The Effect of Coenzyme Q10 Supplementation on Global Longitudinal Strain Values in Acute ST Segment Elevation Myocardial Infarction Patients Treated With Primary Percutaneous Coronary Intervention

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1. Introduction

Cardiovascular diseases, particularly coronary artery disease (CAD), remain one of the leading causes of morbidity and mortality worldwide.[1,2] Acute Myocardial Infarction (AMI) is a life-threatening manifestation of acute CAD that can lead to sudden cardiac death.[3] Subjects with ST-Elevation Myocardial Infarction (STEMI) have a worse long-term prognosis compared to those with Non-ST-Elevation Myocardial Infarction (NSTEMI).[4] Revascularization and pharmacological therapy have successfully reduced mortality from Myocardial Infarction (MI), but subjects still experience progressive left ventricular dilation after MI, even after undergoing Primary Percutaneous Coronary Intervention (PPCI).[5,6,7] Left ventricular remodeling after MI affects long term prognosis, with post-infarction adverse remodeling being a parameter for the risk of cardiovascular events such as ventricular arrhythmias, heart failure, and death in AMI subjects. This makes the identification of at-risk subjects crucial for important prognostic value and therapeutic implications.[8,9]

The strain and strain rate techniques have been developed for echocardiographic examination to quantitatively assess and evaluate changes in left ventricular function both globally and regionally. Echocardiographic assessment of Global Longitudinal Strain (GLS) has been used to predict left ventricular remodeling after MI.[10,11] Peksiene et al. reported that a GLS cutoff value of -12.5% can predict left ventricular remodeling in STEMI subjects after PPCI, with a sensitivity of 78% and specificity of 73%.[12] Lacalzada et al. reported that the optimal cutoff value for GLS as a predictor of left ventricular remodeling in STEMI subjects after PPCI is -12.46%.[13]

Pharmacological management of cardiac remodeling, such as beta-receptor blockers, angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin II receptor blockers (ARBs), has been proven to reduce mortality and is considered standard therapy after myocardial infarction.[14] Supplements can be beneficial as adjunctive therapy for managing cardiac remodeling, with Coenzyme Q10 (CoQ10) potentially offering significant cardiovascular protective effects.[15,16,17] In the early 1980s, Karl Folkers discovered the therapeutic potential of CoQ10 in cardiovascular diseases and used it in subjects with heart failure. Research on CoQ10 has since expanded to other cardiovascular conditions, including hypertension, ischemic heart disease, and myocardial infarction. Decreased levels of CoQ10 in myocardial tissue and serum are associated with disease severity and poorer clinical outcomes in subjects with cardiovascular disease.[18,19] CoQ10 helps reduce oxidative stress, plays a role in ATP synthesis, alleviates the inflammatory response, restores intracellular calcium homeostasis, and reduces cellular apoptosis, thereby potentially decreasing cardiac remodeling after MI.[15,16,17] Therefore, this study aims to determine the effect of CoQ10

supplementation post-MI on left ventricular remodeling, assessed through changes in GLS values.

2. Materials and Methods

Subjects population

The study included acute STEMI subjects (less than 12 hours after symptom onset) who underwent PPCI from January 2024 to Apil 2024. Furthermore, a sequence of GLS measurements were collected within the first 24 hour after PPCI and 8 weeks after the intervention. Relevant clinical parameters (age, hypertension, diabetes, dyslipidemia, gender, body mass index, total ischemia time) along with thorax x-ray, laboratory tests, electrocardiography and echocardiography data were prospectively documented.

Subjects with hemodynamic conditions of Killip class III-IV and NYHA class III-IV, those who received fibrinolytic therapy prior to admission, had a past history of coenzyme Q10 consumption, or were receiving warfarin therapy were excluded. Additionally, subjects with severe valvular heart disease, isolated right ventricular infarction, a history of Percutaneous Coronary Intervention (PCI), Coronary Artery Bypass Grafting (CABG), myocardial infarction, or abnormal heart rhytms detected through electrocardiogram were also excluded from the study.

Coenzyme Q10

Coenzyme Q10 was administered at a dose of 100 mg every 12 hours starting on the second day following primary PCI, after the baseline GLS examination. CoQ10 was taken every morning and evening after meal for 8 weeks until participant underwent a repeat GLS examination.

Coronary Angiography and PCI

Coronary angiography was performed using the conventional Judkins method, along with computerized picture acquisition and storage. An individual proficient in invasive cardiology conducted the analysis offline without knowledge of the results from the other imaging investigations. In cases of single-vessel disease, the affected blood vessel was determined to be the primary factor. The primary responsible vessel in cases of multivessel disease was determined using a combination of electrocardiographic and angiographic markers. PCI was performed based on the operator's judgment, with all subjects demonstrating TIMI 3 flow in the culprit arteries.

Echocardiography and Global Longitudinal Srain Analysis

Three sequential cardiac cycles of apical 4, 2, and 3 chamber view images were stored using optimal machine settings and frame rates of 50-70 frames per second for strain measurement using speckle tracking echocardiography. Two-dimentional speckle-tracking investigations were conducted using the Epiq 7C ultrasound machine manufactured by Philips Medical Systems. These studies utilized QLAB/automated cardiac motion quantification (ACMQ) version 10.85 and QLAB/LV auto-strain version 12.0, both developed by Philips Healthcare. The endocardial border was delineated either manually or automatically during the cardiac cycle using the highest quality image. If speckle visibility was insufficient, the region of interest was manually

adjusted. Tracking data that did not meet specified criteria or was affected by shadows or artifacts was excluded. The software subsequently generated time-domain Left Ventricle (LV) strain curve automatically for each segment. Data for calculating GLS were extracted from the 18 cardiac segments using standard methods of the American Society of Echocardiography. The strain value was obtained from automatic measurements based on the formula : strain (ε) = L– L0/L0, where L represents changes in the length of longitudinal myocardial fibers at the end of systole and L0 represents the initial myocardial fiber length at rest at end diastole. Each inspection was conducted by a single operator. With an intraclass coefficient reliability above 0.90 and minimal differences in GLS values across two operators (-12,94 ± 5.3% vs. -12,76 ± 5,8%), our lab demonstrated strong intraobserver and interobserver variability. The identity of the subject and other data were not disclosed to the operators during any of the offline analysis.

Follow-Up Data and Assessment of Recovery

Each participant in this randomized control trial was monitored for a period of 8 weeks after PPCI. All subject received treatment consisting of beta blockers, ACEIs /ARBs, statins, nitrates, MRAs and dual antiplatelet agents (specifically aspirin in combination with clopidogrel or ticagrelor). The improvement in systolic function was measured by calculating the delta GLS, which represents the difference between GLS measurements taken within the first 24 hour after primary PCI and 8 weeks after the intervention. A lower (more negative) GLS signifies superior left ventricular function. Conversely, a higher value of delta GLS indicates a more effective recovery of function.

Statistical Analysis

The chi-square test was employed to assess disparities between groups. Descriptive discrete characteristics are presented as counts and percentages. Continuous variables that follow a normal distribution are presented as means and standard deviations (SD). The analysis focused on comparing measurements taken at baseline with those taken at follow-up using paired subjects. The Student's t-test was used for normally distributed data, whereas the Wilcoxon test was used for data that were not normally distributed. The t-test or the Mann-Whitney U-test was employed to assess disparities in GLS between each group, depending on the data distribution. Statistically significant was defined as a p-value less than or equal to 0.05 in two-sided testing. Statistical analyses were conducted using SPSS version 26.

Ethical Clearance and Informed Consent

The Ethical Committee of the Faculty of Medicine, Diponegoro University, and the Ethical Committee of Kariadi Central General Hospital Semarang approved the study protocol, which followed the Second Declaration of Helsinki. This research complies with seven (7) WHO 2011 Standards in terms of ethics, referring to the 2016 CIOMS Guidelines: 1) Social Values, 2) Scientific Values, 3) Equitable Assessment and Benefits, 4) Risks, 5) Persuasion and Exploitation, 6) Confidentiality and Privacy, and 7) Informed Consent. The fact that each standard's indicators are met (Ethical Approval No. 1648/EC/KEPK-RSDK/2023) indicates this.

3. Results

The study comprised a total of forty-six subjects with acute onset STEMI, as shown in Table 1. Following the intervention, the participants were divided into two groups: Coenzyme Q10 (standard treatment+ CoQ10 100mg/12hours, comprising 23 subjects) and Placebo (standard treatment+ placebo 1 chewable tablet/12hours, comprising 23 subjects). There were no statistically significant differences in demographic characteristics between the two groups regarding gender, age, and Body Mass Index (BMI). Subjects in both groups were predominantly male, with 14 subjects (60.9%) in the CoQ10 group and 19 subjects (82.6%) in the placebo group (p=0.190). The median age of the participants in the CoQ10 group was 55 (33-74) years, while in the placebo group it was 54 (41-71) years (p=0.768). The average BMI of subjects in both groups indicated overweight status (according to WHO Asia Pacific criteria), with 25±2.5 kg/m² in the CoQ10 group and 24.6±2.3 kg/m² in the placebo group (p=0.604). Based on risk factors for CAD, smoking was the most common risk factor in both groups (47.8% and 65.2%), followed by hypertension, diabetes mellitus, and dyslipidemia. No significant differences were found between the two groups regarding CAD risk factors.

In the clinical characteristics of STEMI, no significant differences were found in the location of the infarct between the two groups, with anterior infarction at 52.2% in the CoQ10 group and 47.8% in the placebo group (p=1.000). The average total ischemic time was 493.39±179.08 minutes in the CoQ10 group, while in the placebo group it was 510.87±179.36 minutes (p=0.742). Most subjects had Killip Class I (95.7% in the CoQ10 group and 82.6% in the placebo group). The average TIMI score was 3 for both the CoQ10 and placebo groups (p=0.973). Of the 23 subjects in the CoQ10 group, 6 subjects (26.1%) underwent complete revascularization, while in the placebo group 8 subjects (34.8%) received complete revascularization (p=0.749). In the CoQ10 group, 43.5% had 2 vessel disease (2VD), while in the placebo group, 39.1% had 3 vessel disease (3VD) (p=0.464).

During hospitalization, all subjects received standard STEMI therapy according to guidelines and adjusted to their clinical condition. All study subjects received dual antiplatelet therapy and statins. All subjects also received ACEIs or ARBs. The most commonly administered ACEIs during hospitalization was ramipril 2.5 mg/24 hours (43.5%) in both the CoQ10 and placebo groups, while the most common ARBs was candesartan 4 mg/24 hours (17.4%) in both groups (p=0.785). During the study, there was an increase in dosage for 10 subjects in the CoQ10 group and 8 subjects in the placebo group (p=0.602). The dosage increases included ramipril 10 mg/24 hours for 1 subject in the CoQ10 group, perindopril 5 mg/24 hours for 5 subjects in the CoQ10 group and 3 subjects in the placebo group, candesartan 8 mg/24 hours for 4 subjects in the CoQ10 group and 3 subjects in the placebo group, and valsartan 80 mg/24 hours for 2 subjects in the placebo group.

Nearly all subjects received beta-blockers, with 100% in the CoQ10 group and 91.3% in the placebo group (p=0.489). The most commonly administered beta-blocker during hospitalization in both groups was bisoprolol 1.25 mg/24 hours (39.2% and 34.8%), followed by bisoprolol 2.5 mg/24 hours, carvedilol 3.125 mg/12 hours, and carvedilol 6.25 mg/12 hours (p=0.994). During the study, there was an increase in dosage for 9 subjects in the CoQ10 group and 9 subjects in the placebo group (p=0.408). The dosage increases included bisoprolol 2.5 mg/24 hours for 2 subjects in the CoQ10 group and 5 subjects in the placebo group, bisoprolol 5 mg/24 hours for 2 subjects in the CoQ10 group, carvedilol 6.25 mg/12 hours for 5 subjects in the CoQ10 group and 4 subjects in the placebo group.

Most subjects also received mineralocorticoid receptor antagonists, with 19 (82.6%) in the CoQ10 group and 18 (78.3%) in the placebo group (p=1.000). After the PPCI procedure, some subjects were still given additional anticoagulants. A total of 8 (34.8%) subjects in the CoQ10 group and 11 (47.8%) subjects in the control group received anticoagulants, including unfractionated heparin, enoxaparin, or fondaparinux for 3-5 days (p=0.550). A total of 15 (65.2%) subjects in the CoQ10 group and 17 (73.9%) subjects in the control group received nitrates, including isosorbide dinitrate or glyceryl trinitrate (p=0.749). Eight (34.8%) subjects in the CoQ10 group and 7 (30.4%) subjects in the control group received insulin during hospitalization. The oral antihyperglycemic medications used during outsubject care included gliclazide at doses of 30 mg and 60 mg, as well as glimepiride 2 mg/24 hours (p=0.352).

All study subjects underwent laboratory tests, including routine blood tests, blood glucose levels, lipid profiles, and kidney function. The average random blood glucose level for the CoQ10 group was 187.35±49.32 mg/dl, while for the placebo group it was 184.3±67.99 mg/dl (p=0.333). The average total cholesterol level for the CoQ10 group was 184.30±36.5 mg/dl, while for the placebo group it was 192.04±48.2 mg/dl (p=0.860). The average LDL level for the CoQ10 group was 118.70±24.33 mg/dl, while for the placebo group it was 113.30±35.39 mg/dl (p=0.272). The average serum creatinine level for the CoQ10 group was 1.11±0.40 mg/dl, while for the placebo group it was 1.17±0.39 mg/dl (p=0.596). No significant differences were found between the two groups for the laboratory parameters. There was a significant improvement in LVEF values in the CoQ10 group, with an increase of 10.39 ± 8.93% ($p < 0.001$). The placebo group also showed a significant improvement in LVEF values, with an increase of 3.21 ± 5.74% ($p = 0.014$). The difference (Δ) in average LVEF values between the CoQ10 group and the placebo group was significantly higher in the CoQ10 group (Δ 10.39 ± 8.93 vs. 3.21 ± 5.74, $p = 0.007$).

The average baseline GLS value in the CoQ10 group was more negative compared to the placebo group, but there was no significant difference between the two groups (-10.13 ± 2.64% vs -9.94 ± 3.38%, $p = 0.835$). In the follow-up data, the average GLS value in the CoQ10 group was more negative than in the placebo group, and there was a significant difference between the two groups (-15.75 ± 2.52% vs -10.64 ± 2.97%, $p < 0.001$). There was a significant improvement in GLS values in the CoQ10 group of 5.62 ± 2.16% ($p < 0.001$). The placebo group also showed a significant improvement in GLS values of 0.70 ± 1.56% ($p = 0.043$). The difference (Δ) in average GLS values between the CoQ10 group and the placebo group showed a significantly higher improvement in the CoQ10 group (Δ 5.62 ± 2.16 vs 0.70 ± 1.56, $p < 0.001$). Comparison of GLS values between Coenzyme Q10 and placebo group is shown in Figure 1.

None of the subjects reported any toxicity related to CoQ10 consumption. Gastrointestinal complaints, such as diarrhea, were observed in 1 subject (4.3%) in the CoQ10 group and 1 subject (4.3%) in the placebo group (p=1.000). Nausea was reported in 2 subjects (8.7%) in the CoQ10 group and 3 subjects (13%) in the placebo group (p=1.000). Abdominal pain occurred in 1 subject in the placebo group (4.3%) but was not found in the CoQ10 group (p=1.000). No allergic reactions/itching or headaches related to CoQ10 use were reported. Statistically, no significant differences were found in safety profiles related to CoQ10 use in this study's subjects.

4. Discussion

Baseline demographic and clinical characteristics were comparable between the two groups. The majority of participants were male, reflecting the demographic trends

often seen in STEMI populations.[13,20] Notably, smoking was the most prevalent risk factor for CAD in both groups, followed by hypertension, diabetes mellitus, and dyslipidemia. The uniformity in CAD risk factors suggests that the findings are representative of typical STEMI patients.[20,21] In terms of clinical outcomes, both groups exhibited similar characteristics regarding infarct location, ischemic times, Killip class classifications, and the average Thrombolysis In Myocardial Infarction (TIMI) scores. The majority of subjects were classified as Killip Class I (89.1%), and had TIMI scores of ≤5, indicating that the patients in this study were of low-risk stratification. The 30-day mortality rate for these patients is estimated to be 2-3% based on Killip class and ≤12.4% based on TIMI score.[22,23]

In this study, the average total ischemic time was notably long, at 502.13 ± 177.44 minutes (8.36 ± 2.95 hours). The study by De Luca et al. indicated that a symptom onset to door-to-balloon time of more than 4 hours is an independent predictor of one-year mortality ($p < 0.05$). Additionally, every 30-minute delay in reperfusion is associated with a 7.5% increase in mortality at one-year follow-up.[24] In this study, 30.4% of patients achieved complete revascularization. Those with incomplete revascularization are at a higher risk for adverse remodeling compared to those with complete revascularization. Sohn et al. further stated that complete revascularization through PCI can decrease the rates of cardiovascular and cerebrovascular events, as well as mortality, in patients with multivessel coronary artery disease, when compared to incomplete revascularization.[25]

The use of medications such as ACE inhibitors or ARBs and beta-blockers has been clinically proven to prevent remodeling and reduce mortality following AMI. The AIRE (Acute Infarction Ramipril Efficacy) study using ramipril reported a 27% reduction in mortality among post-myocardial infarction patients.[26] The use of β-blockers in patients with left ventricular dysfunction after myocardial infarction was demonstrated by the Carvedilol Post Infarct Survival Control in Left Ventricular Dysfunction (CAPRICORN) study, which found that treatment with carvedilol was associated with a 23% reduction in mortality and a 40% reduction in recurrent infarction after a 1.3-year follow-up. [27] The echocardiographic substudy of CAPRICORN assessed left ventricular remodeling and showed that in the carvedilol therapy group, there was a reduction in end-systolic LV volume of 9.2 ml ($p=0.023$) and an increase in LVEF of 3.9% ($p=0.015$) compared to the placebo group over 6 months. Thus, the use of carvedilol in conjunction with ACEIs has a protective effect against ventricular remodeling.[28]

Several studies indicate that assessing GLS is a superior method compared to Left Ventricular Ejection Fraction (LVEF) for evaluating left ventricular injury and function following STEMI.[29,30] GLS provides a more comprehensive view of myocardial function by measuring the deformation of the heart muscle during contraction. Subendocardial longitudinal fibers in the left ventricle are sensitive to ischemic conditions, making them useful for detecting early stages of myocardial dysfunction and possessing prognostic strength in patients at risk of developing heart failure. Global longitudinal strain as the primary outcome, revealed a greater improvement in the CoQ10 group post-intervention compared to the placebo group. The difference in GLS values (Δ 5.62 ± 2.16 vs 0.70 ± 1.56, $p < 0.001$) highlights the beneficial effect of CoQ10 supplementation on myocardial function following acute

STEMI. The significant enhancement in GLS values suggests improved myocardial contractility and function, which is crucial for recovery after ischemic events.

Both groups showed improvements in LVEF and GLS, whether in the CoQ10 group or the placebo group. These improvements in LVEF and GLS are likely due to the beneficial effects of revascularization procedures and the pharmacological management of STEMI patients, including ACE inhibitors/ARBs, beta-blockers, MRAs, and statins, which were administered to both groups and have clinically proven benefits in preventing remodeling and reducing mortality after myocardial infarction. The use of ACE inhibitors/ARBs, beta-blockers, and MRAs has a protective effect against ventricular remodeling by inhibiting the progression of remodeling.

The more pronounced improvement in GLS in the CoQ10 group indicates its potential as an effective adjunct therapy in STEMI management. The mechanisms behind these improvements may involve CoQ10's role in mitochondrial function and oxidative stress reduction, thereby enhancing myocardial energy metabolism and overall cardiac performance. The results of this study are consistent with theories and several studies suggesting that CoQ10 can help reduce oxidative stress and alleviate the inflammatory response by preventing neutrophil activation and matrix metalloproteinases, thus potentially reducing cardiac remodeling following myocardial infarction.[31] Oxidative stress is a pathophysiological mediator of myocardial remodeling in heart failure. CoQ10 supplementation may be beneficial by intervening in the increased production of reactive oxygen species that contribute to post-ischemic injury and the progression to heart failure.[32,33] However, this study did not measure serum levels of CoQ10 or inflammatory factors; both parameters could indicate the cardioprotective pathways of CoQ10.

The effect of CoQ10 suplementation on GLS values in patients with STEMI underwent PPCI has not been previously studied, making this research the first clinical trial in humans to investigate this matter. Nonetheless, other research has explored the impact of CoQ10 on infarct size in both animal models and human subjects. Awad et al. reported that CoQ10 significantly reduced myocardial infarct size by 11.36% compared to the control group in an animal model experiencing ischemia-reperfusion injury.[34] Mohseni et al. found that supplementation with CoQ10 at a dose of 200 mg per day for 12 weeks improved blood pressure, reduced inflammatory markers [serum levels of ICAM-1 (Intercellular Adhesion Molecule-1) and IL-6 (Interleukin-6)], and increased HDL-C (High-Density Lipoprotein Cholesterol) in patients with myocardial infarction.[35] Singh et al. reported that the incidence of nonfatal recurrent infarction and cardiac-related death was significantly lower in the CoQ10 group receiving 120 mg per day compared to the placebo group (15.0% vs. 30.9%, $p < 0.02$) during a 28-day follow-up.[36]

From a safety profile perspective, this study found that subjects receiving CoQ10 did not experience any serious side effects. Gastrointestinal disturbances were observed, but these were not significantly different between the CoQ10 and placebo groups ($p=1.000$). These side effects generally occurred only during the initial treatment phase. All participants tolerated the side effects, with or without the addition of symptomatic medications, without needing to stop CoQ10 treatment. Thus, it can be concluded that CoQ10 at a dose of 100 mg every 12 hours for 8 weeks is safe for use in STEMI patients undergoing PCI. The results are consistent with previous studies that

have safely used higher doses of CoQ10 for longer durations.[37,38] We acknowledge the limitations of this study, which include the lack of measurement of serum Coenzyme Q10 (ubiquinone) levels and inflammatory factors prior to the intervention, as well as the absence of a gold standard evaluation for cardiac remodeling, specifically cardiac magnetic resonance.

5. Conclusions

In conclusion, this study demonstrates that CoQ10 supplementation has a greater effect on the improvement of GLS values in patients with acute STEMI undergoing PPCI, with a favorable safety profile and no significant adverse effects. These findings support the potential of CoQ10 as an adjunct therapy in acute STEMI treatment, warranting further investigation into its long-term benefits and optimal dosing strategies. Future studies should aim to explore the underlying mechanisms of action and confirm these results in larger and diverse populations..

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9. Conflict of Interest

The authors have no conflict of interest to declare.

10. Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due to our local policy but are available from the corresponding author on reasonable request.

Main Points

- Global Longituinal Strain assessment using speckle-tracking echocardiography could be used as predictor of left ventricular recovery after myocardial infarction.
- Coenzyme Q10 as a potential adjunctive therapy that may improve outcomes and provides benefits for myocardial recovery in acute STEMI underwent PPCI.

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Abbreviation List

ACEIs	: Angiotensin Converting Enzyme Inhibitors
ACMQ	: Automated Cardiac Motion Quantification
AIRE	: Acute Infarction Ramipril Efficacy
AMI	: Acute Myocardial Infarction
ARBs	: Angiotensin II Receptor Blockers
BMI	: Body Mass Index
CABG	: Coronary Artery Bypass Grafting
CAD	: Coronary Artery Disease
CAPRICORN	: Carvedilol Post Infarct Survival Control in Left Ventricular Dysfunction
CoQ10	: Coenzyme Q10
GLS	: Global Longitudinal Strain
LV	: Left Ventricle
LVEF	: Left Ventricle Ejection Fraction
MI	: Myocardial Infarction
NSTEMI	: Non ST-elevation Myocardial Infarction
NYHA	: New York Heart Association
PPCI	: Primary Percutaneus Coronary Intervention
SD	: Standard Deviation
STE	: Speckle Tracking Echocardiography
STEMI	: ST-elevation Myocardial Infarction
TIMI	: Thrombolysis in Myocardial Infarction

Figures and Tables

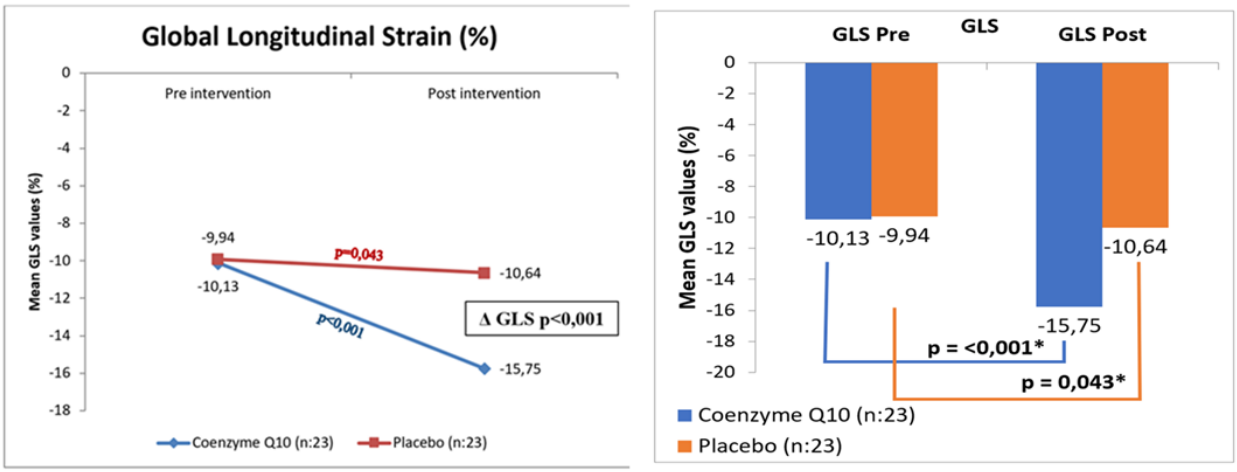

Figure 1. Comparison of GLS values before and after 8 weeks of intervention. Coenzyme Q10 group showed significantly greater improvement in GLS values. GLS, global longitudinal strain

Table 1. Baseline characteristics of the study participants.

Variable	Group		p value
	Coenzyme Q10 (n=23)	Placebo (n=23)	
Age	55,22 ± 8,43	54,48 ± 8,44	0,768§
Gender			
Male	14 (60,9%)	19 (82,6%)	0,190¥
Female	9 (39,1%)	4 (17,4%)	
Body mass index (kg/m^2)	25,01 ± 2,55	24,63 ± 2,38	0,604§
CAD Risk factor			
Hipertension	14 (60,9%)	10 (43,5%)	0,376¥
DM	8 (34,8%)	7 (30,4%)	1,000¥
Smoker	11 (47,8%)	15 (65,2%)	0,372¥
Dislipidemia	5 (21,7%)	6 (26,1%)	1,000¥
Hipertension and DM	5 (21,7%)	3 (13,0%)	0,699¥
STEMI detail			
Infarct location			
Anterior	12 (52,2%)	11 (47,8%)	1,000¥
Non Anterior	11 (47,8%)	12 (52,2%)	
Killip class			
Killip I	22 (95,7%)	19 (82,6%)	0,346¥
Killip II	1 (4,3%)	4 (17,4%)	
TIMI STEMI score	3 (1-5)	3 (1-5)	0,973‡
Door to Balloon (minute)	130,78±77,83	131,30±52,32	0,488‡
Total Ischemic Time (minute)	493,39±179,08	510,87±179,36	0,742§
Complete revascularisation	6 (26,1%)	8 (34,8%)	0,749¥
Vessel Disease			
1VD	6 (26,1%)	8 (34,8%)	0,464¥
2VD	10 (43,5%)	6 (26,1%)	
3VD	7 (30,4%)	9 (39,1%)	
Culprit lesion			
LAD	12 (52,2%)	11 (47,8%)	0,542¥
LCX	1 (4,3%)	0 (0%)	
RCA	10 (43,5%)	12 (52,2%)	
Laboratorium Parameter			
Ureum (mg/dl)	26,3±7,83	28,57±7.05	0,309§
Creatinin (mg/dl)	1,11±0.40	1,17±0,38	0,596‡
Glucose ad random (mg/dl)	187,35 ± 49,32	184,30 ± 67,98	0,333‡
HbA1c (%)	6,81 ± 1,99	6,67 ± 1,87	0,834‡
Lipid Profile			
Total Cholesterol (mg/dl)	184,30 ± 36,52	192,04 ± 48,24	0,860‡
Trigliserid (mg/dl)	149,87 ± 59,65	158,26 ± 51,23	0,482‡
HDL (mg/dl)	33,39 ± 8,82	33,26 ± 7,60	0,957§
LDL (mg/dl)	118,70 ± 24,33	113,30 ± 35,39	0,272‡

§ Independent-t; ¥ Chi-Square; ‡ Mann-Whitney

Abbreviations: CAD: coronary artery disease; DM: Diabetes Mellitus; STEMI: ST elevation myocardial infarction; VD: Vessel Disease; LDL: Low Density Lipoprotein; HDL: High Density Lipoprotein; LAD: Left Anterior Descending; LCX: Left Circumflex

Table 1. Baseline characteristics of the study participants.

Variable	Group		p value
	Coenzyme Q10 (n=23)	Placebo (n=23)	
Medicamentosa			
Aspilet	23 (100%)	23 (100%)	–
Ticagrelor	23 (100%)	21 (91,3%)	0,489¥
Clopidogrel	0 (0%)	2 (8,7%)	0,489¥
ACE-i/ARB	23 (100%)	23 (100%)	–
In hospital			
Ramipril 2,5mg/24hour	10 (43,5%)	10 (43,5%)	0,785¥
Ramipril 5mg/24hour	2 (8,7%)	1 (4,3%)	
Perindopril 2,5mg/24hour	5 (21,7%)	4 (17,4%)	
Perindopril 5mg/24hour	2 (8,7%)	2 (8,7%)	
Candesartan 4mg/24hour	4 (17,4%)	4 (17,4%)	
Valsartan 40mg/12hour	0 (0%)	2 (8,7%)	
Follow up			
Ramipril 2,5mg/24hour	10 (43,5%)	10 (43,5%)	0,602¥
Ramipril 5mg/24hour	1 (4,3%)	1 (4,3%)	
Ramipril 10mg/24hour	1 (4,3%)	0 (0%)	
Perindopril 2,5mg/24hour	0 (0%)	1 (4,3%)	
Perindopril 5mg/24hour	7 (30,4%)	5 (21,7%)	
Candesartan 4mg/24hour	0 (0%)	1 (4,3%)	
Candesartan 8mg/24hour	4 (17,4%)	3 (13,0%)	
Valsartan 80mg/12hour	0 (0%)	2 (8,7%)	
Beta blocker	23 (100%)	21 (91,3%)	0,489¥
In hospital			
Bisoprolol 1,25mg/24hour	9 (39,2%)	8 (34,8%)	0,994¥
Bisoprolol 2,5mg/24hour	8 (34,8%)	8 (34,8%)	
Carvedilol 3,125mg/12hour	5 (21,7%)	4 (17,4%)	
Carvedilol 6,25mg/12hour	1 (4,3%)	1 (4,3%)	
Follow up			
Bisoprolol 1,25mg/24hour	5 (21,7%)	3 (13,0%)	0,408¥
Bisoprolol 2,5mg/24hour	10 (43,5%)	13 (56,6%)	
Bisoprolol 5mg/24hour	2 (8,7%)	0 (0%)	
Carvedilol 6,25mg/12hour	6 (26,1%)	5 (21,7%)	
Statin			
Atorvastatin 40mg/24hour	23 (100%)	23 (100%)	–
MRA			
Spironolacton 25mg/24hour	19 (82,6%)	18 (78,3%)	1,000¥
Anticoagulant	8 (34,8%)	11 (47,8%)	0,550¥
Fondaparinux 2,5mg/24hour	6 (26,1%)	7 (30,4%)	0,734¥
Enoxaparin 0,6cc/12hour	1 (4,3%)	3 (13,0%)	
Heparine 500 U/hour	1 (4,3%)	1 (4,3%)	
Nitrat	15 (65,2%)	17 (73,9%)	0,749¥
ISDN 5mg/8hour	5 (21,7%)	7 (30,4%)	0,726¥
Nitrokaf R 2,5mg/12hour	10 (43,5%)	10 (43,5%)	
Insulin (*in hospital*)	8 (34,8%)	7 (30,4%)	1,000¥
Glicazide 30mg/24hour	1 (4,3%)	3 (13,0%)	0,352¥
Glicazide 60mg/24hour	4 (17,4%)	3 (13,0%)	
Glimepiride 2mg/24hour	3 (13,0%)	1 (4,3%)	

§ Independent-t; ¥ Chi-Square; ‡ Mann-Whitney; Abbreviations: ACEi: Angiotensin Converting Enzyme inhibitor; ARB: Angiotensin Receptor Blocker; MRA: Mineralocorticoid Receptor Antagonist; ISDN: Isosorbid Dinitrat

Table 2. Comparison of LVEF (Biplane) value before and before and after 8 weeks intervention in each group.

LVEF (B) %	Group		p value
	Coenzyme Q10 (n=23)	Placebo (n=23)	
Pre	52,42 ± 6,84	49,77 ± 7,76	0,226§
Post	62,81 ± 8,91	52,98 ± 6,82	**<0,001§***
p	**<0,001†***	**0,014¶***	
Delta	10,39 ± 8,93	3,21 ± 5,74	**0,007‡***

* Significant (p < 0,05) § Independent t; ‡ Mann-Whitney; † Wilcoxon; ¶ Paired t. GLS, global longitudinal strain.

Table 3. Comparison of GLS value before and after 8 weeks intervention in each group.

GLS	Group		p value
	Coenzyme Q10 (n=23)	Placebo (n=23)	
Pre test	-10,13 ± 2,64	-9,94 ± 3,38	0,835§
Post test	-15,75 ± 2,52	-10,64 ± 2,97	**<0,001§***
p value	**<0,001¶***	**0,043¶***	
Delta GLS	5,62 ± 2,16	0,70 ± 1,56	**<0,001§***

* Significant (p < 0,05); § Independent t; ¶ Paired t. GLS, global longitudinal strain.

PERSETUJUAN / PENOLAKAN MENJADI SUBYEK PENELITIAN	Nama : No RM : Tgl Lahir/Umur : Jenis Kelamin : Ruang : No Register : Kelas : Tgl Masuk : Nama DPJP : Nama PPJP : *(Tempelkan stiker identitas pasien jika tersedia)*

JUDUL PENELITIAN: Pengaruh Suplementasi Koenzim Q10 Terhadap Perubahan Nilai Global Longitudinal Strain pada Pasien Paska Infark Miokard Akut Elevasi Segmen ST yang Menjalani Intervensi Koroner Perkutan Primer

PEMBERIAN INFORMASI

Nama Peneliti : dr. Carina Adriana
Pemberi Informasi : dr. Carina Adriana
Penerima Informasi :
Diberikan pada tanggal / jam :

No	JENIS INFORMASI	ISI INFORMASI	Tanda (√)/paraf Penerima informasi
1	Judul Penelitian	Pengaruh Suplementasi Koenzim Q10 Terhadap Perubahan Nilai Global Longitudinal Strain pada Pasien Paska Infark Miokard Akut Elevasi Segmen ST yang Menjalani Intervensi Koroner Perkutan Primer	
2	Perkenalan Peneliti	Perkenalkan saya dr. Carina Adriana dari bagian Jantung dan Pembuluh Darah RSUP dr.Kariadi.	
3	Tujuan Penelitian	Mengetahui pengaruh pemberian Koenzim Q10 sebagai tambahan terapi standar terhadap nilai Global Longitudinal Strain ventrikel kiri.	
4	Manfaat Penelitian	Apabila hipotesis penelitian ini benar maka Bapak/Ibu yang mendapatkan Koenzim Q10 akan mengalami perbaikan parameter Global Longitudinal Strain ventrikel kiri.	
5	Prosedur Penelitian	• Bapak/Ibu yang terpilih secara acak akan kami berikan Koenzim Q10 dengan dosis 100mg/12 jam selama minimal 8 minggu, selain obat-obatan jantung rutin lainnya. • Kami akan melakukan pemeriksaan ekokardiografi 2 kali untuk mengukur nilai GLS, yaitu di awal penelitian dan setelah 8 minggu pemberian obat. • Bapak/Ibu tidak dipungut biaya untuk pengobatan dan pemeriksaan.	
6	Lama Waktu Partisipasi Subyek	8 minggu	
7	Risiko Penelitian	Koenzim Q10 memiliki tolerabilitas yang baik dalam uji klinis dengan tingkat efek samping yang rendah. Efek samping yang dilaporkan antara lain diare, nyeri perut, mual.	
8	Alternatif Lain	Tidak menjadi subjek penelitian.	
9	Tanggung Jawab Bila Terjadi Efek Samping	Jika Bapak/Ibu mengalami efek samping dari obat ini maka Bapak/Ibu dapat menghubungi kami melalui nomor telepon (dr. Carina Adriana / 085641516100) dan kami akan segera menindaklanjuti keluhan Anda. RSUP Dr. Kariadi Semarang akan bertanggungjawab terhadap pasien yang menjadi subyek penelitian apabila terjadi efek samping akibat aktivitas penelitian ini.	
10	Kerahasiaan Subyek Penelitian	Dirahasiakan dan tidak akan dipublikasikan kecuali dengan ijin peserta.	
11	Kebebasan Menyetujui / Menolak	Bila pada saat pelaksanaan penelitian, subyek penelitian menyatakan untuk berhenti, maka tidak akan mempengaruhi sikap maupun pelayanan yang diberikan terhadap yang bersangkutan sebagai pasien di RSUP Dr.Kariadi Semarang.	
12	Informasi Tambahan	Penelitian ini sudah mendapatkan persetujuan etik dari komisi etik penelitian RSUP Dr.Kariadi dan persetujuan pelaksanaan penelitian dari Bagian Diklit RSUP Dr.Kariadi. Jika ada hal yang masih ingin ditanyakan atau diperjelas, anda dapat langsung menanyakan kepada saya (dr. Carina Adriana / 085641516100) atau Bagian Diklit RSUP Dr. Kariadi di nomor (024) 8413476 ext. 8033	
Dengan ini menyatakan bahwa saya telah menerangkan hal-hal di atas secara benar dan jelas dan memberikan kesempatan untuk bertanya dan/atau berdiskusi			Tanda tangan Pemberi Informasi
Dengan ini menyatakan bahwa saya telah menerima informasi sebagaimana di atas yang saya beri tanda/paraf di kolom kanannya, dan telah memahaminya			Tanda tangan Penerima Informasi

Keterangan :
1. **Bila pasien tidak kompeten/tidak mau menerima informasi,maka penerima informasi adalah keluarga terdekat atau wali**
2. **Isi informasi tidak boleh disingkat**

Lanjut ke halaman 2

PERSETUJUAN MENJADI SUBYEK PENELITIAN

Yang bertanda tangan di bawah ini saya,
Nama : ……
Umur.....tahun, laki-laki / perempuan*
No. KTP : .....
Alamat : ……
dengan ini menyatakan **SETUJU** untuk menjadi responden penelitian terhadap saya / Ayah / Ibu / Anak / Keluarga saya,*
Nama : ……
Umur.....tahun, laki-laki / perempuan*
No. KTP : .....
Alamat : ……
Saya memahami tujuan dan manfaat peneltian tersebut sebagaimana telah dijelaskan seperti di atas kepada saya, termasuk risiko dan komplikasi yang mungkin timbul.
Saya juga menyadari bahwa oleh karena ilmu kedokteran bukanlah ilmu pasti, maka keberhasilan tindakan kedokteran bukanlah keniscayaan, melainkan sangat bergantung kepada Tuhan Yang Maha Esa, oleh sebab itu saya membebaskan **RSUP Dr. Kariadi / dokter/Petugas lainnya** dari tanggung jawab hukum apabila risiko dan komplikasi yang tidak diharapkan benar-benar terjadi di kemudian hari.

Semarang, tanggal……Jam……

Yang menyatakan,	Peneliti	Saksi
(……)	(……)	(.....)

PENOLAKAN MENJADI SUBYEK PENELITIAN

Yang bertanda tangan di bawah ini saya,
Nama : ……
Umur.....tahun, laki-laki / perempuan*
No. KTP : .....
Alamat : ……
dengan ini menyatakan **TIDAK SETUJU** untuk menjadi responden penelitian terhadap saya / Ayah / Ibu / Anak / Keluarga saya,*,
Nama : ……
Umur.....tahun, laki-laki / perempuan*
No. KTP : .....
Alamat : ……
Saya memahami tujuan dan manfaat penelitian tersebut sebagaimana telah dijelaskan seperti di atas kepada saya, termasuk risiko dan komplikasi yang mungkin timbul.
Saya juga menyadari bahwa oleh karena ilmu kedokteran bukanlah ilmu pasti, maka keberhasilan tindakan kedokteran bukanlah keniscayaan, melainkan sangat bergantung kepada Tuhan Yang Maha Esa, oleh sebab itu saya membebaskan **RSUP Dr. Kariadi / dokter/Petugas lainnya** dari tanggung jawab hukum apabila akibat tindakan yang tidak saya setujui terdapat risiko dan komplikasi yang tidak diharapkan benar-benar terjadi di kemudian hari.

Semarang, tanggal……Jam……

Yang menyatakan,	Peneliti	Saksi
(……)	(……)	(.....)

Keterangan : *) Pilih salah satu