HUE UNIVERSITY
MEDICAL PHARMACY UNVERSITY

TRAN THI TRUC LINH

INVESTIGATING THE RELATIONSHIP BETWEEN CARDIAC MANIFESTATIONS AND THE TREATMENT TARGETS FROM ESC-EASD GUIDELINES FOR TYPE 2 DIABETIC PATIENTS WITH HYPERTENSION

Speciality : Endocrinology
Code : 62 72 01 45

SUMMARY OF MEDICAL DOCTORAL THESIS

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The work was completed at the Hue University- Medicine and Pharmacy Hue University

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The Objection 3: Assoc. Prof. , MD,PhD

Can be found the thesis in:

1. National Library
2. The Library of Medicine and Pharmacy Hue University

LIST OF WORKS OF RESEARCH HAS PUBLISHED AUTHOR RELATED TO THE THESIS

1. **Tran Thi Truc Linh, Nguyen Hai Thuy,** "Researching relationship between the plasma levels of NT-proBNP and changes of left ventricular morphology and diastolic function in hypertension type 2 diabetes mellitus", *Journal of Vietnamese Cardiology*, Vol 65, pp. 365-369.
2. **Tran Thi Truc Linh, Nguyen Hai Thuy,** "Intimal-Medial Thickness of carotid artery (IMTc) in the type 2 diabetic patients with hypertension", *Journal of Medicine and Pharmacy,* Vol 22+23, pp. 28-35.

BACKGROUND

Diabetes (DM) and Hypertension (HT) are the chronic diseases which have been increasing all over the world rapidly. Combining two disease have effected the serious burden of cardiovascular system. The significant development of the mortality and morbidity causing cardiovascular diseases (CVD) in patients with DM and HT which have been encouraged many cardiology and diabetes associations recommended that cardiovascular risk assessment should become the first aim in the recent time. Besides the traditional cardiovascular risks, ESC-EASD has added the nontraditional cardiovascular risk factors such as biomarkers and imaging is necessary in order to detect target organs damage in subclinical.

In Vietnam, the application of ESC-EASD guideline and the awareness of diabetic heart disease in preclinical stage have limited. Therefore, we are essential to research "Investigating the relationship between cardiac manifestations and the treatment targets from ESC-EASD guidelines on type 2 diabetic patients with hypertension". Concluding the objectives:

1. To review the recommended treatment goals of ESC-EASD, a number of cardiovascular risk factors and cardiac manifestations (serum NTproBNP levels and morphology, structure left ventricular function on echocardiography) in type 2 diabetic patients (T2DM) with hypertension.

2. To determine the relationship and the change between the treatment targets, cardiovascular risk factors and cardiac manifestations after 12 months of follow-up.

The scientific and practical meaning

- To evaluate the treatment effects of ESC-EASD guideline in Vietnamese health clinic. Determinating the importance of nontraditional risk factors for cardiovascular damage in subclinical and predicting cardiovascular events.

- Throughout the research proves that the role of diagnosed cardiovascular or target organs in preclinical is much valuable and independent with the treatment targets of the guidelines.

Structure thesis:

It consists of 126 pages (excluding references and appendices), with 4 chapters, 40 tables, 5 charts, 13 diagrams, 6 pictures and 109 references. Introduction 3 pages, overview 38 pages, subjects and methods 21 pages, results 28 pages, discussions 33 pages, conclusion 2 pages, recommendations and follow-up researchs 1 page.

Chapter 1: OVERVIEW

1.1. DIABETES AND HYPERTENSION

1.1.1. Epidemiology

The incidence of hypertension (HTN) are twofold higher in those with T2DM relative to similar aged individuals without DM and 75% T2DM have hypertension, or patients with HTN are more likely to develop T2DM about 2.5 times after five years diagnosed with HTN. A meta-analysis 89 studies showed that HTN in T2DM rates typically were high in all regions; most studies presented rates above 50%, and many presented rates above 75%.

1.2. CARDIOVASCULAR RISK FACTORS

1.2.1. Traditional cardiovascular risk factors

- The elements of time (ages, duration of diagnosed diabetes, a duration of diagnosed hypertension) and gender: in almost the studies, age and duration of diagnosed disease are always the important and indispensable risk factors. Moreover, the results of the study showed that cardiovascular complications particularly high rate in women with T2DM. Smoking is the independent risk of cardiovascular disease due to atherosclerosis. Physical activity plays the important role to help blood glucose control and is associated with cardiovascular complications in DM. Body mass index (BMI) and waist circumference (WC) in T2DM patients are both the predictor factors and the cardiovascular risk of DM. Fasting plasma

glucose (FPG) and HbA1C, postprandial plasma glucose are some independent and direct risk fators of death. Dyslipidemia is often accompanied with T2DM with typical manifestations include increased levels of triglycerides and decreased HDL.C. FIELD, ACCORD study on T2DM patients showed that the rate of cardiovascular events have been significantly higher in dyslipidemia group.

1.2.2. Nontraditional cardiovascular risk factors

- **Microalbuminurea:** HOPE study demonstrated that microalbuminuria has increased the cardiovascular events with the relative risk 1.83 (95%CI: 1.64-2.05). Among these, the risk of T2DM was 1.97 (95%CI: 1.68-2.31) higher than patients without T2DM, similar to IDNT, RENAAL, PREVEND research.

- **C-reactive protein high sensitivity (Hs-CRP):** is a factor representing the state of endothelial dysfunction and test applications common in patients with hypertension and diabetes. Hs-CRP is associated with insulin resistance, indices of systolic blood pressure, pulse pressure, hypertension and other signs of endothelial dysfunction other.

- **Thickness middle class internal carotid artery (IMTc)**: tends to increase cardiovascular disease atherosclerosis in diabetic and hypertensive subjects with increasing progression of the thickness IMTc. IMTc is a sign of atherosclerosis which is associated with other cardiovascular risks.

1.3 Diabetes hypertension and cardiovascular complications

1.3.1. Pathogenesis of diabetes heart disease (DHD: Diabetic Heart Disease)

The most comprehensive access of diabetic heart disease is a combination of three groups of diseases, including: (1) diabetic cardiomyopathy (DMD), (2) hypertensive heart disease (HHD) and (3) due to coronary artery disease atherosclerosis and contribute to this very complex mechanism [79].

1.3.3. Characteristics of diabetic heart disease: (1) Morphology disorders of diabetic cardiomyopathy, (2) Regional wall motion abnormalities related coronary artery disease (3) Dysfunction of the diabetic heart disease.

1.4. SOME ASSESSMENT METHODS OF HEART VULNERABILITY

1.4.1. NT-proBNP concentrate in heart damage: NT-proBNP was one of the diuretic peptides which synthesized and secreted from ventricular myocardial cells, capable of diagnosis, prognosis and risk stratification of cardiovascular diseases. NT-proBNP value of 125 pg/ml are considered simple markers in patients with suspected heart failure symptoms, the good value for negative predictive.

1.**4.2. Electrocardiogram (ECG) and other methods:** the classic method used since 1914 by Lewis which is still worth using nowadays, transesophageal echocardiography, coronary reserve rate measurement, computing tomography multi-slice, magnetic resonance imaging, myocardial perfusion imaging, stress test, coronary angiography via skin, intravascular ultrasound.

1.4.3. Transthoracic echocardiography: have been considered as methods for early detection of diabetic cardiomyopathy through assessment of left ventricular morphology, abnormal wall motion, and diastolic function, Tei index.

1.4. TREATMENT AND ESC-EASD RECOMMENDATIONS

1.4.1. Lifesstyle intervention : Non-drug treatments involves positive lifestyle changes such as diet, stopping smoking and physical activity.

1.4.2. Pharmacological treatment: blood pressure management, glucose control, management of dyslipidaemia. Re-examination and control to achieve the targets of ESC-EASD guidelines.

Chapter 2: SUBJECTS AND METHODS

2.1. Research subjects

2.1.1 The inclusion criteria: patients diagnosed with hypertensive type 2 diabetes entered the Can Tho Central Hospital from 7/2011 to 7/2013 to satisfy diagnostic criteria for diabetes by ADA, IDF, ESC-EASD, classified type 2 of diabetes according to Asia-Pacific Type 2 Diabetes Policy Group in 2005 with diagnosed hypertension by criteria of ESC-EASD 2007: ≥ 130 mmHg and/or ≥ 80 mmHg, measuring at least 2 times or using of antihypertensive drugs. Besides that hypertensive type 2 diabetes without ischemic heart disease excluded by ESC criteria in 2013.

2.1.2 The exclusion criteria: type 1 diabetes, gestational diabetes, under 6-month discovered type 2 diabetes, acute complications, with ischemic heart disease, myocardial infarction or systolic heart failure before joining in the study, non-diabetic heart disease: heart muscle disease (hypertrophic cardiomyopathy, myocardial infection, inflammation of the heart muscle), heart valve disease (stenosis aortic valve insufficiency, aortic valve diseases), arrhythmias heart (atrial fibrillation, atrial flutter), cardiopulmonary diseases (sleep apnea, pulmonary embolism, pulmonary hypertension), septic shock, burns, respiratory failure, liver failure, severe renal impairment and patients not agree to participate study.

2.2. RESEARCH METHODOLOGY

2.2.1. Study Design: A monitoring and prospective stydy.

2.2.2. Sample size: the formula applied in the sample size of intervention study for a group of patients, tracking the change in LVMI for monitoring the development of heart complications in hypertension type 2 diabetes. The sample size should be monitored on 43 patients. The actual patient at the initial time were 116 and the patients followed-up after a minimum period of 12 months were 47.

2.2.3. Methods of collecting informations

2.3. Statistical analysis: the data collected existing sample and statistical analysis software SPSS 16.0.

CHAPTER 3: STUDY RESULTS

3.1. CHARACTERISTICS OF STUDY SUBJECTS ACCORDING TO THE ESC-EASD GUIDELINES

Table 3.1. Characteristics of BMI, WC, blood pressure

Target facts	Achievement		Non achievement		$\overline{X} \pm SD$ (unit measurements)
	Quantity	%	Quantity	%	
BMI < 25 kg/m^2	84	72.4	32	27.6	22.62 ± 4.84 (kg/m^2)
WC < 90cm (male), < 80cm (female)	41	35.3	75	64.7	86.24 ± 13.27 (cm)
Systolic <140 mmHg and Diastolic <85 mmHg	47	40.5	69	59.5	143.88 ± 28.37(mmHg) 81.21 ± 12.73 (mmHg)

. The percentage of patients did not achieve blood pressure goal and WC is higher than another group.

Table 3.2. Characteristics of glycaemic control

Target facts	Achievement		Non achievement		$\overline{X} \pm SD$ (unit measurements)
	Quantity	%	Quantity	%	
FPG < 7.2 mmol/L	30	25.9	86	74.1	11.29 ± 5.61
Post-pradial < 10 mmol/L	26	22.4	90	77.6	14.40 ± 4.80
HbA1C < 7%	39	33.6	77	66.4	8.36 ± 2.49
All glycemic targets	11	9.5	105	90.5	

The proportion of patients achieved fasting plasma glucose (FPG), Post-pradial, HbA1C and all glycaemic targets were very low.

Table 3.3. Characteristics of dyslipidaemia management

Target facts (mmol/L)	Achievement		Non achievement		$\overline{X} \pm SD$ (mmol/L)
	Quantity	%	Quantity	%	
TC < 4.5	46	39.7	70	60.3	5.17 ± 1.47
TG < 2.3	69	59.5	47	40.5	2.45 ± 1.97
LDL.C < 2.5	24	20.7	92	79.3	3.33 ± 1.06
HDL.C ≥ 1	75	64.7	41	35.3	1.07 ± 0.29
Non-HDL.C < 3.3	33	28.4	83	71.6	4.10 ± 1.42
All lipid targets	12	10.3	104	89.7	

The percentage of patients did not achieve TC, LDL.C, Non-HDL.C goal and all lipid targets were higher. But the proportion of patients did not achieved TG, Non-HDL.C were lower.

3.2. CHARACTERISTICS OF OTHER CARDIOVASCULAR RISK FACTORS

Table 3.4. Characteristics of traditional cardiovascular risk factors

Factors	Group	Quantity	%	$\overline{X} \pm SD$ (years)
Age	< 60	37	31.9	65.6 ± 9.90
	≥ 60	79	68.1	
Duration of DM	< 10	91	78.4	6.10 ± 4.89
	≥ 10	25	21.6	
Duration of HT	< 10	96	82.8	3 (0-31)
	≥ 10	20	17.2	
Gender	Male	17	14.7	
	Female	99	85.3	

Smoking	Yes	12	10.3	
	No	104	89.7	
Physical activity	Little	83	71.6	
	Yes	33	28.4	

The group of over 60 years old, female, little physical activity, no-smoking, duration of DM < 10 years, duration of HT < 10 years were higher the percentages.

Table 3.5. Characteristics of Hs-CRP, UACR, eGFR

Risk factor (unit measurements)	No		Yes	
	Quantity	%	Quantity	%
Hs-CRP ≥ 3 mg/dl	88	75.9	28	24.1
Median (Min -Max)	0.63 (0.01-19.8)			
UACR ≥ 3 mg/mmol	65	56.0	51	44.0
Median (Min -Max)	1.74 (0 – 369.92)			
eGFR < 60 ml/ph/1.73 m^2	85	73.3	31	26.7
$\overline{X} \pm SD$ (ml/ph/1.73 m^2)	72.84 ± 18.07			

Hs-CRP ≥ 3mg/dl, eGFR < 60 ml/ph/1.73 m^2 và UACR ≥ 3 mg/mmol had lower propotion than the others groups.

Table 3.6. Characteristics of IMTc, carotid plaques

Risk factor (unit measurements)	No		Yes	
	Quantity	%	Quantity	%
IMTc ≥ 0.9 mm	27	23.3	89	76.7
Left: $\overline{X} \pm SD$ (mm)	1.33 ± 0.70			
Right: $\overline{X} \pm SD$ (mm)	1.20 ± 0.68			
Carotid plaque	61	52.6	55	47.4
+ one side			36	65.5
+ two sides			19	34.5

IMTc ≥ 0.9 mm had the high percentages, but the group of having carotid plaque were lower proportion than the group without plaque.

3.3. CARDIAC MANIFESTATIONS OF STUDY SUBJECTS AT THE BEGINNING PERIOD.

Table 3.7. Characteristics of NT-proBNP following to age, gender, eGFR

Factor	Group	Quantity	NT-proBNP (pg/ml) Median (Min – Max)	p
Gender	Male	17	73.24 (4.99 -737.6)	> 0.05
	Female	99	137.4 (4.99 - 1528)	

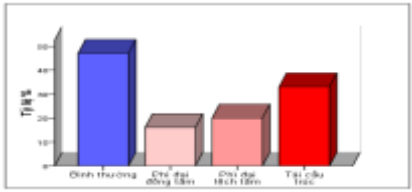
Age	≥ 75	28	197.3 (28.42 – 1528)	**< 0.05**
	< 75	88	115.3 (4.99 – 811.6)	
eGFR ml/ph/1.73m^2	< 60	31	284.4 (34.43 – 1119)	**< 0.001**
	≥ 60	85	105.8 (4.99 – 1528)	
Total		116	134.40 (4.99 – 1528)	

Average of serum NT-proBNP levels were different between two groups of age ≥ 75 and < 75. In addition, NT-proBNP concentration were not same between two groups of eGFR ≥ 60 and < 60 ml/ph/1.73m^2, (p< 0.05).

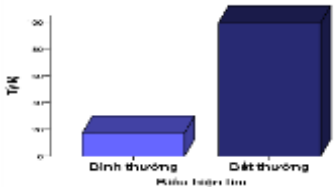
Table 3.8. Distribution of NT-proBNP following to age, gender, eGFR

Factor	**Group**	**NT-proBNP (pg/ml)**			**Total n**	**p**
		< 125 n (%)	**125 - 450 n (%)**	**> 450 n (%)**		
Gender	Male	9 (52.94%)	3 (17.64%)	5 (29.42%)	17	> 0.05
	Female	48 (48.5%)	38 (38.4%)	13 (13.1%)	99	
Age	≥ 75	9 (32.1%)	12 (42.9%)	7 (25%)	28	> 0.05
	< 75	48 (54.5%)	29 (33%)	11 (12.5%)	88	
eGFR ml/ph/1.73m^2	< 60	10 (32.3%)	13 (41.9%)	8 (25.8%)	31	> 0.05
	≥ 60	47 (55.3%)	28 (32.9%)	10 (11.8%)	85	
Total		57 (49.14%)	41 (35.34%)	18 (15.52%)	116	

The proportion of NT-proBNP in many concentration levels were not different according to age, gender, eGFR, p> 0.05.



Graph 3.1. Proportion of left



Graph 3.2. Proportion of

ventricular morphology forms **cardiac manifestations**

- Left ventricular morphology abnormal were 59.5% in which had 47.8% restructures, 29% eccentric hypertrophy, 23.2% concentric hypertrophy.
- 85.3% hypertensive type 2 diabetes had abnormal in cardiac manifestations by biochemical and echocardiography.

Table 3.9. Distribution of the left ventricular manifestations

Group		Normal		Abnormal	
		Quantity	%	Quantity	%
Diastolic function		29	25	87	75
Stage	I			76	87.4
	II			11	12.6
Tei index		68	58.6	48	41.4

Diastolic dysfunction were 75% in which the first stage was the highest 87.4 %. The percentages of Tei index abnormal were 41.1%.

3.4. RELATIONSHIP BETWEEN CARDIAC MANIFESTATIONS AND THE TREATMENT TARGETS OF ESC-EASD GUIDELINES OR SOME OTHER RISK FACTORS

3.4.1. Relationship beween cardiac manifestations and the targets

Bảng 3.10. Relationship beween cardiac manifestations and BMI, WC, blood pressure

Target facts (unit measurements)		Cardiac manifestations		Total (n=116)
		Normal (n=17)	Abnormal (n=99)	
BMI (kg/m^2)	≥ 25	2	30	32
	< 25	15	69	84
	OR (95% CI); p	3.26 (0.70 – 15.16); 0.148		
WC (cm)	≥ 80 (female); ≥ 90 (male)	10	65	75
	< 80 (female); <90 (male)	7	34	41
	OR (95% CI); p	1.34 (0.47 – 3.83); 0.586		
Blood pressure	≥ 140/85	6	63	69
	< 140/85	11	36	47

(mmHg)	OR (95% CI); p	**3.21 (1.09 – 9.41); 0.028**

Not achieving the blood pressure target were abnormal cardiac manifestations higher than 3.21 times another group, with $p < 0.05$.

Bảng 3.11. Relationship beween cardiac manifestations and glycemia

Target facts (unit measurements)		**Cardiac manifestations**		**Total (n=116)**
		Normal (n=17)	**Abnormal (n=99)**	
FPG (mmol/L)	≥ 7,2	9	77	86
	< 7,2	8	22	30
	OR (95% CI); p	**3.11 (1.07 – 9.01); 0.031**		
Post-prandial (mmol/L)	≥ 10	11	79	90
	< 10	6	20	26
	OR (95% CI); p	2.16 (0.71 – 6.53); 0.168		
HbA1C (%)	≥ 7	9	68	77
	< 7	8	31	39
	OR (95% CI); p	1.95 (0.69 – 5.53); 0.204		
All glycemic targets	1-2	12	93	105
	3	5	6	11
	OR (95% CI); p	**6.46 (1.71 – 24.43); 0.002**		

The group of fasting plasma glucose and the group of achieving 1-2 glycemic targets were abnormal cardiac manifestations higher than 3.11, 6.46 times others groups, respectively ($p < 0.05$) .

Bảng 3.12. Relationship beween cardiac manifestations and lipid

Target facts (unit measurements)		**Cardiac manifestations**		**Total (n=116)**
		Normal (n=17)	**Abnormal (n=99)**	
TC (mmol/L)	≥ 4.5	10	60	70
	< 4.5	7	39	46
	OR (95% CI); p	1.08 (0.38 – 3.07); 0.890		
TG (mmol/L)	≥ 2.3	7	40	47
	< 2.3	10	59	69
	OR (95% CI); p	0.97 (0.34 – 2.76); 0.952		
LDL.C (mmol/L)	≥ 2.5	15	77	92
	< 2.5	2	22	24
	OR (95% CI); p	0.47 (0.10 – 2.20); 0.518		
HDL.C (mmol/L)	< 1	6	35	41
	≥ 1	11	64	75
	OR (95% CI); p	1,00 (0,34 - 2,94); 0,996		

Non-HDL.C (mmol/L)	≥ 3.3	14	69	83
	< 3.3	3	30	33
	OR (95% CI); p	0.49 (0.13 – 1.84); 0.285		
All lipid targets	1 - 4	15	89	104
	5	2	10	12
	OR (95% CI); p	1.19 (0.24 – 5.96); 0.688		

In the group without achieving lipid targets were not decrease the risk of abnormal cardiac manifestations, ($p < 0.05$).

3.4.1.1. Correlation between cardiac morphological parameters and the targets of ESC-EASD guidelines.

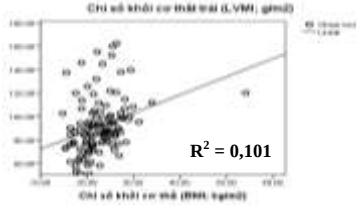


Chart 3.1. Correlation between LVMI and BMI

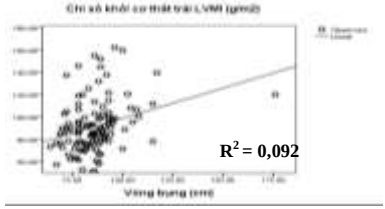
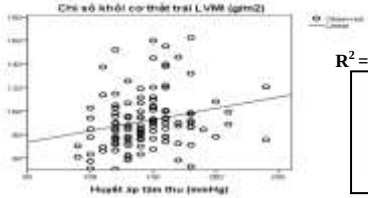


Chart 3.2. Correlation between LVMI and WC

The positive correlation of LVMI and BMI, $r = 0.317$; $p < 0.001$ with the regression equation: $y = 56.56 + 1.55x$.

The positive correlation of LVMI and WC, $r = 0.303$; $p < 0.001$, with the regression equation: $y = 45.02 + 0.54x$.



The positive correlation of LVMI and systolic blood pressure , $r = 0.232$; $p < 0.05$, with the regression equation: $y = 63.93 + 0.19x$

Chart 3.3. Correlation between LVMI and Systolic blood pressure

3.4.1.2. Correlation between left ventricular function parameters and the targets of ESC-EASD guidelines.

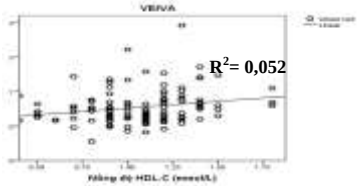


Chart 3.6. Correlation between E/A

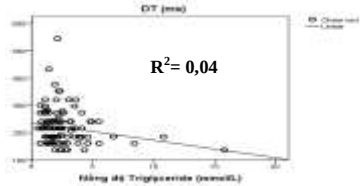


Chart 3.7. Correlation between DT

and HDL.C **and TG**

The positive correlation of E/A and HDL.C, r = 0.299; p < 0.05, with the regression equation: y = 0.57 + 0.2 x

The negative correlation of DT and TG, r = - 0.20; p < 0.05, with the regression equation: y = 235.7 – 6.43 x

3.4.2. Relationship beween cardiac manifestations and the cardiovascular risk factors

Bảng 3.13. Relationship beween cardiac manifestations and duration of diseases

Risk factors (unit measurements)		Cardiac manifestations		Total (n=116)
		Normal (n=17)	Abnormal (n=99)	
Duration of DM (years)	≥ 10	2	23	25
	< 10	15	76	91
	OR (95% CI); p	2.27 (0.48 – 10.67); 0.358		
Duration of HT (years)	≥ 10	1	19	20
	< 10	16	80	96
	OR (95% CI); p	3.80 (0.47 – 30.46); 0.299		

The frequency of abnormal cardiac mannifactions in group having duration of DM ≥ 10 years and duration of HT ≥ 10 years were higher than 2.27, 3.8 times, respectively, p > 0,05.

Bảng 3.14. Relationship beween cardiac manifestations and the other risk factors

Risk factors (unit measurements)		Cardiac manifestations		Total (n=116)
		Normal (n=17)	Abnormal (n=99)	
Hs-CRP (mg/dl)	≥ 3	1	27	28
	< 3	16	72	88
	OR (95% CI); p	6.00 (0.76 – 47.46); 0.068		
UACR (mg/mmol)	≥ 3	7	44	51
	< 3	10	55	65
	OR (95% CI); p	1.14 (0.40 – 3.25); 0.802		
eGFR (ml/ph/1.73 m^2)	< 60	3	28	31
	≥ 60	14	71	85
	OR (95% CI); p	1.84 (0.49 – 6.90); 0.554		
IMTc (mm)	≥ 0.9	11	78	89
	< 0.9	6	21	27
	OR (95% CI); p	2.03 (0.67 – 6.12); 0.204		
Carotid plaque	Yes	4	51	55
	No	13	48	61

	OR (95% CI); p	**3.45 (1.05 – 11.33); 0.038**

The patient group having carotid plaque were the frequency of abnormal cardiac mannifactions higher 3.45 times than the group without plaque.

Bảng 3.15. Correlation beween LVMI, NT-proBNP and other risk factors

Factors	LVMI		NT-proBNP		E/A	
	r	p	r	p	r	p
Duration of DM	0.06	> 0.05	**0.21**	**<0.05**	-0.05	> 0.05
Duration of HT	**0.22**	**< 0.05**	0.16	>0.05	-0.17	> 0.05
Hs-CRP	**0.32**	**< 0.0001**	**0.23**	**<0.05**	-0.11	> 0.05
UACR	0.08	> 0.05	**0.35**	**<0.0001**	-0.05	> 0.05
eGFR	-0.17	> 0.05	**-0.20**	**<0.05**	**0.20**	**< 0.05**
IMTc	0.09	> 0.05	0.14	> 0.05	-0.11	> 0.05

The positive correlation between NT_proBNP and duration of DM, Hs-CRP, UACR and the negative correlation of NT-proBNP and eGFR with $p < 0.05$. The positive correlation of LVMI and duration of HT, $r = 0.224$; $p < 0.05$, with the regression equation: $y = 86.73 + 0.87$ x. The positive correlation of LVMI and log (Hs-CRP), $r = - 0.324$; $p < 0.0001$, with the regression equation: $y = 82.75 + 4.25$ x.

The positive correlation of E/A and eGFR, $r = 0.20$; $p < 0.05$, with the regression equation: $y = 0.58 + 0.003$ x.

3.4.3. Multivariate regression correlation between cardiac manifestations and the targets of ESC-EASD guidelines with other cardiovascular risk factors

Table 3.16. Linear regression factors related LVMI

Factors	LVMI			
	B	Standardized Coefficients	t	p
Constant	32.88		2.12	**0.03**
BMI	0.35	0.07	0.36	0.71
WC	0.29	0.16	0.83	0.41
Duration of HT	0.91	0.23	2.83	**0.005**
SBP	0.15	0.18	2.13	**0.03**
Log (Hs-CRP)	9.19	0.30	3.63	**0.0001**

Multivariate analysis showed that the independent risk factors affecting LVMI included duration of HT, systolic blood pressure (SBP), log (Hs-CRP), with R= 0.515, Adjusted R^2= 0.265, p< 0.0001.

Table 3.17. Logistic regression factors related diastolic dysfunction

Factors	Diastolic dysfunction		
	OR	**95% CI**	**p**
BMI ≥ 25 kg/m^2	1.48	0.68 – 3.25	0.2
BP ≥ 140/85 mmHg	0.75	0.32 – 1.75	0.51
FPG ≥ 7.2 mmol/L	0.61	0.24 – 1.54	0.29
Non-HDL.C ≥ 3.3 mmol/L	5.02	1.58 – 15.92	**0.006**
Hs-CRP ≥ 3 mg/dl	2.24	1.01 – 4.98	**0.04**
Carotid plaque	0.70	0.32 – 1.56	0.38

Multivariate logistic analysis showed that Hs-CRP ≥ 3 mg/dl and NonHDL.C ≥ 3,3 mmol/L were the independent risk factors of diastolic dysfunctions significantly with p<0.05.

Table 3.18. Logistic regression factors related abnormal Tei index

Factors	Abnormal Tei index		
	OR	**95% CI**	**p**
Duration of DM ≥ 10 years	2.90	1.29 – 6.52	**0.01**
Achieving glycemic control < 3 targets	0.10	0.01 – 0.81	**0.03**
Hs-CRP ≥ 3 mg/dl	0.39	0.17 – 0.88	**0.02**
IMT ≥ 0.9 mm	0.32	0.12 – 0.88	**0.02**

Multivariate logistic analysis showed that Duration of DM ≥ 10 years, achieving glycemic control< 3 targets, Hs-CRP ≥ 3 mg/dl, IMT ≥ 0.9 mm were the independent risk factors of abnormal Tei index.

Table 3.19. Logistic regression factors related cardiac manifestations

Factors	**Cardiac manifestations**		
	OR	**95% CI**	**p**
BMI ≥ 25 kg/m^2	**2.74**	**1.21 – 6.24**	**0.02**
BP ≥ 140/85 mmHg	0.75	0.29 – 1.91	0.54
Achieving glycemic control < 3 targets	0.22	0.06 – 0.87	**0.03**

Hs-CRP ≥ 3 mg/dl	3.13	1.30 – 7.52	**0.01**
Carotid plaque	1.11	0.47 – 2.62	0.81

Multivariate logistic analysis showed that the independent risk factors of cardiac manifestations were BMI ≥ 25 kg/m^2 (OR=2,74), achieving glycemic control< 3 targets (OR=0,22), Hs-CRP ≥ 3 mg/dl (OR= 3,13), with p < 0,05.

3.5. ASSESSMENT OF THE PARAMETERS BELONG TO ESC- EASD GUIDELINES, OTHER RISK FACTORS BEFORE AND AFTER 12 MONTHS ON SOME RANDOMIZED SELECTIVE SUBJECTS

After a minimum follow-up period of 12 months, there were 47 patients who were randomly evaluated the second time.

3.5.1. Changes of the treatment targets parameters after 12 months

Table 3.20. The average changes of treatment targets factors before and after follow-up

Target facts (units measurements)	Before (n=47) $\overline{X}$ ± SD	After (n=47) $\overline{X}$ ± SD	Diff Mean	95% CI		p
BMI (kg/m^2)	23.13 ± 5.89	22.55 ± 5.69	**- 0.58**	**-0.94**	**-0.22**	**<0.005**
WC (cm)	87.36 ± 17.30	86.23±16.74	**- 1.13**	**-1.98**	**- 0.28**	**<0.05**
FPG (mmol/L)	12.63 ± 5.54	10.83 ± 5.74	**- 1.79**	**- 3.51**	**-0.07**	**<0.05**
HbA1C (%)	8.49 ± 2.69	9.03 ± 2.98	+ 0.54	-0.30	1.38	>0.05
TC (mmol/L)	5.11 ± 1.28	5.47 ± 1.66	+ 0.35	- 0.17	0.88	>0.05
TG (mmol/L)	2.26 ± 1.73	2.75 ± 1.81	+ 0.49	- 0.06	1.04	>0.05
HDL.C (mmol/L)	1.06 ± 0.27	1.18 ± 0.24	**+ 0.12**	**0.05**	**0.20**	**<0.005**
LDL.C (mmol/L)	3.33 ± 0.96	3.41 ± 1.14	+ 0.08	- 0.28	0.45	>0.05
Non-HDL.C (mmol/L)	4.06 ± 1.27	4.29 ± 1.58	+ 0.23	- 0.26	0.72	>0.05

Average of BMI, WC, FPG declined and HDL.C concentration increased higher than before follow-up significantly, p < 0.05.

Table 3.21. The proportion changes of treatment targets factors before and after follow-up

Target facts (units measurements)	Before (n=47)		After (n=47)		p
	Achievement	Non achievement	Achievement	Non achievement	
BMI < 25 kg/m^2	34 (72.3%)	13 (27.7%)	37 (78.7%)	10 (21.3%)	> 0.05
VB < 80/F , < 90/M	19 (40.4%)	28 (59.6%)	20 (42.6%)	27 (57.4%)	> 0.05
FPG < 7.2 mmol/L	9 (19.1%)	38 (80.9%)	12 (25.5%)	35 (74.5%)	> 0.05
HbA1C < 7%	14 (29.8%)	33 (70.2%)	14 (29.8%)	33 (70.2%)	> 0.05
TC < 4.5mmol/L	18 (39.3%)	29 (61.7%)	14 (29.8%)	33 (70.2%)	> 0.05

TG < 2.3 mmol/L	**32 (68.1%)**	**15 (31.9%)**	**23 (48.9%)**	**24 (51.1%)**	**< 0.05**
LDL.C < 2.5mmol/L	6 (12.8%)	41 (87.2%)	7 (14.9%)	40 (85.1%)	> 0.05
HDL.C ≥ 1mmol/L	**29 (61.7%)**	**18 (38.3%)**	**43 (91.5%)**	**4 (8.5%)**	**<0.0001**
Non-HDL.C< 3.3mmol/L	11 (23.4%)	36 (76.6%)	13 (27.7%)	34 (72.3%)	> 0.05

The proportion of achieving TG target decreased and the proportion of achieving HDL.C target increased higher than before follow-up significantly, $p < 0.05$.

3.5.2. Changes of other risk factors after 12 months

Table 3.22. Characteristics of changes in UACR

Parameters	Before (n=46)	After (n=46)	Diferences	p
UACR (mg/mmol)	6.68 (0 – 209.49)	2.3 (0 – 253.81)	10.02 (-5.13 – 25.17)	**< 0.01**
Microalbbuminurea	15 (75%)	20 (60.6%)	5 (38.5%)	**< 0.005**
Macroalbbuminurea	5 (25%)	13 (39.4%)	8 (61.5%)	
Total	20 (43.5%)	33 (71.7%)	13 (28.2%)	

Average of UACR, the proportion of microalbbumin, macroalbbumin at two assessments times were increase after follow-up significantly, $p < 0.05$.

Table 3.23. Characteristics of changes in carotid lesions

Parameters		Before (n=47)	After (n=47)	Diferences	p
IMTc (mm)	Left	1.34 ± 0.62	1.69 ± 0.78	0.35(0.20 – 0.51)	**<0.0001**
	Right	1.26 ± 0.81	1.60 ± 1.07	0.34 (0.13 – 0.54)	**<0.005**
IMTc ≥ 0.9 mm		36 (76.6%)	41 (87.2%)	5 (11.4%)	> 0.05
Plaque (Yes)		25 (53.2%)	33 (70.2%)	8 (17%)	**< 0.05**

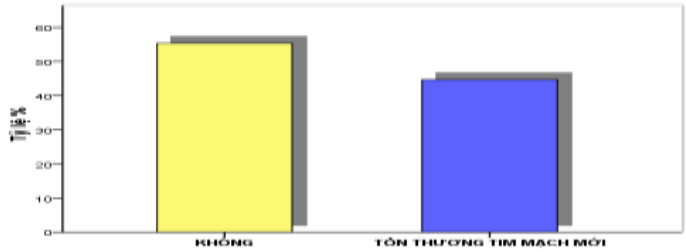
3.5.3. Changes of cardiac manifestations after 12 months

Table 3.24. Characteristics of changes in NT-proBNP levels and echocardiography

Target facts (units measurements)	Before (n=47) $\overline{X}$ ± SD	After (n=47) $\overline{X}$ ± SD	Diff Mean	95% CI		p
NT-proBNP (pg/ml)	113.5 (5–1044)	93.65 (11.51–5538)	+ 137.72	-119.79	395.24	>0.05
LVMI (g/m^2)	91.00 ± 23.64	74.93 ± 20.18	- 16.07	-21.74	-10.40	**<0.0001**
RWT	0.42 ± 0.06	0.45 ± 0.09	0.03	0.003	0.07	**<0.05**
E/A	0.74 ± 0.19	0.70 ± 0.20	-0.04	-0.09	0.02	> 0.05
DT (ms)	231.09 ± 72.07	214.94 ± 62.33	-16.14	-30.24	- 2.06	**< 0.05**
IVRT (ms)	104.19 ± 28.88	89.43 ± 27.95	-14.77	-25.79	- 3.74	**< 0.05**

Chỉ số Tei	0.74 ± 0.21	0.83 ± 0.18	0.09	0.01	0.16	**< 0.05**
EF (%)	72.92 ± 6.05	72.42 ± 8.16	-0.50	- 3.23	2.23	>0.05

Average of LVMI, RWT, DT, IVRT and Tei index were different significantly, p < 0.05.



Graph 3.3. Proportion of new diagnosed cardiac manifestations

To have 21 hypertensive type 2 diabetes patients had new diagnosed abnormal in cardiac manifestations were 45%

Table 3.25. Relations between changes of treatment targets factors and new diagnosed cardiac manifestations

Difference (after-before)	**Beta**	**SE**	**Wald**	**p**	**0R (95% CI)**
BMI (kg/m^2)	0.20	0.25	0.62	0.43	1.22 (0.75 – 1.98)
WC (cm)	0.002	0.10	0.001	0.98	1.00 (0.82 – 1.23)
FPG (mmol/L)	0.03	0.05	0.35	0.55	1.03 (0.93 – 1.14)
HbA1C (%)	0.08	0.11	0.58	0.44	1.09 (0.88 – 1.34)
TC (mmol/L)	0.07	0.17	0.17	0.68	1.07 (0.77 – 1.49)
TG (mmol/L)	**0.59**	**0.28**	**4.41**	**0.03**	**1.80 (1.04 – 3.12)**
LDL.C (mmol/L)	0.15	0.24	0.36	0.54	1.16 (0.72 – 1.85)
HDL.C (mmol/L)	- 1.08	1.19	0.82	0.36	0.34 (0.03 – 3.50)
Non-HDL.C (mmol/L)	0.10	0.18	0.33	0.56	1.11 (0.78 – 1.58)

Multivariate analysis showed that the changes of TG concentration was the independent risk factors affecting new diagnosed abnormal in cardiac manifestations, p< 0.05.

Table 3.26. Characteristics of the differences in the ischemic heart diseases groups

Factors (units measurements)	Ischemic heart diseases **(IHD)**		**p**
	Yes (n = 8) $\overline{X}$ ± SD	**No (n = 39)** $\overline{X}$ ± SD	
HbA1C (%)	11.05 ± 3.21	7.97 ± 2.27	**0.002**

NT-proBNP (pg/ml)	344.46 ± 304.35	170.41 ± 200.22	**0.044**
SBP (mmHg)	152.5 ± 31.96	139.23 ± 24.43	0.191
Carotid plaque (Yes)	2/8 (25%)	23/39 (58.97%)	0.123

Average of HbA1C, NT-proBNP in the group with ischemic heart diseases were different to without ischemic heart diseases, p < 0.05.

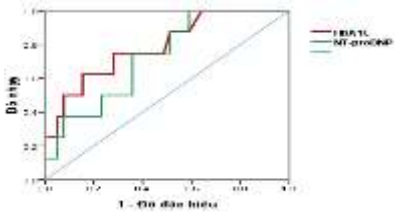


Chart 3.8. ROC curve of HbA1C, BNP plasma concentration in predicting the ischemic heart diseases (IHD)

Biến số	AUC	95% CI	Cutoff	Sens (%)	Spec (%)	p
HbA1C (%)	0.79	0.62 – 0.96	8.8	75%	71.8%	**<0.01**
NT-proBNP(pg/ml)	0.73	0.56 – 0.90	136.1	75%	64.1%	**<0.05**

Table 3.27. Logistic regression factors related the IHD

Risk factors	Ischemic heart diseases					
	B	SE	Wald	p	OR	95% CI
SBP (mmHg)	-0,002	0.005	0,. 16	0.73	0.99	0.98- 1.01
HbA1C ≥ 8.8%	-2.17	0.99	4.81	**0.03**	0.11	0.02 – 0.79
NT-proBNP ≥ 136 pg/ml	-2.53	1.11	5.17	**0.02**	0.08	0.01– 0.71
Carotid plaque (Yes)	1.66	1.02	2.67	0.10	5.26	0.72 – 38.52

Multivariate analysis showed thatHbA1C, NT-proBNP were the independent risk factors affecting the ischemic heart diseases, p< 0.05.

Chapter 4: DISCUSSION

4.1. CHARACTERISTICS OF STUDY SUBJECTS ACCORDING TO THE ESC-EASD GUIDELINES

4.1.1. **Body mass index (BMI):** BMI of study subjects with hypertension type 2 diabetes was 22.62 ± 4.84 kg/m^2, and 72.4% achieved BMI target <25 kg/m2 (Table 3.1), which was suitabble for the general characteristics of diabetic patients in Vietnam. There were not as same as Gomez-Marcos et al (2011), IM Ruckert (2012), p <0.05.

4.1.2. Waist circumference (WC): 64.7% patients had abnormal WC and average of WC was 86.24 ± 13.27cm (Table 3.1), lower than Gomez-Marcos (2011), $p < 0.05$. Abdominal obesity was increases cardiovascular risk significantly.

4.1.3. Blood pressure: Average of systolic blood pressure was 143.88 ± 28.37 mmHg or diastolic blood pressure was 81.21 ± 12.73 mmHg and 40.5% patients achieved blood pressure target (Table 3.1), similarly to Huelsmann M. (2008), or IM Ruckert (2012). The majority of hypertension in type 2 diabetes is very difficult to control because the combination of complex pathophysiological mechanisms have still been studied.

4.1.4. Glucose and HbA1C: average of FBG was 11.29 ± 5.61 mmol/L and 74.1% people didn't gain the target; post-prandial glucose was 14.40 ± 4.80 mmol/L and there were 77.6% not achievements; average concentration of HbA1C was 8.36 ± 2.49% and 66.4% didn't achieve this goal. Only 11 patients accounted for 9.5% achieved all three glycemic targets (Table 3.2). It was similar to Gomez-Marcos (2011), Ho Thi Hoai Thuong, Nguyen Hai Thuy (2012), and Nguyen Ngoc Chat (2010).

4.1.5. Lipid profile: the percentages of reaching lipid targets were 64.7% HDL.C, 59.5% TG; 39.7% TC, 28.4% Non-HDL.C, 20.7% LDL.C and 10.3% patients achieved all lipid goals. It was different with Gomez-Marcos et al (2011), Ichikawa (2013), but as same as Ho Thi Hoai Thuong Nguyen Hai Thuy (2012).

4.2. CHARACTERISTICS OF OTHER CARDIOVASCULAR RISK FACTORS

4.2.1. Age: Average age was 65.60 ± 9.90 years old (Table 3.4), the youngest was 45 and the oldest is 90 years old, as same as the age of diabetic patients in the world from 40 to 59 and gradually increases to 75 years old.

4.2.2. Gender: The study result accounted for 85.3% of women patients which was 5 times higher than 14.7% of men (Table 3.4), similarly to the domesticl researches.

4.2.2. Duration of DM (DDM) and duration of HT (DHT): average of DDM was 6.10 ± 4.89 years and 78.4% had DDM <10 years (Table 3.4). Similarly, median of DHT was 3 years, with the percentage of DHT <10 years was higher than the group of DHT over 10 years (Table 3.4).

4.2.4. Smoking: has been proven to be one risk factor of cardiovascular diseases for a long time. The percentage of smokers in this study accounted for 10.3%, lower than non-smokers (Table 3.4).

4.2.5. Physical activity: the state of little physical activity in study was a high proportion of 71.6% (Table 3.4), similar to Ruckert IM (2012).

4.2.6 High sensitivity of C-reactive protein: median of Hs-CRP was 0.63 mg/dl in which increased from 19.8 mg/dl to 0.01 mg/ dl. There were 24% Hs-CRP ≥ 3 mg / dl who had high cardiovascular risk (Table 3.5). It was same as Masson S. (2013) but lower than Vinagre I. (2014).

4.2.7. Urine albumin to creatinine ratio (UACR): median of UACR was 1.74 mg/mmol, the highest of 369.92 mg/mmol, and 44% patients had UACR ≥ 3 mg / mmol (Table 3.5) which was similar to Zinman B. (2014), but higher than Puttnam W. (2011).

4.2.8. Estimated glomerular filtration rate (eGFR-MDRD): Average of eGFR-MDRD was 72.84 ± 18.07 ml/min/1,73m2. The proportion of eGFR <60 ml/min/1,73m2 was 26.7% (Table 3.5) which was lower than Nguyen Kim Luong (2010) and similar to Zinman (2014).

4.2.9 Carotid intima-media thickness (IMTc): IMTc in the left was 1.33 ± 0.70 mm thicker than in the right 0.68 ± 1.20 mm and the high proportion of IMTc mm above 0.9mm was 76.7%. The

percentages of carotid plaque was 47.4% in which had 65.5% in one side and 34.5% in two sides (Table 3.6).

4.3. CARDIAC MANIFESTATIONS OF STUDY SUBJECTS AT THE BEGINNING PERIOD.

4.3.1. N-Terminal Pro-B-Type natriuretic peptide (NT-proBNP): average of NT-proBNP was 134.4 pg/ml, didn't differ between men and women. However, the difference in age groups <75 and ≥ 75 years old, and between two groups of eGFR <60 and ≥ 60 ml/min/1.73m^2, p <0.001. There was 49.14% NT-proBNP levels above 125 pg/ml (Table 3.7 and 3.8).

4.3.2. Characteristics of morphological parameters and left ventricular function: mean of LVMI was 91.53 ± 23.61 g/m^2 and RWT was 0.42 ± 0.08 and it had 59.5% abnormal left ventricular morphology in which included in 23.2% of concentric hypertrophy 29% eccentric hypertrophy and 47.8% left ventricular restructuring. It were 75% diastolic dysfunction and 41.4% of abnormal Tei index (Table 3.9). In addition, there were 85.3% hypertensive type 2 diabetes with abnormal cardiac manifestations (Chart 3.2). The result study showed that asymptomatic cardiovascular damages has been detected early by echocardiography very high and it was the leading cause of death for cardiovascular diseases

4.4. RELATIONSHIP BETWEEN CARDIAC MANIFESTATIONS AND THE TREATMENT TARGETS OF ESC-EASD GUIDELINES OR SOME OTHER RISK FACTORS

4.4.1. Relationship beween cardiac manifestations and the targets:

BMI, WC: The frequency of cardiac manifestations in the groups which didn't achieve BMI target, was higher than 3.26 times, with p > 0.05 (Table 3.10). There was the positive correlation between BMI, VB and LVMI. Every BMI unit was able to increase 1.55 g/m^2 LVMI (Graph 3.1) as same as one milimeter of WC could be increase 0.54 g/m^2 LVMI, p < 0.001 (Graph 3.2).

Blood pressure (BP): The hypertensive type 2 diabetes were

able to control BP who was cardiac manifestation risk higher than 3.21 times ((Table 3.10) and there was the positive correlation of sytolic blood pressure and LVMI. One unit of SBP could add much more 0.19 g/m^2 of LVMI, $p < 0.05$ (Graph 3.3). Moreover, non achieving of BP target was able to have diastolic dysfunction higher than 2.69 times, $p< 0.05$. The result was suitable with the influence of hypertensive pathogenesis in diabetic heart diseases.

Glucose and HbA1C: The group of fasting plasma glucose and the group of achieving 1-2 glycemic targets were abnormal cardiac manifestations higher than 3.11, 6.46 times others groups, respectively (Table 3.11). It suggested that glycemic management have significantly affected to cardiac manifestation. However, they didn't note the correlation between the glycemia parameters and echocardiography variables.

Lipid profile: the prevalence of cardiac manifestations was as same as two groups of achieving or without achieving lipid targets, $p > 0.05$ (Table 3.12). There were the positive correlation of HDL.C with E/A (Graph 3.4) and the negative correlation of TG with DT (Graph 3.5). Dyslipideamia affected to relax left ventricular which was the fundamental pathogenesis of diabetic cardiomyopathy.

4.4.2. Relationship beween cardiac manifestations and the cardiovascular risk factors

Duration of disease: DDD ≥ 10 years, DHD ≥ 10 years were able to have the risk of cardiac manifestations 2.27; 3.8 times higher than the group of DDM < 10 years and DHD < 10 years, respectively, $p> 0.05$ (Table 3.13). There were the correlation of DHD with LVMI and DDD with NT-proBNP. However, our study was different from the studies because there didn't find the correlation between function parameters, Tei index and DDD, DHD.

Hs- CRP: The cardiac manifestation prevalence of Hs-CRP ≥ 3 mg/dl group was higher than 6 times of another group (Table 3.14). There were the positive correlation between log Hs-CRP and LVMI, NT-proBNP (Table 3.15). The research proved that the strong relationship between Hs-CRP and cardiovascular

complications.

UACR and eGFR-MDRD: the risk of abnormal cardiac manifestations in UACR group ≥ 3 mg/mmol higher than 1.14 times, p > 0.05 (Table 3.14). There was the positive correlation between UACR and NT-proBNP, p <0.0001 (Table 3.15). Besides, the study found that there were the negative correlation between eGFR with NT-proBNP and a positive correlation between eGFR with E / A (Table 3.15), p <0.05. The group of eGFR <60 ml/min/1.73m^2 had risk of abnormal heart manifestations higher than 1.84 times, with p> 0.05 (Table 3.14).

IMTc: The group of IMTc ≥ 0.9 mm had risk of abnormal heart manifestations higher than 2.03 times, with p> 0.05 (Table 3.15). However, it was not the correlation between IMTc and LVMI, function variables.

Multivariate logistic analysis showed that Hs-CRP ≥ 3 mg/dl were the independent risk factors of cardiac manifestations in hypertensive type 2 diabetes with OR= 4.6, p<0.01 (Table 3.16). The study showed that the nontraditional cardiovascular risk factors was important in predicting cardiac manifestations.

3.5. ASSESSMENT OF THE PARAMETERS BELONG TO ESC- EASD GUIDELINES, OTHER RISK FACTORS BEFORE AND AFTER 12 MONTHS ON SOME RANDOMIZED SELECTIVE SUBJECTS

After a minimum follow-up period of 12 months, there were 47 patients who were randomly evaluated the second time.

- ***Changes of BMI, WC:*** Similarly, Gomez-Marcos et al (2011) after the intervention time, BMI reduced by 0.39 kg/m^2 and waist circumference decreased 1.30 cm, significantly. The percentages of BMI control <25 kg/m^2 in our study increased by 6.4% (Table 3.20, Table 3.21), with p> 0.05, but higher than the domestic and foreign authors.

- ***Changes of FPG and HbA1C:*** FPG reduced by 1.79 kg/m^2 and the

proportion of FPG <7.2 mmol/L in our study increased by 6.4%. p > 0.05. HbA1C increased by 0.54% while the prevalence of HbA1C < 7% was similar to in the beginning (Table 3.20, Table 3.21), with p> 0.05. In practice, glycemia management is the biggest challenge.

- ***Changes of lipid profile:*** there were the change of averages and proportion in lipid targets. Among them, the change in the percentage of achieving lipid control had significant in TG and HDL.C, with p <0.05.

4.5.2. Changes of other risk factors after 12 months

: there were 46 patients who were avaluated UACR before and after 12 months. The prevalence of microalbuminurea increased by 13 cases (28.2%); including 5 cases of microalbuminurea and 8 cases of macroalbuminurea (Table 3.22).

- ***Changes of carotid lesions:*** IMTc were increase 0.35 mm in the left, 0.34 mm in the right, while the percentage of IMTc ≥ 0.9 mm increased 11.4% and had more 17% of new diagnosed carotid plaque, p < 0.05 (Table 3.23). Among them, there were 2 patients (4.08%) who had unstable plaque and 4.08% new plaques.

- ***Changes of NT-proBNP and echocardiography index:*** average of LVMI after 12 months reduced by 16.07 g/m^2. Tei index was incease and DT, IVRT reduced after follow-up, p < 0.05. The reduction of LVMI tended differently from the increasing of NT-proBNP concentration, p > 0.05 (Table 3.24). The reason of differences were able to be caused by renal complications. It is worth noting that the increase of Tei index seems contrary to the decline of DT and IVRT, but it was really reasonable because the heart rate did not change.

4.5.3. Characteristics of the new diagnosed cardiac manifestations after 1 year and the role of biomarkers predicted ischemic heart disease

The new cardiac manifestations were diagnosed 45% by echocardiography, p<0.05 (Graph 3.4) and the change of TG level was its independent risk with OR=1.8, p<0.05 (Table 3.25). After 12

months, the results showed that the target organ damage were increase significantly.

NT-proBNP and HbA1C were different between the groups with and without ischemic heart disease, p <0.05 (Table 3.26). The cutoff of HbA1C was 8.8% and NT-proBNP was 136.1 pg/ml which were capable of predicting risk of IHD (Chart 3.8). Multivariate logistic regression, SBP, HbA1C and carotid plaque were the independent risks of IHD, with p <0.05 (Table 3.27).

CONCLUSION

Through the survey of 116 hypertension type 2 diabetes without ischemic heart disease in two times before and after 12 months, we concluded as:

1. Characteristics of study subjects according to the ESC-EASD guidelines, some other risk factors and cardiac manifestations (NTproBNP and echocardiogram) at the beginning

The proportion of patients achieving the target treatment from ESC-EASD guidelines were BMI (72.4%), waist circumference (35.3%), bood pressure (40.5%), fasting plasma glucose (25.9%), postprandial (22.4%), HbA1C (33.6%), controlling all glycemic targets (9.5%), HDL.C (64.7%), cholesterol (39 , 7%), triglycerides (59.5%), LDL.C (20.7%), Non-HDL.C (28.4%) and reached all of lipidemia targets (10.3%).

The percentage of cardiovascular risk factors recorded by 68.1% patients ≥ 60 years old, 89.7% female, 71.6% less physical activity. In addition, 24.1% Hs-CRP ≥ 3 mg/dl, 44% UACR ≥ 3 mg/mmol, 26.7% eGFR <60 ml/min/1.73 m^2, 76.7% IMTc ≥ 0.9 mm and 47.4% plaques.

The prevalence of abnormal cardiac manifestations was 85.3%. The median of NT-proBNP concentration was 134.4 pg/ml, and 50.86% NT-proBNP ≥ 125 pg/ml. Abnormal left ventricular morphology was 59.5%, in which included in 23.2% concentric hypertrophy, 29% eccentric hypertrophy and 47.8% restructuring.

The percentage of diastolic dysfunction was 75% and 41.4% Tei index ≥ 0.75.

2. Relationship and change of the treatment targets from ESC-EASD, cardiovascular risk factors and cardiac manifestations after 12 months of follow-up.

- **Throughout 116 patients** recorded by risk of abnormal cardiac manifestations associated with the target of blood pressure (OR = 3.21), fasting plasma glucose (OR = 3.11), achieved < 3 glycemic targets (OR = 6.46) and carotid plaque (OR = 3.45), p <0.05.

The independent risks of LVMI included systolic blood pressure, duration of hypertension, Hs-CRP. The independent risks of diastolic dysfunction were blood pressure, fasting plasma glucose, Non-HDL.C, carotid plaque. Abnormal Tei index ≥ 0.75 associated with duration of diabetes ≥ 10 years**,** achieved < 3 glycemic targets hypertension, Hs-CRP and IMTc ≥ 0.9 mm, (p< 0.001).

The independent risks of cardiac manifestations were BMI ≥ 25 kg/m^2 (OR=2.74), Hs-CRP ≥ 3 mg/dl (OR=3.13) and achieved <3 glycemic targets, p<0.05.

Assessing after 12 months of 47 patients follow-up recorded by average reduction of 0.58 kg/m^2 BMI, 1.13 cm waist circumference, 1.79 mmol/L fasting plasma glucose, 0.12 mmol/L HDL.C. There were decrease in the percentage of 19.2% Triglycerides targets and increase the achieving proportion of 29.8% HDL.C, p <0.05.

Increasing in the proportion of microalbuminuria was 28.2% and in average of IMTc were 0.35 mm in the left, 0.34 mm in the right and 17% carotid plaque.

Reducing LVMI was 16.04 g/m^2 and increased 0.03 RWT. In addition, there were decrease DT, IVRT in 16.14 ms, 14.77ms, respectively and increase 0.09 Tei index, with p <0.05. Results showed that 45% of patients with new abnormal cardiac manifestations after a year and was associated with the increase of triglycerides concentration (p <0.05).

17% new diagnosed ischemic heart diseases related to systolic blood pressure, HbA1C, carotid plaque, p <0.05. The predicting ability of ischemic heart disease of HbA1C level with an area under the curve was 0.79 (95% CI: 0.62-0.96; p <0.01), a sensitivity of 75%, a specificity of 71.8% with the cut-off value of 8.8% and of NT-proBNP concentration was 136.1 pg/ml with an area under the curve was 0.73 (95% CI: 0.56- 0.90; p <0.05), sensitivity of 75%, specificity of 64.1%.

REQUEST

- Treatment of type 2 diabetic patients should combine glycemic control and management of metabolic disorders, especially with hypertensive type 2 diabetic patients which have many cardiovascular risk factors.
- ESC/EASD guidelines is general, but as applying to diabetic patients with hypertension should add more nontraditional cardiovascular risk factors which have highly valued in predicting the cardiovascular events and mortality, that should be applied routinely to this object.
- Every year, hypertensive diabetic patient should be examined the target organ damage in preclinical stage in order to detect new cardiovascular lesions as well as the progression of cardiovascular complications.