balloon first or Rotablator. If there is no atherosclerotic

plaque causing stenosis of >50% of the other branch (LAD or LCX), an LM-LAD (or LM-LCX) stent was implanted. Perform POT (Proximal Optimization Technique), IVUS assess stent expansion, stent apposition and complications; consider kissing balloon if necessary, then check with at least 2 angles projector. If atherosclerotic plaque is present with >50% stenosis of the other branch (LAD or LCX), switch to a 2-stent strategy.

+ 2 stents strategy: dilatation with non-compliant balloon which have diameter ratio 1:1 with coronary artery diameter, then use one of the techniques: Crush, D-K Crush, TAP, T-stent, V-stent, Culotte, Kissing stent, then perform Kissing balloon, perform POT, IVUS assess expansion, stent apposition and complications, then check again with at least 2 angles projector.

In-hospital follow up after procedure

- End of procedure: record vital signs, evaluate PCI results: TIMI flow, residual stenosis, coronary dissection, residual Syntax, complications. ECG immediately after the procedure and when there have any clinical abnormalities. HS-Troponin T 8 ±2 hours, 24-48 hours after PCI and when there are abnormal clinical manifestations. Transfer patient to the department, echocardiography, serum creatinine 24 hours after the procedure. Remove the compression bandage 4-6 hours after PCI with the radial artery, 18-24 hours with the femoral artery.

Medical treatment at discharge

All patients were monitored at Tam Duc Heart Hospital after discharged. Aspirin 81 mg/day, up to the end of 12-month follow-up. Clopidogrel: all patients after intervention, dose is 75 mg/day, 6 months. Or continue after 6 months if intolerant to aspirin.

Patients with atrial fibrillation: when CHA2DS2-VASc score ≥ 1 in men and ≥ 2 in women: use novel anticoagulation and DAPT 1 month after PCI. Then, clopidogrel 75 mg/day and new anticoagulation up to 12 months.

Antianginal drugs: patients continue to be prescribed the same as before PCI. Statins: 20-40 mg Atorvastatin/day or 10-20 mg Rosuvastatin/day. Or Ezetimibe: 10 mg/day when indicated.

Short-term outcomes evaluation

Direct medical examination or indirect by phone once a month. Collected variables include: CCS angina, Composite cardiovascular events: all-cause death, MI, repeat reperfusion, stroke. And major bleeding. Investigation: Echocardiography, ECG, LDL-c.

CHAPTER 3.

RESULTS

Table 3.1. Overall characteristic

Characteristics	n	Mean ± SD
Overall age (year)	177	65,94 ± 10,85
Female age (year)	58	69,03 ± 9,25
Male age (year)	119	64,44 ± 11,28
Overall BMI (kg/m^2)	177	23,82 ± 2,94
Female BMI (kg/m^2)	58	23,37 ± 3,39
Male BMI (kg/m^2)	119	24,12 ± 2,76

Comments: 177 patients participated in the study. Male: 119 patients (67.2%), female 58 patients (32.8%), mean age: 65.94 ± 10.85 years old, the lowest is 32 and the highest is 91. Mean BMI is 23.82 ± 2.94 kg/m2, BMI between men and women is relatively equivalent.

Table 3.2. Cardiovascular risk factor characteristic

Characteristic	Yes (n)	(%)	No (n)	(%)
Smoking	25	14,1%	152	85,9%
Hypertension	159	89,8%	18	10,2%
Diabetes	78	44,1%	99	55,9%
Dyslipidaemias	156	88,1%	21	11,9%
Family history of CAD	20	11,3%	157	88,7%

Comments: CAD risk factors: HTN, dyslipidaemias are predominant.

Table 3.3. Anginal symptom characteristic before PCI

Anginal classification	n	%
CCS I	1	0,6%
CCS II	84	47,5%
CCS III	92	51,9%
CCS IV	0	0%

Comments: CCS II and CCS III angina are predominant with CCS II accounting for 47.5%, CCS III accounting for 51.9%, the rest is CCS I which accounting for 0.6%, no report any case has CCS IV.

3.2.3 Lesion characteristics by coronary angiography

Table 3.8. Coronary artery lesion characteristic

	yes (n)	(%)	no (n)	(%)
LM	33	18,6%	144	81,4%
Proximal LAD	102	57,6%	75	42,4%
LAD	175	98,9%	2	1,1%
LCX	176	99,4%	1	0,6%
RCA	177	100%	0	0%
Left coronary artery predominance	5	2,82%	172	97,18%

Comments: The rate of coronary artery lesion in the LM is 18.6%, the LAD is 98.9%, the LCX is 99.4% and the RCA is 100%, the incidence of stenosis ≥ 70% of proximal LAD was 57.6%.

Table 3.10. Coronary artery lesion characteristic by Syntax score before and after PCI

Characteristic	**Mean ± SD**	**Variable range (min – max)/ percentage of overall study**			
Syntax score before PCI	15,84 ± 3,85	7 - 22			
		100%			
Residual syntax score after PCI	3,37 ± 2,97	0	1-4	5-8	>8
		23,7%	44,6%	22%	9,7%

Comments: Average Syntax score: 15.84 ± 3.85 (from 7 to 22), average residual Syntax score is 3.37 ± 2.97, residual Syntax score 0 and 1- 4 are predominate.

3.2.4. Characteristic of diseased coronary artery intervention

Table 3.11. Percentage of diseased coronary artery are revascularized

Characteristic	**Ratio with study population**		**Ratio with every coronary artery lesion**	
LM	33/177	18,6%	33/33	100%
Proximal LAD	102/177	57,6%	102/102	100%
LAD	151/177	85,3%	151/175	86,3%
LCX	84/177	47,5%	84/176	47,7%
RCA	103/177	58,2%	103/177	58,2%

Comments: Percentage of coronary lesions revascularized in which 100% of LM and proximal LAD lesions were revascularized.

Bảng 3.12. Average number of stent

Characteristic	**Stent number/study population** (mean ± SD)	**Stent number /every coronary artery lesion**
LM	0,18 ± 0,38	1
LAD	1,11 ± 0,63	1,3
LCX	0,54 ± 0,63	1,1
RCA	0,79 ± 0,81	1,4
Stent/patient	2,61 ± 0,95	
Average stent diameter (mm)	2,92 ± 0,42	
Average stent length (mm)	22 ± 15,4	

Comments: Average number of stents per coronary artery in the whole study population: LM: 0.18 ± 0.38 stents/whole sample and 1 stent/every lesion and all cases of LM significant stenosis were stenting; LAD: 1.11 ± 0.63 stent; LCX: 0.54 ± 0.63 stent and RCA: 0.79 ± 0.81 stent and the number of stent/patient is 2.61 ± 0.95 stents.

3.3. ASSESSMENT RESULTS OF TREATMENT WITH PERCUTANEOUS INTERVENTION FOR PATIENT WHICH HAVE THREE CHRONIC CORONARY ARTERY STENOSIS AT 12 MONTH FOLLOW UP

3.3.1. Successful regarding PCI technique on patient with three chronic coronary artery stenosis

Table 3.15. Successful rate of PCI procedure

Characteristic	Yes (n)	(%)	No (n)	(%)
TIMI III at revascularized vessels	177	100%	0	0%
Residual stenosis <20%	177	100%	0	0%
Success on coronary angiography	171	96,6%	6	3,4%
Successful PCI procedure	171	96,6%	6	3,4%
Success on clinical condition	171	96,6%	6	3,4%

Comments: The PCI success rate based on angiography and procedure success was 96.6% (there were 6 cases of slow flow or loss of side branch flow). There were 3 cases of periprocedural myocardial infarction, accounting for 1.67%.

3.3.3. Results after PCI on patients with three chronic coronary artery stenosis during hospital course

Bảng 3.4. Percentage of improvement in angina before and after PCI

Characteristic	Before PCI (n=177)	After PCI (n=177)	p
Change from CCS>1 to CCS≤ 1 after PCI (n%)	1 (0,5%)	174 (98,3%)	**<0,001**
Become no angina (n%)	0 (0%)	174 (98,3%)	

Comments: The percentage of no angina symptoms or CCS ≤ 1 is reached up to 98.3% compared with 100% with chest pain before PCI.

Table 3.17. In-hospital cardiovascular events rate

Characteristic	Yes (n)	(%)	No (n)	(%)
Stroke	0	0%	177	100%
Myocardial infarction	3	1,7%	174	98,3%
Death	0	0%	177	100%
Revascularization after PCI	0	0%	177	100%
Composite cardiovascular events	3	1,7%	174	98,3%

Comments: Composite cardiovascular events: 1.7%, of which MI: 1.7%.

Table 3.18. In-hospital bleeding percentage

Characteristic	Yes (n)	(%)	No (n)	(%)
Major bleeding/BARC	3	1,7%	174	98,3%
Access site bleeding	0	0%	100	100%
Other sites bleeding	3	1,7%	174	98,3%

Comments: The overall rate of major bleeding was 1.7%, in which all cases of major bleeding occurred in the upper gastrointestinal tract: with symptoms of melena, fecal occult red blood cell test (+) and upper gastrointestinal endoscopy showed hemorrhagic images, there were no cases of severe bleeding at the access site.

3.3.6. Results of PCI after 12 month follow up on patient with three chronic coronary artery stenosis

Table 3.5. Rate of improvement in angina symptomp, investigations after 12 month follow up on study population

Đặc điểm	Before PCI (n=177)	12 months after PCI (n=177)	p
Change from CCS>1 to CCS≤ 1 after PCI (n%)	1 (0,5%)	165 (93,2%)	**<0,001**
Become no angina	0 (0%)	158 (89,3%)	
Mean EF (%) (Simpson)(Mean±SD)	60,34 ± 11,75	68,06 ± 11,69	**<0,001**
Reduction LDL ≥50% (n%)	0 (0%)	87 (49,2%)	
LDL-C ≤1,4 mmol/L (n%)	7 (4,0%)	36 (20,3%)	**<0,001**

Comments: 12 months of follow-up after PCI, there was a statistically significant improvement in angina and investigations. The rate of change in CCS ≤ I was 93.2%, the rate of change in angina symptoms was 89.3%. Mean LVEF (%) measured by Simpson method, there was an improvement of 68.06 ± 11.69% compared to 60.34 ± 11.75% after 12 months of intervention.

Table 3.6. Major bleeding after 12 month follow up of PCI, corresponding with NOAC or anaemia group of patients

Characteristic	Major bleeding		RR (CI 95%)	p
	no	yes		
Anticoagulation (n%)	8 (66,7%)	4 (33,3%)	40,75 (6,5 - 256,5)	**<0,001**
No anticoagulation (n%)	163 (98,8%)	2 (1,2%)		
Anaemia (n%)	21 (84,0%)	4 (16,0%)	14,29 (2,46-82,85)	**0,004**
No anaemia (n%)	150 (98,7%)	2 (1,3%)		
Overall (n%)	171/177 (96,6%)	6/177 (3,4 %)		

Comments: The rate of major bleeding in the whole study population was 3.4% (6 cases). Anticoagulation increased the risk of major bleeding 40.75 times (95% CI: 6.5 - 265.5) compared with the group without anticoagulation with p<0.001. In the anemia group, the risk of major bleeding increased 14.29 times (95% CI:2.46 - 82.85) compared with the group without anemia. Statistic significant difference between pre-PCI anemia and major bleeding with p = 0.004.

Table 3.7. Rate of composite cardiovascular events at 12 month follow up after PCI on study population

Characteristic	yes (n)	(%)	no (n)	(%)
Myocardial infarction	11	6,2%	166	93,8%
Stroke	1	0,6%	176	99,4%
Death	0	0%	177	100%
Revascularization after PCI	7	4,0%	170	96%
Composite CV events	19	10,7%	158	89,3%

Comments: The composite CV event was 10.7% (19 cases). In which: + MI was 6.2% (11 cases): 3 cases of MI related to PCI procedure due to reduction or loss of side branch flow <1.5mm, the remaining 8 cases were non-STEMI occurred between 6-12 months after stenting, in which 7 cases were revascularized, 1 case was diagnosed with non-STEMI but patient and family did not agree to have coronary angiography. +The stroke 0.6% (1 case).+The rate of revascularization after PCI is 4% (7 cases): revascularization 7 cases with diagnosis are non-STEMI, 4 cases of focal in-stent restenosis, 3 cases due to lesion progression outside the stent.+No patient died during the study course.

Table 3.8. Result of composite CV in complete revasularization vs incomplete revascularization after 12 months

Characteristic	Composite CV events		p
	No	yes	
Complete revascularization	41 (97.6%)	1 (2.4%)	
Incomplete revascularization	117 (86.7%)	18 (13.3%)	**0,048**
Overall (n%)	158 (89.3%)	19 (10.7%)	

Comments: Composite cardiovascular events in the whole study were 10.7%, incomplete revascularization group (residual Syntax >0) is 13.3% and complete revascularization group (residual Syntax =0) is 2.4%, p=0.048.

3.3.7. Relationship between clinical condition, investigations, and CAD risk factors with composite cardiovascular events in patients with three chronic coronary artery stenosis which had been PCI

Table 3.9. Relationship between risk factors with composite cardiovascular events at 12 month follow up on study population

Characteristic	Composite CV events		RR (CI 95%)	p
	no	yes		
Smoking (n%)	18 (90%)	2 (10%)	0,86 (0,16-4,64)	>0,05
Hypertension (n%)	142 (89,3%)	17 (10,7%)	0,62 (0,11-3,35)	>0,05
Diabetes (n%)	64 (82,1%)	14 (17,9%)	4,31 (1,4-13,25)	**<0,05**
Dyslipidaemias (n%)	140 (89,7%)	16 (10,3%)	0,93 (0,24-3,67)	>0,05
BMI>23 (n%)	83 (88,3%)	11 (11,7%)	0,98 (0,35-2,7)	>0,05
Family history with CAD (n%)	18 (90,0%)	2 (10,0%)	0,76 (0,16-3,74)	>0,05
Residual syntax > 8 (n%)	151 (88,8%)	19 (11,2%)	1,126 (1,067-1,187)	>0,05

Comments: the group has diabetes had a composite cardiovascular events risk 4.31 times higher (CI 95%: 1.4-13.25) compared with the group does not have diabetes on the study population with $p<0.05$.

CHAPTER 4.
DISCUSSION

4.2.1. Characteristic of study population

General characteristics: Gender: male predominates with 67.2%. This result is consistent with the author Kevin R. B. et al., studied 2175 patients with three chronic coronary artery stenosis, the male predominance rate was 81.5%. Study from Nguyen Lan Viet and colleagues at Bach Mai Hospital are 68.1% male. Age: mean age is 65.94 ± 10.85 years old. This result is consistent with William S. W. et al., studied 330 patients with three chronic coronary artery stenosis, the average age of patients was 63±10 years old. BMI: average BMI is 23.82 ± 2.94 kg/m2 (according to Asian obesity criteria). In study of Nguyen Lan Viet et al., the mean BMI of the chronic coronary artery disease study group was 22.9 ± 2.3 kg/m2. Jeehoon K. et al., 729 patients with three chronic coronary artery disease, average BMI 24.7 ± 3.3 kg/m2.

Risk factors for coronary artery disease: 89.8% had hypertension, 88.1% had dyslipidaemias, 44.1% had diabetes, smoking was 14.1% and family history of coronary artery disease was 11.3%. This result is consistent with study of Kevin R. B. et al., include 2175 patients with three chronic coronary artery disease underwent PCI, the rate of hypertension was 78.9%, dyslipidaemias was 78.3%, diabetes was 31.1%, smoking is 11.9%.

Angina: all patients participating in the study had symptoms of angina, with angina CCS II accounting for 47.5% and angina CCS III

accounting for 51.9%. Angina CCS I had a low rate of 0.6%, there were no patients with CCS IV angina. Our results are consistent with study of William S. W. et al, include 330 with three chronic coronary artery disease underwent PCI, which angina CCS II is 33%, CCS III is 23%.

4.2.3. Characteristic of lesion on coronary angiography

Characteristics of lesions according to coronary artery: the rate of significant stenosis is 18.6%, LAD is 98.9%, LCX is 99.4% and RCA is 100%, stenosis ≥ 70% of proximal LAD is 57.6%. The results of this study are consistent with study from Neuza H. L. et al., include 358 patients with three chronic coronary artery disease, the ratio of each vessels: LAD accounted for 98%, LCX accounted for 89%, RCA accounted for 82%.

Syntax and residual syntax: the average Syntax score is 15.84 ± 3.85. Our results are consistent with study of Jeehoon K. et al., studying 729 patients with three chronic coronary artery stenosis with Syntax score ≤ 22, average Syntax score 14.5 ± 5.2. The proportion of patients with residual Syntax score > 8 in our study is low (9.7%), indicating that the residual burden of atherosclerosis after PCI is not high.

4.2.4. Characteristic of PCI for coronary artery lesions

Percentage of each reperfused coronary artery: 18.6% LM, 85.3% LAD, 47.5% LCX and 58.2% RCA were reperfused, in which 100% LM lesions and 100% proximal LAD lesions are stenting. The rate of patients who were completely reperfused (residual Syntax = 0) was 23.7%, consistent with study from Jeehoon K. et al., studied 729 patients with three chronic artery stenosis with Syntax ≤ 22, the rate of patients with complete reperfusion (residual Syntax= 0) was 21.5%. LM and/or proximal LAD reperfusion showed an improved in

prognosis compared with medical treatment, therefore all LM and/or proximal LAD significant stenosis in our study were stented.

Average number of stents: the average number of stents per vessel was: LAD 1.11 ± 0.63 stent, LCX 0.54 ± 0.63 stent, RCA 0.79 ± 0.81 stent and all LM lesions were being stented, in which number of stent/LAD: 1.3, number of stent/LCX: 1,1, number of stent/RCA: 1.4. The average number of stents/patient was 2.61 ± 0.95 stent consistent with study from Jeehoon K. et al., which studied 729 patients with three chronic coronary artery disease with Syntax score ≤ 22 who received PCI, the average number of stents/ patient is 1.9 ± 0.9.

4.3. EVALUATE RESULTS OF PCI IN PATIENTS HAVE THREE CHRONIC CORONARY ARTERY STENOSIS WITH 12 MONTHS FOLLOW UP

4.3.1. PCI technique success in patients have three chronic coronary artery stenosis

The successful rate on coronary angiography is 96.6%. The procedure successful rate is 96.6%. The clinical successful rate is 96.6%. Our results are consistent with study of Samuel C. C. and colleagues, which included 46 patients with three coronary artery stenosis who underwent PCI: the angiography successful rate was 100% and the procedure successful rate was 95.66%. Abel Y. L. Q. et al. studied 87 patients with three coronary arteries diease were implanted drug-eluting stents, the successful rate of the procedure was 97.7%. The successful rate of the procedure is related to the following factors: the general condition of the patient, the anatomy of the lesion, the technique and facilities, the successful rate of our procedure is high, likely because of the good lesion preparation, the new generation stent able to cross through lesion easily are favorable factors for high

success.

4.3.3. Results after PCI in patients with three chronic coronary artery stenosis during hospital stay

Improvement of Angina: We evaluated angina during hospital stay after PCI, because angina occured immediately after the procedure or within 24 hours after PCI could be caused by coronary artery spasm, coronary artery wall overdistension by stent or procedural complications such as acute stent thrombosis, incomplete reperfusion, and the incidence of angina were significantly reduced at hospital discharge compared with post-procedure. The rate of angina pectoris resolution or conversion to CCS ≤ I was 98.3% after PCI, consistent with study from Kini et al., studied 1362 patients with chronic coronary artery disease who underwent PCI: the rate of angina resolution at hospital discharge was 95 %.

Composite cardiovascular events: According to table 3.17, composite cardiovascular events (death, MI, stroke, repeat revascularization) was 1.7%, of which MI was 1.7%. Our results are consistent with study of Mohamed L. et al., included 243 diabetic patients and 401 non-diabetic patients with multivessel stenosis who were implanted drug-eluting stents, composite cardiovascular events (death, MI, stroke, repeat revascularization) in hospital course is 2%.

Major bleeding during hospital stay: The incidence of major bleeding depends on a variety of factors including: anticoagulation, patient general characteristics, interventional procedures, and in particular based on the different definition of bleeding. We use the BARC criteria that are widely used in coronary artery revascularization clinical studies and recommended by the Interventional Associations. BARC major bleeding includes: type 3,

type 4, type 5. The rate of major bleeding during hospital stay: 1.7%. Our results are consistent with Yohei N. et al., who had study of 4062 chronic coronary artery disease undergoing PCI, major bleeding during hospital stay was 1.65%.

4.3.6. Results at 12 month follow up after PCI in patients with three chronic coronary artery stenosis

Improvement of angina symptoms after 12 months of PCI: according to the results of Table 3.26, all patients had angina symptoms before PCI, after 12 months of intervention, there was an improvement in angina. The percentage of conversion to CCS ≤ I was 93.2%, the rate of conversion to CCS 0 was 89.3% (compared to before PCI: the rate of CCS 0 was 0% and the rate of CCS I was 0.6%). Our results are consistent with study of Head S. J. and colleagues, who studied 546 patients with three chronic coronary artery stenosis who underwent PCI, after 12 months the rate of residual chest pain was 10.5%. Especially in our study, after considering the risk factors for coronary artery disease and medication between the two groups are similar, the conversion rate of CCS 0 in the complete revascularization group (residual Syntax = 0) was 97.6%, which was higher than 74.1% in the incomplete revascularization group (residual Syntax >0) with p= 0.048. However, when analyzing the correlation with residual Syntax > 8: study results in Table 3.28: angina characteristics, LVEF and LDL-C are not related to residual Syntax score > 8 and < 8. Results This result can be explained because our study selected the revascularized vessels according to dobutamine echocardiography, therefore we can reduce residual narrow branches with large myocardial distribution area.

Major bleeding after 12 months of intervention: In our study, the radial artery approach was mainly used, accounting for 76.3%, thus reducing bleeding complications at the access site. Therefore, bleeding after PCI is associated with antiplatelet therapy or possibly oral anticoagulation. According to Table 3.29, the rate of major bleeding was 3.4%. This result is consistent with Sara A. et al., studied 424 patients were implanted drug-eluting stents, 12 months follow-up, the rate of major bleeding according to BARC criteria was 3.5%.

Correlation between anaemia, anticoagulation at hospital admission and major bleeding after 12 months of follow-up: according to the study results in Table 3.29, after 12 months of PCI, the group with pre-PCI anaemia increased the probability of major bleeding by 14,29 times (95% CI: 2.46-82.85) compared with the no-anaemia group, this result is consistent with study of Line D. et al., studied 2837 patients with chronic coronary artery disease were stent implantation, group with anaemia increased the risk of major bleeding by 2.18 times after 3 years follow-up. According to our study, patients taking NOAC due to atrial fibrillation after PCI increased the risk of major bleeding by 40.75 times (CI 95%: 6.5 - 265.5).

Composite cardiovascular events during 12-month follow-up: The composite cardiovascular events in our study included: death, stroke, MI, repeat revascularization. According to the results of Table 3.30, our composite cardiovascular event rate was 10.7%. Due to the low frequency of events and limited sample size, our study decided not to analyze each event alone. Our composite cardiovascular event rate was consistent with Patrick S. et al., which studied 299 patients with three chronic coronary artery disease with Syntax score ≤ 22, had PCI with drug-eluting stents, followed up for 12 months, the composite

cardiovascular event rate (death, stroke, MI, repeat revascularization) was 13.5%. Chang W. N. et al., studied 167 patients with three chronic coronary artery stenosis with a Syntax score ≤ 22, who had PCI with drug-eluting stents for 12-month follow-up, composite cardiovascular events (death, MI, revascularization) was 8.4%.

The rate of revascularization after PCI was 4% (7 cases): revascularization 7 cases was diagnosed of non- ST segment elevation myocardial infarction, 4 cases of in-stents restenosis with focal type < 10mm, 3 cases due to progression of pre-existing lesions beyond the stent area. Thus, in-stent restenosis alone accounted for 2.26% (4/177), this is a low rate of in-stent restenosis after coronary stenting in patients with three-vessel stenosis, this can explain by our study was using new generation drug-eluting stent, lesions with Syntax score ≤ 22, large average stent diameter of 2.92 ± 0.42 mm, novel intervention techniques as well as very strictly controlled risk factors of atherosclerosis.

Composite cardiovascular events at 12 months were different between the complete (residual Syntax = 0) and incomplete (residual Syntax > 0) revascularization groups: After assesment for similarity in the general characteristics of the complete revascularization (residual Syntax = 0) and incomplete group (residual Syntax > 0), composite cardiovascular events of incomplete revascularization group (residual Syntax > 0) was 13.3% and complete revascularization group (residual Syntax = 0) was 2.4% with p=0.048. In the group of incomplete revascularization, high residual ischemic myocardium area may be the cause of cardiovascular events and angina after coronary revascularization. Head S. J. et al studied 544 patients with three chronic coronary artery stenosis who underwent

PCI by drug-eluting stents, the rate of composite cardiovascular events (death, MI, stroke, repeat revascularization) after 5 years in the complete revascularization group (residual Syntax = 0) was 32.7% and lower than in the incomplete revascularization group (residual Syntax > 0) was 42.6% with p<0.01. Young B. S. et al, 873 three coronary artery stenosis who underwent PCI with drug-eluting stents after 35 months of follow up, complete revascularization group (residual Syntax = 0) had composite cardiovascular events (death, MI, repeat revascularization) was lower than in the incomplete revascularization group (residual Syntax > 0) (HR 0.64; 95% CI 0.46–0.88; p < 0.01).

4.3.7. The relationship between clinical, investigations and coronary artery risk factors with composite cardiovascular events in patients with three chronic coronary artery stenosis undergoing PCI

According to Table 3.33, there is a relationship between the diabetes group and the composite cardiovascular events with p<0.05. In Diabetes group had composite cardiovascular event rate which increased by 4.31 times (95% CI: 1.4-13.25, p<0.05). Our results are consistent with results of Elvin K. et al, who studied 3167 diabetic patients and 3167 non-diabetic patients who were implanted drug-eluting stents, after 12 months of follow-up, the rate of composite cardiovascular events increased by 1.5 times in the diabetes group (95% CI: 1.29-1.74, p<0.0001.13.9% vs 9.4%). Ibrahim A. et al, diabetes increases cardiovascular events: 1,659 diabetic and 3,559 non-diabetic patients who were implanted drug-eluting stents, after 1-year follow-up, the diabetes group had an increased risk of death (5.6 vs. 4%; p < 0.01), MI (4.8 vs 3.4%; p = 0.05), stroke (1.7 vs 0.9%; p < 0.05), composite cardiac events (10.9 vs 7.1%; p < 0.001).

CONCLUSION

The study of 177 patients who diagnosed with three chronic coronary artery stenosis and Syntax score ≤ 22, underwent percutaneous intervention at Tam Duc Heart Hospital from January 2017 to July 2021, we would like to demonstrate some conclusions:

1. Clinical and investigations characteristics in patients with three chronic coronary artery stenosis with Syntax ≤ 22 undergoing percutaneous intervention.

• The mean age was 65.94 ± 10.85, male accounted for 67.2%.

• Risk factors for coronary artery disease: hypertension 89.8%, dyslipidemias 88.1%, diabetes 44.1%, smoking 14.1%, family history of coronary artery disease 11.3% and mean BMI 23.82 ± 2 ,94 kg/m2

• CCS III angina accounted for 51.9%, CCS II angina accounted for 47.5%, CCS I angina accounted for 0.6%.

• Comorbidities: chronic kidney disease accounted for 20.3%, atrial fibrillation requiring novel oral anticoagulation 6.8%, anemia 14.1%, COPD 11.9%.

• Mean LVEF 60.34 ± 11.75%. The rate of LVEF > 50% accounted for 81.4%.

• Risk stratification by dobutamine echocardiography: intermediate risk 21.5%, high risk 78.5%.

• Percentage of each coronary artery lesion: LM is 18.6%, LAD is 98.9%, LC is 99.4% and RCA is 100%.

• Average Syntax score of 15.84± 3.85, with a range from 7 to 22. Residual Syntax score: 3.37 ± 2.97.

• Percentage of each coronary artery has revascularization: LM is 18.6%, LAD is 85.3%, LCX is 47.5% and RCA is 58.2%.

• The average number of stents/patient is 2.61 ± 0.95.

2. Results of treatment with percutaneous intervention in patients with three chronic coronary artery stenosis with Syntax ≤ 22 after 12 months

• During hospital stay: the rate of chest pain resolution or conversion to CCS ≤ 1 was 98.3%, composite cardiovascular events were 1.7%, major bleeding was 1.7%.

• At 30-day follow-up: the rate of chest pain resolution or conversion to CCS ≤ 1 was 98.3%, composite cardiovascular events were 1.7%, major bleeding was 1.7%.

• At 3-month follow-up: the rate of chest pain resolution or conversion to CCS ≤ 1 was 98.3%, composite cardiovascular events were 1.7%, major bleeding was 2.3%.

• At 6-month follow-up: the rate of chest pain resolution or conversion to CCS ≤ 1 was 98.3%, composite cardiovascular events were 1.7%, major bleeding was 2.3%.

• At 12-month follow-up:

+ There was an improvement in angina compared with pre-PCI in the general population, the rate of conversion to CCS ≤ I was 93.2%, the rate of angina resolution was 89.3%. The complete revascularization group (residual Syntax = 0) improved angina 97.6% better than the incomplete revascularization group (residual Syntax > 0) 74.1%.

+ The mean LVEF (%) improved after 12 months of intervention was 68.06 ± 11.69% compared to 60.34 ± 11.75% before the intervention.

+ The composite cardiovascular event in the general population was 10.7%, the rate of complete revascularization group (residual Syntax = 0) was lower than incomplete revascularization group (residual Syntax > 0) (2.4% versus 13.3%). No patient died during the study.

+ Diabetes increased the risk of composite cardiovascular events by

5.64 times compared with the non-diabetic group.

+ Major bleeding: Using novel anticoagulants increased the risk of major bleeding by 40.75 times compared with the group not using novel anticoagulants. Anemia before intervention increases the risk of major bleeding by 14.29 times compared with the group without anemia.

LIST OF PUBLISHED ARTICLE RELATING TO THESIS

1. Hồ Minh Tuấn, Phạm Thái Giang, Vũ Điện Biên (2022), Evaluation of clinical characteristics and investigations in patients with triple chronic coronary artery stenosis, Vol.17, No.1, Journal of Clinical Medicine and Pharmacy 108.
2. Hồ Minh Tuấn, Phạm Thái Giang, Vũ Điện Biên (2022), Evaluation of intervention results in patients with chronic triple coronary artery stenosis at 12 months, Vol.17, No.1, Journal of Clinical Medicine and Pharmacy 108.