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# Six-Month Metabolic, Inflammatory, and Elastographic Outcomes with Adjunctive Ademetionine After Coronary Artery Bypass Grafting in Patients with Metabolic Dysfunction-Associated Fatty Liver Disease

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## Abstract

**Background:** Metabolic dysfunction-associated fatty liver disease (MAFLD) frequently coexists with advanced coronary artery disease. Coronary artery bypass grafting (CABG) may produce transient hepatic injury and systemic inflammation, while residual metabolic-inflammatory abnormalities can persist during follow-up.

**Objective:** To evaluate six-month metabolic, inflammatory, and liver-elastography outcomes in patients with stable exertional angina and MAFLD receiving standard post-CABG therapy with or without adjunctive ademetionine.

**Methods:** This comparative cohort analysis included 100 patients with stable exertional angina and MAFLD who underwent CABG for multivessel coronary artery disease. After CABG, 50 patients received standard therapy alone and 50 received standard therapy plus ademetionine (400 mg intravenously daily for 10 days, followed by 500 mg orally twice daily for 6 months). Serum adiponectin, leptin, ghrelin, interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and liver elastography were evaluated. Perioperative routine laboratory changes were also summarized from the source dissertation.

**Results:** At six months, adjunctive ademetionine was associated with higher adiponectin (7.2 ± 0.16 vs. 4.7 ± 0.18 μg/mL; $P < 0.001$) and ghrelin (693.8 ± 17.5 vs. 523.9 ± 16.9 pg/mL; $P <$

0.001), and with lower leptin (22.2 ± 0.5 vs. 29.2 ± 0.6 ng/mL; P < 0.001), IL-6 (8.4 ± 0.4 vs. 11.1 ± 0.3 pg/mL; P < 0.001), and TNF-α (11.5 ± 0.4 vs. 15.1 ± 0.44 pg/mL; P < 0.001). Liver stiffness was lower with ademetionine (Young modulus 7.2 ± 0.1 vs. 8.86 ± 0.09 kPa; P < 0.001), as was the reported fibrosis grade (1.50 ± 0.12 vs. 1.92 ± 0.12; P < 0.05).

**Conclusion:** In patients with MAFLD after CABG, adjunctive ademetionine was associated with a more favorable six-month adipokine, inflammatory, and elastographic profile. Because random allocation and baseline comparability of the two treatment subgroups were not documented in the source dissertation, these findings should be interpreted as associative and require prospective randomized validation.

**Keywords:** Metabolic Dysfunction-Associated Fatty Liver Disease; Coronary Artery Bypass Grafting; Ademetionine; Adiponectin; Leptin; Ghrelin; Interleukin-6; Tnf-A; Liver Elastography

## Introduction

Metabolic dysfunction-associated fatty liver disease (MAFLD) is increasingly recognized as a multisystem metabolic disorder rather than an isolated hepatic condition. It shares major cardiometabolic drivers with coronary artery disease, including obesity, insulin resistance, atherogenic dyslipidemia, and hypertension, and is associated with an increased burden of cardiovascular events [1-5].

In patients with advanced coronary atherosclerosis, CABG remains an established revascularization strategy. Cardiopulmonary bypass, perioperative hemodynamic shifts, anesthetic exposure, and systemic inflammatory activation may nevertheless transiently affect liver function [6-10]. This interaction is particularly relevant in patients with pre-existing steatosis or fibrosis, in whom hepatic reserve may be reduced.

Routine aminotransferases and bilirubin may normalize during postoperative recovery even when metabolic and inflammatory abnormalities persist. Adiponectin, leptin, ghrelin, IL-6, and TNF-α may therefore provide complementary information regarding postoperative metabolic-inflammatory status. The source dissertation also used liver elastography to assess hepatic stiffness and reported persistent abnormalities six months after CABG under standard therapy.

Ademetionine (S-adenosyl-L-methionine) participates in methylation and transsulfuration pathways and is used as a hepatoprotective agent in hepatobiliary practice. The dissertation therefore evaluated whether adding ademetionine to standard post-CABG therapy was associated with improvement in metabolic hormones, inflammatory cytokines, and liver stiffness. The present article reports these six-month comparative outcomes in the structured format of the accompanying reference article.

## Materials and Methods

### *Study Design and Participants*

This comparative clinical cohort was derived from a dissertation study conducted in Uzbekistan. The overall study included 100 patients with stable exertional angina and comorbid MAFLD and 20 patients with stable angina without identified liver pathology. The present treatment analysis is restricted to the 100 patients with MAFLD who underwent CABG for multivessel coronary artery disease. The mean age of the MAFLD cohort was 63.3 ± 0.8 years; 63 patients were men and 37 were women.

After CABG, the MAFLD cohort was divided into two subgroups of 50 patients each. One subgroup received standard post-CABG therapy; the second received the same standard therapy plus ademetionine (Heptral), 400 mg intravenously daily for 10 days followed by 500 mg orally twice daily for six months. The dissertation does not describe random sequence generation, allocation concealment, or blinding; therefore, the treatment comparison is reported as observational rather than randomized.

### *Clinical and Laboratory Assessment*

Clinical evaluation included symptoms, medical history, physical assessment, complete blood count, routine serum biochemistry, lipid profile, and coagulation-related measurements. Instrumental assessment included coronary angiography, 12-lead electrocardiography, 24-hour blood-pressure monitoring, echocardiography, abdominal ultrasonography, and liver elastography.

Adiponectin was measured by solid-phase immunoassay using a MAGLUMI X3 analyzer. Leptin was measured by sandwich immunoassay using a FineCare FIA Meter Plus platform. Ghrelin was measured using a MAGLUMI X3 analyzer. Serum IL-6 and TNF-α were assessed by immunoassay using the FineCare FIA Meter Plus platform.

### *Liver Elastography*

Liver elastography was performed using a Mindray DC-80 system. The median Young modulus (kPa) was used as the quantitative liver-stiffness measure. The interquartile range-to-median ratio (IQR/Med) was used as a reliability indicator, with values below 30% considered acceptable in the dissertation. A numerical fibrosis grade was also reported.

### *Outcomes*

The principal outcomes were six-month serum adiponectin, leptin, ghrelin, IL-6, TNF-α, median Young modulus, IQR/Med, and reported fibrosis grade. Selected perioperative routine laboratory measures were included to contextualize the early postoperative hepatic response and subsequent recovery.

### *Statistical Analysis*

Statistical analyses in the source dissertation were performed using SPSS version 31.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were reported as mean ± the dispersion/error term used in the source tables (M±m). The dissertation reports Mann-Whitney and Kruskal-Wallis procedures for continuous between-group comparisons, $\chi^2$ or Fisher exact tests for categorical variables, and Pearson correlation analysis where applicable. No unreported patient-level analyses were reconstructed for the present manuscript. Two-sided $P < 0.05$ was considered statistically significant.

### *Ethics Approval and Informed Consent*

The study protocol was reviewed and approved by the Ethics Committee of Tashkent State Medical University. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. All participants were informed about the objectives, procedures, potential risks, and intended scientific use of the collected data. Written informed consent was obtained from all participants before enrollment. Participant confidentiality was maintained throughout the study.

## Results

### *Cohort Characteristics and Perioperative Hepatic Response*

The MAFLD cohort comprised 100 CABG recipients (63 men and 37 women; mean age 63.3 ± 0.8 years). Conventional biochemical indices demonstrated an early postoperative deterioration followed by substantial recovery. Total bilirubin increased from 16.3 ± 0.56 µmol/L before CABG to 22.8 ± 0.6 µmol/L on postoperative day 2 and decreased to 15.2 ± 0.5 µmol/L at six months. ALT changed from 56.6 ± 1.9 to 76.5 ± 2.04 and then 49.1 ± 1.7 U/L; AST changed from 46.9 ± 1.7 to 67.2 ± 1.9 and then 37.9 ± 1.4 U/L. CRP increased from 5.7 ± 0.2 mg/L preoperatively to 7.5 ± 0.3 mg/L on day 2 and decreased to 5.4 ± 0.2 mg/L at six months.

**Table 1. Selected perioperative laboratory changes reported in the MAFLD CABG cohort**

| Variable | Pre-CABG (n=100) | Day 2 (n=100) | 6 months, standard therapy (n=50) | Reported significance |
|---|---|---|---|---|
| Total bilirubin, micromol/L | 16.3 ± 0.56 | 22.8 ± 0.6 | 15.2 ± 0.5 | Day 2 vs baseline p<0.001; day 2 vs 6 mo p<0.001 |
| ALT, U/L | 56.6 ± 1.9 | 76.5 ± 2.04 | 49.1 ± 1.7 | Day 2 vs baseline p<0.001; 6 mo lower than baseline p<0.01 |
| AST, U/L | 46.9 ± 1.7 | 67.2 ± 1.9 | 37.9 ± 1.4 | Day 2 vs baseline p<0.001; 6 mo lower than baseline p<0.001 |
| CRP, mg/L | 5.7 ± 0.2 | 7.5 ± 0.3 | 5.4 ± 0.2 | Day 2 vs baseline p<0.001; day 2 vs 6 mo p<0.001 |
| Albumin, g/L | 41.9 ± 0.45 | 38.3 ± 0.49 | 39.9 ± 0.43 | Day 2 vs baseline p<0.001; day 2 vs 6 mo p<0.05 |

*Values are reproduced from the dissertation. The six-month standard-therapy column contains 50 patients and should not be interpreted as a fully paired 100-patient repeated-measures analysis.*

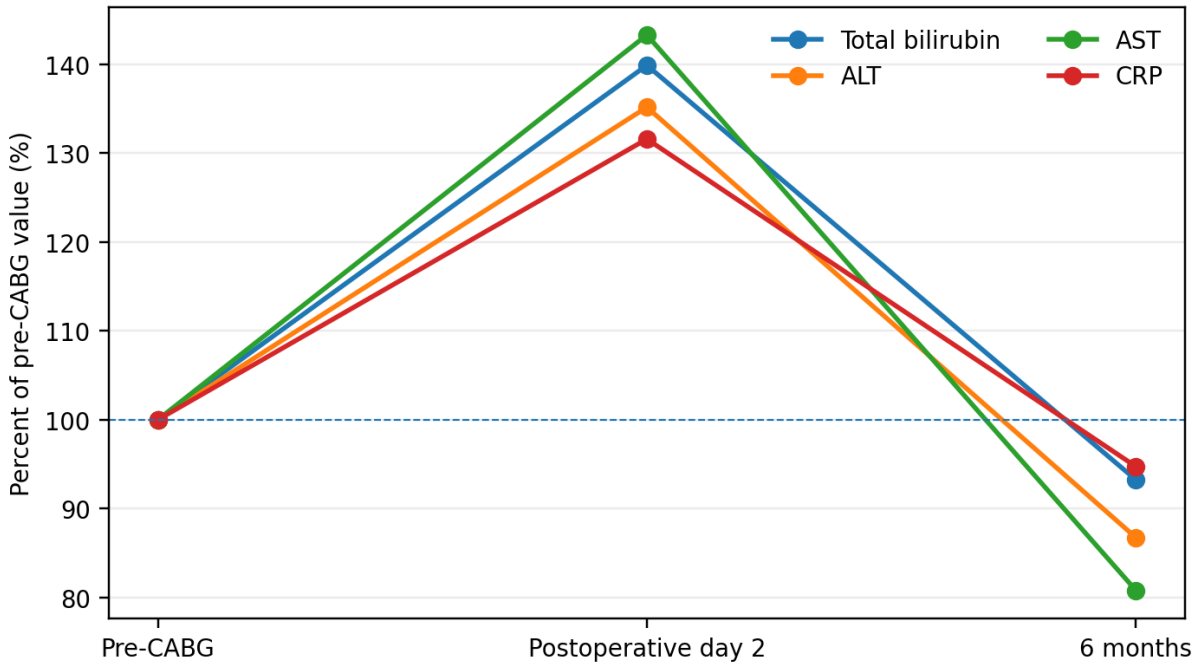


**Figure 1. Relative perioperative changes in bilirubin, ALT, AST, and CRP after CABG. Values are normalized to the pre-CABG level (100%) to permit visualization of markers with different measurement units. Source values are from the dissertation.**

***Six-Month Metabolic Hormone Outcomes***

At six months, adiponectin was higher in patients receiving adjunctive ademetionine than in those receiving standard therapy alone (7.2 ± 0.16 vs. 4.7 ± 0.18 µg/mL; P < 0.001). Leptin was lower in the ademetionine group (22.2 ± 0.5 vs. 29.2 ± 0.6 ng/mL; P < 0.001), whereas ghrelin was higher (693.8 ± 17.5 vs. 523.9 ± 16.9 pg/mL; P < 0.001).

**Table 2. Six-month metabolic and inflammatory biomarkers by treatment group**

| Outcome | Standard therapy (n=50) | Standard therapy + ademetionine (n=50) | p value |
|---|---|---|---|
| Adiponectin, microg/mL | 4.7 ± 0.18 | 7.2 ± 0.16 | <0.001 |
| Leptin, ng/mL | 29.2 ± 0.6 | 22.2 ± 0.5 | <0.001 |
| Ghrelin, pg/mL | 523.9 ± 16.9 | 693.8 ± 17.5 | <0.001 |
| IL-6, pg/mL | 11.1 ± 0.3 | 8.4 ± 0.4 | <0.001 |
| TNF-alpha, pg/mL | 15.1 ± 0.44 | 11.5 ± 0.4 | <0.001 |

*Data are reproduced from the source dissertation. The source notation M±m does not consistently specify whether the second term represents SD or SEM.*

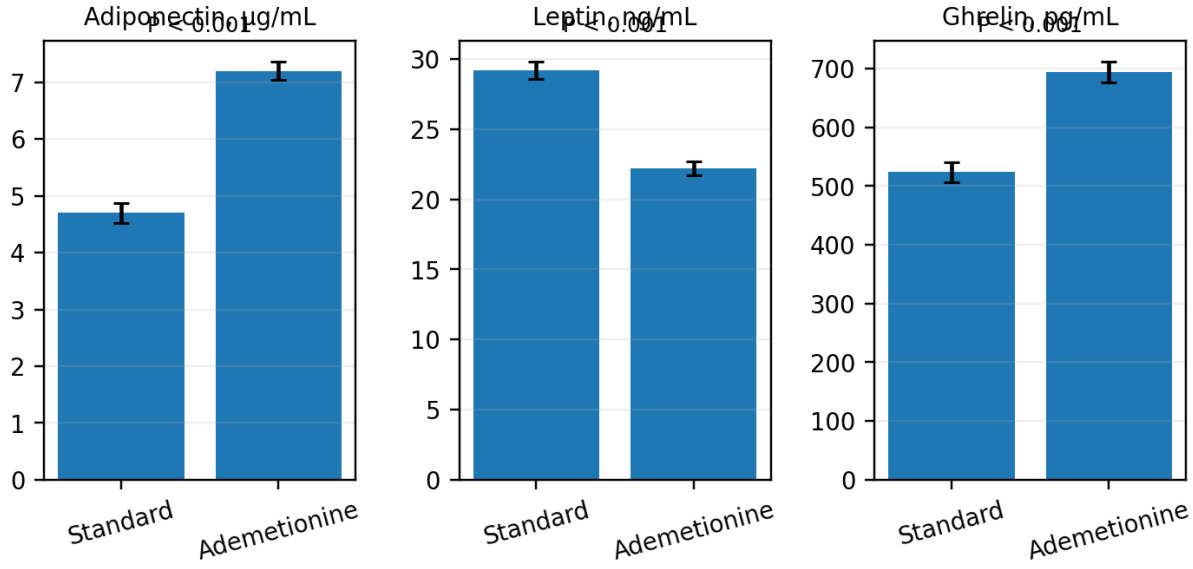


**Figure 2. Six-month adiponectin, leptin, and ghrelin concentrations in patients receiving standard therapy alone versus standard therapy plus ademetionine after CABG. Error bars reproduce the reported M±m values from the dissertation.**

***Six-Month Inflammatory Cytokines***

IL-6 was lower with adjunctive ademetionine than with standard therapy alone (8.4 ± 0.4 vs. 11.1 ± 0.3 pg/mL; P < 0.001). TNF-α showed the same direction of association (11.5 ± 0.4 vs. 15.1 ± 0.44 pg/mL; P < 0.001). These findings indicate lower circulating inflammatory activity in the ademetionine subgroup at six months, although causality cannot be established from the available study design.

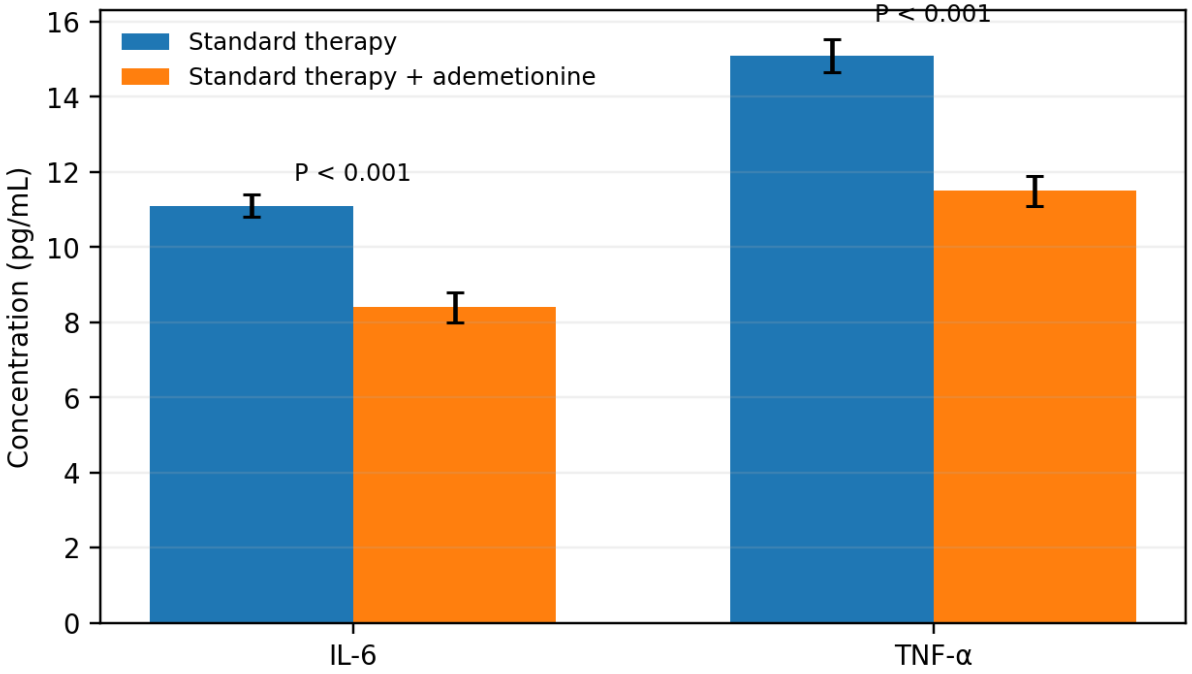


**Figure 3. Serum IL-6 and TNF-α concentrations six months after CABG according to treatment group. Error bars reproduce the reported M±m values from the dissertation.**

***Six-Month Liver Elastography***

Elastography reliability was acceptable in both groups according to the source criterion: IQR/Med was below 30% and did not differ significantly (17.1 ± 0.62% with standard therapy vs. 17.5 ± 0.68% with ademetionine; P > 0.05). The median Young modulus was lower with ademetionine (7.2 ± 0.1 vs. 8.86 ± 0.09 kPa; P < 0.001), and the reported fibrosis grade was also lower (1.50 ± 0.12 vs. 1.92 ± 0.12; P < 0.05).

**Table 3. Six-month liver elastography by treatment group**

| Elastography outcome | Standard therapy (n=50) | Standard therapy + ademetionine (n=50) | p value |
|---|---|---|---|
| IQR/Med, % | 17.1 ± 0.62 | 17.5 ± 0.68 | >0.05 |
| Young modulus median, kPa | 8.86 ± 0.09 | 7.2 ± 0.1 | <0.001 |
| Reported fibrosis grade | 1.92 ± 0.12 | 1.50 ± 0.12 | <0.05 |

*IQR/Med <30% was considered an acceptable elastography reliability criterion in the source dissertation.*

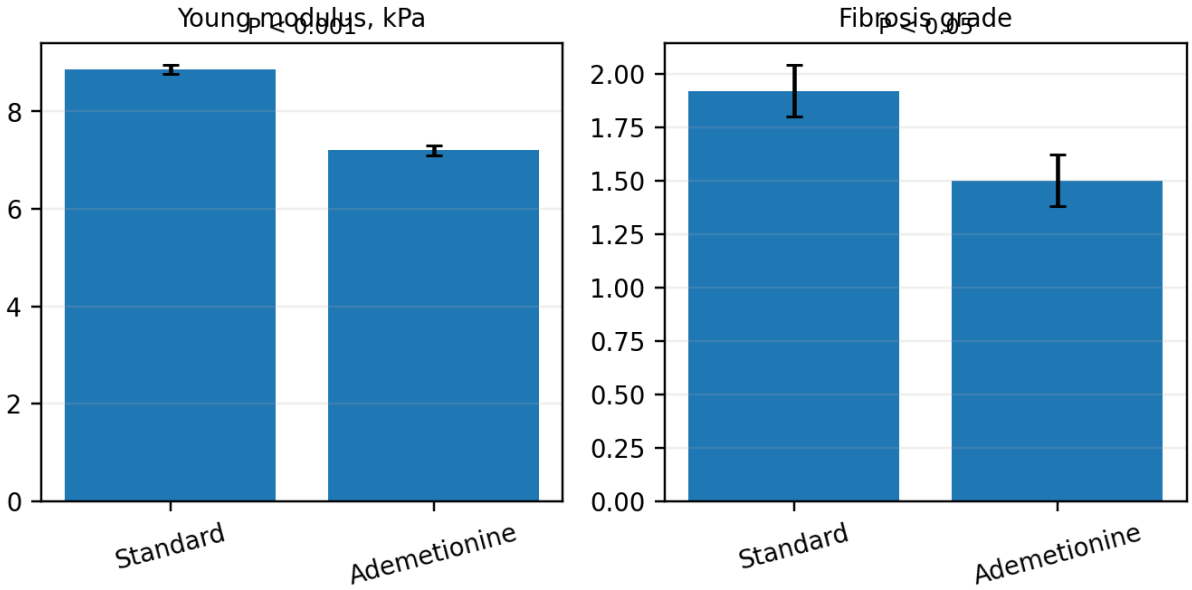


**Figure 4. Liver stiffness and reported fibrosis grade six months after CABG according to treatment group. Lower Young modulus and fibrosis grade were observed in the ademetionine subgroup.**

## Discussion

The present comparative cohort study demonstrated that patients with stable angina and MAFLD who received adjunctive ademetionine after CABG had a more favorable six-month metabolic, inflammatory, and elastographic profile than patients receiving standard therapy alone. The most pronounced between-group differences involved adiponectin, leptin, ghrelin, IL-6, TNF-α, and liver stiffness.

The perioperative biochemical trajectory is consistent with transient hepatic stress after major cardiac surgery. Bilirubin, aminotransferases, and CRP increased on postoperative day 2, while most routine indices improved by six months. This pattern may reflect the combined effects of cardiopulmonary bypass, systemic inflammatory activation, altered hepatic perfusion, operative stress, medication exposure, and subsequent postoperative recovery [7-10,13].

The adipokine findings may be clinically relevant. Adiponectin is linked to insulin sensitivity, endothelial protection, and anti-inflammatory signaling, whereas elevated leptin commonly accompanies obesity, insulin resistance, and chronic inflammatory activation. Higher adiponectin and lower

leptin in the ademetionine group therefore indicate a more favorable metabolic phenotype at six months. Ghrelin was also higher with ademetionine, supporting a broader difference in metabolic-hormonal regulation between the two subgroups.

Persistent cytokine activation was another important observation. IL-6 and TNF-α remained elevated during follow-up under standard therapy, whereas both were lower in the ademetionine subgroup. This is compatible with reduced systemic inflammatory activity; however, the observational comparison does not establish that ademetionine itself caused the difference. Unmeasured variation in baseline metabolic status, concomitant treatment, rehabilitation, diet, body-weight change, or adherence may have contributed.

The elastography findings provide an organ-level correlate of the biomarker results. The lower Young modulus in the ademetionine group suggests lower liver stiffness at six months. Nevertheless, liver stiffness is influenced not only by fibrosis but also by inflammation, congestion, and steatosis. Accordingly, the numerical fibrosis grade and Young modulus should not be interpreted as direct histologic fibrosis regression in the absence of liver biopsy.

From a clinical perspective, patients with MAFLD after CABG may appear biochemically recovered when evaluated only by aminotransferases and bilirubin, while residual metabolic-inflammatory dysregulation persists. A broader follow-up approach combining metabolic biomarkers with validated noninvasive liver assessment may better characterize recovery in selected high-risk patients. The present data support further prospective investigation rather than routine treatment recommendations.

### *Clinical Implications and Study Limitations*

Several limitations should be acknowledged. First, the dissertation does not document randomization, allocation concealment, or blinding; therefore, the treatment comparison is observational. Second, baseline biomarker and elastography values are not reported separately for the two 50-patient treatment subgroups, preventing confirmation of baseline balance or adjusted change-from-baseline effects. Third, only aggregate summary data were available, limiting multivariable adjustment and sensitivity analyses. Fourth, the source notation M±m does not consistently distinguish standard deviation from standard error. Fifth, adherence, postoperative weight change, diet, physical activity, and detailed concomitant medication exposure were not reported. Finally, the dissertation contains a MELD-derived measure requiring raw-data verification; it has therefore not been used as a principal outcome in this article.

## Conclusions

Among patients with stable angina and MAFLD after CABG, adjunctive ademetionine was associated at six months with higher adiponectin and ghrelin, lower leptin, IL-6, and TNF-α, and lower liver stiffness than standard therapy alone. These findings suggest a potentially favorable metabolic-inflammatory and hepatic recovery profile. Because treatment allocation and subgroup baseline comparability were not documented, causal efficacy cannot be established. A prospectively registered randomized study with standardized liver elastography and repeated biomarker measurements is required for confirmation.

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