Lowered Postoperative LDL-C/HDL-C Ratio Reduces Later Cardiovascular Events after Abdominal Aortic Aneurysm Surgery

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Purpose: To examine the relationship between the incidence of later cardiovascular events after abdominal aortic aneurysm (AAA) surgery and postoperative lipid levels.

Methods: Atherosclerotic risk factors including postoperative serum lipid levels were examined in 116 patients aged 70 or less undergoing an elective AAA surgery. Later cardiovascular events after AAA surgery occurred in 21 patients, including cerebral infarction (n = 4), catheter intervention or surgery for coronary artery disease (CAD) (n = 10) and other vascular disease.

Results: Postoperative cholesterol levels during the average follow-up period of 55.6 ± 44.3 (months) were 49.0 ± 15.7 (mg/dL) for high-density lipoprotein cholesterol (HDL-C), 97.9 ± 31.2 (mg/dL) for low-density lipoprotein cholesterol (LDL-C), which were both significantly improved compared to preoperative values (p <0.001). Cox hazard analysis indicated that preexistent CAD significantly increased in the risk for later cardiovascular events (hazard ratio 5.67; 95%CI 1.92–16.8; p = 0.002) and lowered postoperative LDL-C/HDL-C ratio <1.5 decreased in the risk after AAA surgery (hazard ratio 0.10; 95%CI 0.01–0.83; p = 0.033). Patients with postoperative LDL-C/HDL-C ratio <1.5 (n = 22) had a significantly better cardiovascular event-free rate than those with that ratio ≥1.5 (n = 94) (p = 0.014).

Conclusion: Lowered postoperative LDL-C/HDL-C ratio <1.5 can decrease in the risk for later cardiovascular events after AAA surgery. These results may support the rationale for postoperative aggressive lipid-modifying therapy.

Keywords: abdominal aortic aneurysm, dyslipidemia, cholesterol, lipid-modifying therapy, cardiovascular events

INTRODUCTION

Abdominal aortic aneurysm (AAA) is an asymptomatic condition with a high mortality rate related to rupture, which has been the cause of 1 to 2% of all deaths in the Western world.1,2) AAA principally develops from arteriosclerosis, which is often associated with other arteriosclerotic cardiovascular disorders like coronary artery disease (CAD).1,3–6) The reported mean 5 year crude survival in patients with AAA after surgical repair was approximately 70%, while the expected survival in a control population matched for age and gender was close to 80%.7,8) The survival was further reduced by about 10% in cases with significant CAD.8) For the primary
prevention of atherosclerotic disease, such as CAD, the importance of adequate control of dyslipidemia has been reported, recently, and lipid-modifying therapies like statin treatment have an established role in the treatment of occlusive atherosclerotic disease.9–11) Although the value of lipid-modifying therapies in the etiology of AAA remains to be controversial, Golledge et al. described the role of high-density lipoprotein cholesterol (HDL-C) levels in predicting the risk of AAA development.12)

Patients with AAA are at high risk for developing other atherosclerotic cardiovascular disorders, but few reports have described the value of secondary prevention for atherosclerotic disease after AAA surgery.13) We have previously reported that lowered preoperative HDL-C <35 mg/dL was one of significant predictors for developing later cardiovascular events after AAA surgery.14) In this previous paper, we conducted detailed investigation on the preoperative characteristics of patients with or without later cardiovascular events.14) The next point should be the issue as to whether postoperative lipid-modifying therapy can decrease in the risk for later cardiovascular events and improve the prognosis after AAA surgery, even in the high-risk patient group. For that purpose, we retrospectively analyzed the postoperative serum lipid levels and other atherosclerotic risk factors related to cardiovascular events occurrence in patients undergoing AAA surgery. The purpose of this study was to examine the relationship between the incidence of later cardiovascular events after AAA surgery and atherosclerotic risk factors, in particular postoperative serum lipid levels.

**Patients and Methods**

This retrospective study was performed on 116 patients aged 70 or less undergoing an elective repair of non-ruptured AAA between August 1988 and February 2011 in the Division of Cardiovascular Surgery, Aishin Memorial Hospital. All patients were Japanese and consisted of 108 male and 8 female patients with a mean age of 64.1 ± 5.0 years (range from 50 to 70 years). To limit the influence of aging on cardiovascular events, we limited the patient population in this study to those who were ≤70 years old at the time of surgery. Either preoperatively or postoperatively, 92 patients (79.3%) received treatment for hypertension (HTN); 12 (10.3%) for diabetes mellitus (DM) and 45 (38.8%) received statins for dyslipidemia. There was a history of CAD without an indication for percutaneous catheter intervention (PCI) or coronary artery bypass grafting (CABG) in 35 (30.2%) patients.

There were no patients with inflammatory or infectious aneurysm in this study.

The diagnosis of AAA was established by the findings of enhanced computed tomography (CT) in all cases, and AAA greater than 50 mm in diameter were determined to have an indication for surgery. Patients with an indication for AAA surgery received preoperative coronary artery evaluation by traditional coronary angiography (CAG) or coronary CT (CTCAG). A patient was diagnosed as having CAD, when CAG or CTCAG demonstrated stenosis that was equal to or had exceeded 50% (≥50%) in at least one major coronary artery or in its main branch. The treatment option for the CAD, such as PCI or CABG, was determined by the strategy resembling the Guidelines proposed by American College of Cardiology (ACC) and American Heart Association (AHA) Task Force Report in 1993 and its updated version.15,16) Patients who had a severe CAD with an indication for PCI or CABG at preoperative evaluation or those with perioperative coronary events were excluded from this study. Patients presenting with CAD without an indication for PCI or CABG were defined as having a “known” CAD in this study. The procedure of AAA repair was a prosthetic aortic replacement with a bifurcated or tube graft in all patients, in this study. Patients with a known CAD received perioperative medical treatment with continuous infusion of trinitroglycerin (TNG) at 0.2 to 0.3 µg/kg/min and/or diltiazem (DTZ) at 0.5 to 2.0 µg/kg/min. All smokers were requested to stop smoking before AAA surgery. There were no operative deaths, and the etiologic source of AAA was considered to be atherosclerosis in all patients.

Follow-up of the patient after discharge has been performed periodically in principle at the outpatient clinic in our institute. The mean follow-up period was 55.6 ± 44.3 (months) after AAA surgery. Patients, who were referred to other hospital or lost to follow-up within 3 months after discharge, were excluded from this study. During follow-up at the outpatient clinic, the patient’s blood pressure was controlled to a target systolic pressure of less than 140 mmHg and a diastolic pressure of less than 90 mmHg. Patients with HTN received angiotensin-converting enzyme inhibitors or angiotensin-II receptor blockers concurrently with additional oral calcium-channel blockers as appropriate. The β-blockers were selected in those with CAD unless patients presented with bradycardia, chronic obstructive pulmonary disease (COPD), or severe heart failure. The summary of patient profile is shown in Table 1.

Cardiovascular events during the follow-up period
were defined as the occurrence of cerebral infarction, surgery for other vascular disease, the need for PCI or CABG due to CAD, and deaths from unknown causes. Clinical features including the age and gender, atherosclerotic risk factors, and postoperative lipid levels were recorded and subjected to multivariate analysis to evaluate the rate of freedom from cardiovascular events. The endpoint of this study was defined as the time at cardiovascular events occurrence or time at the end of follow-up for a maximum of 10 years. In patients with multiple cardiovascular events, the time at the first event was defined as the endpoint of the study.

For the measurement of serum lipid levels, blood samples for biochemical assay were in principle collected after an overnight fast, and the serum was separated and analyzed for total cholesterol (TC), HDL-C, and triglycerides (TG) using automated assay. Low-density lipoprotein cholesterol (LDL-C) levels were calculated by Friedewald formula. The LDL-C levels during the follow-up period were in principle controlled with a target value of at least less than 130 mg/dL using lipid-modifying medications including statins (n = 45) and fibrates (n = 17), according to the physician’s preference. The data of postoperative lipid levels of each patient were determined by the optimum value (the lowest LDL-C, the highest HDL-C, and the lowest LDL-C/HDL-C ratio) of laboratory data obtained 3 months or later after AAA surgery. This study was approved by the Hospital Ethics Committee, and all patients received a full explanation of surgery and related risks, and postoperative treatment strategy by surgeons.

**Statistical analysis**

Continuous variables are presented as the mean ± standard deviation (SD) and compared using the Student’s t-test for parametric and Mann-Whitney U-test for non-parametric analyses. Chi-square test was employed for comparisons of nominal valuables. The rate of freedom from cardiovascular events (CVE-free rate) was analyzed by the Kaplan-Meier method and comparisons between the two groups were performed by the log-rank test. The endpoint of each patient for calculating these curves was the day of cardiovascular events occurring or the last follow-up day as described above. A Cox proportional hazard model was applied to determine the effects of valuables on cardiovascular events during the follow-up period. Differences were statistically considered significant at p <0.05. All statistical analysis was performed using Dr. SPSS II version 11.0.1 J (SPSS Inc., Chicago, Illinois).

### Table 1 Summary of patient profile

|                        | Value  |
|------------------------|--------|
| The number of patients | 116    |
| Age (years)            | 64.1 ± 5.0 |
| Male/Female            | 108/8  |
| Follow up period (months) | 55.6 ± 44.3 |
| HTN treatment (%)      | 92 (79.3%) |
| DM treatment (%)       | 12 (10.3%) |
| Statin treatment (%)   | 45 (38.8%) |
| Preexistent CAD (%)    | 35 (30.2%) |
| Cardiovascular events (%) | 21 (18.1%) |
| SBP (mmHg) at outpatient | 125.4 ± 18.5 |
| DBP (mmHg) at outpatient | 70.6 ± 11.7 |

| Lipid levels          | Preoperative levels | Postoperative levels | p value |
|-----------------------|---------------------|----------------------|---------|
| HDL-C (mg/dL)         | 39.8 ± 11.6         | 49.0 ± 15.7          | <0.001  |
| LDL-C (mg/dL)         | 124.8 ± 29.9        | 97.9 ± 31.2          | <0.001  |
| LDL-C/HDL-C           | 3.41 ± 1.22         | 2.47 ± 1.25          | <0.001  |
| TG (mg/dL)            | 141.1 ± 70.5        | 100.5 ± 72.9         | 0.028   |

CVE: cardiovascular events; OR: odds ratio; CI: confidence interval; HTN: hypertension; DM: diabetes mellitus; CAD: coronary artery disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TG: triglyceride
Later cardiovascular events occurred in 21 patients, including cerebral infarction (n = 4), catheter intervention (PCI) or surgery for coronary artery disease (CAD) (n = 10), surgery for other vascular diseases (n = 10), and death from unknown cause (n = 1). There were 5 deaths other than cardiovascular events, including deaths from lung cancer (n = 2; at 31 and 102 months after surgery), esophageal cancer (n = 1; 87 months after surgery), pneumonia (n = 1; 91 months after surgery), and head injury (n = 1; 6 months after surgery). The postoperative HDL-C levels (postoperative 49.0 ± 15.7 vs. preoperative 39.8 ± 11.6 (mg/dL)), LDL-C levels (postoperative 97.9 ± 31.2 vs. preoperative 124.8 ± 29.9 (mg/dL)) and LDL-C/HDL-C ratio (postoperative 2.47 ± 1.25 vs. preoperative 3.41 ± 1.22) were all significantly improved compared to preoperative values (p <0.001) (Table 1). The postoperative TG levels (100.5 ± 72.9 mg/dL) were also lower than preoperative levels (141.1 ± 70.5 mg/dL) (p = 0.028).

Subsequently, clinical factors that may be related to the development of cardiovascular events were assessed with multivariate analysis using Cox proportional hazard model with stepwise method to identify correlations with the later event occurrence. Since the main issue of this study was to examine whether the improvement of postoperative serum lipid levels could reduce the risk for later cardiovascular events, the analysis was, in principal, limited to postoperative serum lipid levels and atherosclerotic risk factors. The items assessed included an age at surgery, a treatment of HTN and DM, preexistent CAD, the postoperative serum HDL-C levels >60 mg/dL, LDL-C levels <100 mg/dL, LDL-C/HDL-C ratio <1.5, and TG levels. The cut-off value of HDL-C, LDL-C, and LDL-C/HDL-C ratio was determined by reference to previous reports and receiver-operating characteristics curves (ROC curves) using statistical software.

The results are shown in Table 2. Cox hazard analysis indicated that the preexistence of CAD significantly increased in the risk for later cardiovascular events (hazard ratio 5.67; 95%CI 1.92–16.8; p = 0.002) and the lowering of postoperative LDL-C/HDL-C ratio <1.5 decreased in the risk after AAA surgery (hazard ratio 0.10; 95%CI 0.01–0.83; p = 0.033). In contrast, the increase in postoperative serum HDL-C levels >60 mg/dL (hazard ratio 0.81; p = 0.758), decrease in postoperative serum LDL-C levels <100 mg/dL (hazard ratio 0.50; p = 0.229) did not significantly reduce the risk for later cardiovascular events.

According to the relationship between the postoperative LDL-C/HDL-C ratio and cardiovascular events occurrence, we divided the 116 patients, examined in this study, into the following two groups to compare clinical features: 1) those with postoperative LDL-C/HDL-C ratio <1.5 (Low ratio group: n = 22); 2) those with postoperative LDL-C/HDL-C ratio ≥1.5 (High ratio group: n = 94). In univariate analysis of clinical factors, there were no significant differences in the age, gender, systolic and diastolic blood pressure at the outpatient clinic, incidence of a treatment of DM, and statin treatment between the two groups (Table 3). A treatment of HTN was more common among the Low ratio group than the High ratio group (p = 0.006) and the prevalence of CAD tended to be higher in the High ratio group than in the Low ratio group.

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**Table 2** Relationship between postoperative risk factors and cardiovascular events by Cox proportional hazard analysis

| Hazard Ratio | 95% CI      | p value |
|--------------|-------------|---------|
| Age          | 0.99        | 0.91–1.09 | 0.880   |
| preexistent CAD | 5.67      | 1.92–16.8 | 0.002   |
| HTN          | 1.63        | 0.35–7.56 | 0.534   |
| DM           | 0.74        | 0.19–2.85 | 0.665   |
| HDL-C >60    | 0.81        | 0.20–3.19 | 0.758   |
| LDL-C <100   | 0.50        | 0.16–1.55 | 0.229   |
| LDL/C/HDL <1.5 | 0.10      | 0.01–0.83 | 0.033   |
| TG           | 1.00        | 0.99–1.01 | 0.416   |

CI: confidence interval; HTN: hypertension; DM: diabetes mellitus; CAD: coronary artery disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TG: triglyceride
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Fig. 1  Kaplan-Meier curves indicating freedom from cardiovascular events in the group of patients who exhibited the ratio of LDL-C/HDL-C <1.5 and those who did not. LDL-C: low-density lipoprotein; HDL-C: high-density lipoprotein

Table 3  Comparative studies of clinical features between the two groups

|                          | LDL-C/HDL-C <1.5 (Group A; n=22) | LDL-C/HDL-C ≥1.5 (Group B; n=94) | p value |
|--------------------------|----------------------------------|----------------------------------|--------|
| Age                      | 63.6 ± 5.3                       | 64.2 ± 5.0                       | 0.609  |
| Male/Female              | 19/3                             | 89/5                             | 0.174  |
| HTN treatment (%)        | 22 (100%)                        | 70 (74.5%)                       | 0.006  |
| DM treatment (%)         | 4 (18.2%)                        | 8 (8.5%)                         | 0.237  |
| Statin treatment (%)     | 10 (45.5%)                       | 35 (37.2%)                       | 0.476  |
| preexistent CAD (%)      | 3 (13.6%)                        | 32 (34.0%)                       | 0.073  |
| Cardiovascular events (%)| 1 (4.5%)                         | 20 (21.3%)                       | 0.067  |
| SBP (mmHg) at outpatient | 125.6 ± 26.9                     | 125.4 ± 16.2                     | 0.978  |
| DBP (mmHg) at outpatient | 74.4 ± 16.2                      | 69.7 ± 10.4                      | 0.252  |
| pre HDL-C (mg/dL)        | 43.6 ± 12.8                      | 38.8 ± 11.2                      | 0.119  |
| pre LDL-C (mg/dL)        | 119.1 ± 35.5                     | 126.9 ± 28.1                     | 0.367  |
| pre LDL-C/HDL-C          | 3.00 ± 1.30                      | 3.52 ± 1.19                      | 0.117  |
| pre TG (mg/dL)           | 124.7 ± 83.8                     | 144.9 ± 67.1                     | 0.238  |
| post LDL-C (mg/dL)       | 63.7 ± 17.9                      | 45.5 ± 13.0                      | 0.095  |
| post LDL-C (mg/dL)       | 66.9 ± 24.8                      | 105.2 ± 28.1                     | <0.001 |
| post LDL-C/HDL-C         | 1.14 ± 0.26                      | 2.78 ± 1.19                      | <0.001 |
| post TG (mg/dL)          | 81.9 ± 39.2                      | 105.1 ± 77.0                     | 0.175  |
| Follow up period (months)| 81.3 ± 41.7                      | 49.6 ± 42.9                      | 0.003  |

CVE: cardiovascular events; OR: odds ratio; CI: confidence interval; HTN: hypertension; DM: diabetes mellitus; CAD: coronary artery disease; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TG: triglyceride; pre: preoperative; post: postoperative
(p = 0.073). Difference in the preoperative lipid levels between the two groups did not reach statistical significance, but the postoperative LDL-C levels in the Low ratio group were significantly lower than those in the High ratio group (p < 0.001) and postoperative HDL-C levels in the Low ratio group tended to be higher than those in the High ratio group (p = 0.095). The mean follow-up period was 81.3 ± 41.7 (range 13 to 120) months for the Low ratio group, which was significantly higher than those for the High ratio group (49.6 ± 42.9 (range 3 to 120) months) (p = 0.003). The difference in the follow-up period between the two groups may result from the difference in the prevalence of cardiovascular events occurrence, which was the endpoint of this study.

Figure 1 shows a comparison of Kaplan-Meier curves indicating the rate of freedom from cardiovascular events between the two patient groups divided based on the postoperative LDL-C/HDL-C ratio. As shown in the Fig. 1, there was a significant difference in the freedom from cardiovascular events depending on the postoperative LDL-C/HDL-C ratio. Patients with postoperative LDL-C/HDL-C ratio <1.5 had a significantly better cardiovascular event-free rate than those with LDL-C/HDL-C ratio ≥1.5 (p = 0.014 by the log-rank test).

Regarding the relationship between statin treatment and later occurrence of cardiovascular events; the events occurred in 13 of 45 patients (28.9%) who had received statin treatment, whereas, they occurred in only 8 of 71 patients (11.3%) who had not received the treatment. The occurrence of cardiovascular events depended much on the LDL-C/HDL-C ratio as described above, rather than on the presence or absence of statin treatment in our study.

**DISCUSSION**

In the previous literature, the 5 year crude survival rate in patients having undergone AAA repair was reported to be about 70%, which was less than the expected survival of 80% in a matched population. In patients with AAA, comorbidity of HTN, dyslipidemia, COPD, CAD and other cardiovascular diseases are frequently found prior to surgery, most of which are also determinants of long-term survival after AAA surgery. The reported risk factors affecting long-term survival included an increasing age, presence of heart disease, HTN, COPD, renal insufficiency, and continuing smoking. Of these, cerebral and cardiovascular diseases are responsible for approximately two-thirds of late deaths, thus appropriate management of these conditions would be essential to ameliorating long-term survival.

The importance of adequate control of dyslipidemia has been emphasized recently for the primary prevention of atherosclerotic disease but the evidence for the role of lipids in the development and management of AAA remains to be controversial. Some recent reports, however, described the significant association between lipid levels and AAA. Hobbs et al. reported a highly significant association between LDL-C and small AAA, and LDL-C was thought to be an initiating factor in the development of an AAA. Golledge et al. indicated that HDL-C appeared to be the most important lipid in predicting the risk of AAA development. Preoperative HDL-C levels are also one of significant predictors for developing later cardiovascular events after AAA surgery in our previous report. Therapeutic approaches to dyslipidemia like those in the treatment of CAD may be beneficial for the secondary prevention of atherosclerotic disease after AAA surgery.

Since an increasing age is consistently identified as a strong risk factor for atherosclerotic disease like AAA, the age distribution of the study group may have a significant influence on the results from the study like this investigation. For example, the Tromso study included a very wide range of ages (25 to 82 years), thus, the results may not reflect the true risk factors because the risk period for the development of an AAA did not occur for many patients aged <50 years. To minimize the influence of aging on the later events during the follow-up period, the subjects in this study were limited to those aged 70 or less at surgery.

In the analyses of lipid levels, in all cases, the postoperative LDL-C, LDL-C, and LDL-C/HDL-C ratio were all significantly improved compared to preoperative values (p <0.001). This was probably due to postoperative management of atherosclerotic risk factors including statin treatment, although aggressive lipid-modifying medications were not always given to patients during the follow-up period. Lifestyle guidance such as diet and exercise therapy has been intensively conducted by medical personnel in the outpatient clinic throughout the follow-up period, which may have contributed to the improvement of lipid levels. The reason for the higher incidence of HTN among the Low ratio group (patients with LDL-C/HDL-C ratio <1.5) than the High ratio group was not clear, but those with HTN who visited the hospital, regularly, might have good adherence to the lifestyle guidance.

Cox proportional hazard analysis indicated that the
preexistence of CAD significantly increased the risk for later cardiovascular events (hazard ratio 5.67; p = 0.002) and the lowering of postoperative LDL-C/HDL-C ratio <1.5 decreased in its risk after AAA surgery (hazard ratio 0.10; p = 0.033). Isolated postoperative LDL-C and HDL-C values per se were not identified as predictors for later cardiovascular events. Presence of CAD has been reported to be a strong predictor of the late survival after AAA surgery.\(^{7,8,21}\) There was about a three-fold higher risk for the development of cardiovascular events in those with the preoperative HDL-C levels <35 mg/dL. Preoperative LDL-C/HDL-C ratio was also predictive, but the value was less than simple HDL-C levels.\(^{14}\) HDL-C has been reported to oppose atherosclerosis by removing cholesterol from foam cells, by inhibiting the oxidation of LDL-C, and by limiting the inflammatory processes that underlie atherosclerosis.\(^{9}\)

In the analyses of postoperative lipid levels, in this study, we investigated an LDL-C/HDL-C ratio as an important marker, in addition to LDL-C and HDL-C levels. In guidelines for cardiovascular disease risk management, LDL-C is the principal target of lipid-lowering therapy; however, recent evidence has suggested more appropriate targets, including non-HDL-C, apolipoprotein B, and ratios of total/HDL-C, LDL-C/HDL-C.\(^{11,24}\) The ratio of LDL-C/HDL-C reflects both lipid levels of LDL-C and HDL-C, and it has been reported that lowering the ratio by lipid-lowering therapy is associated with a lower incidence of cardiovascular events in the setting of primary prevention.\(^{11}\) Current study also indicated that the lowering of postoperative LDL-C/HDL-C ratio <1.5 decreased in the risk for later cardiovascular events. In addition, patients with postoperative LDL-C/HDL-C ratio <1.5 had a significantly better cardiovascular event-free rate than those with that ratio ≥1.5 (p = 0.014). These results could be consistent with findings from previous reports.\(^{11}\)

In the analyses of atherosclerotic risk factors and postoperative lipid levels between the two groups divided, based on the LDL-C/HDL-C ratio shown in Table 3, the difference in the preoperative lipid levels between the two groups did not reach statistical significance. The postoperative LDL-C levels in the Low ratio group were, however, significantly lower than those in the High ratio group (p <0.001) and postoperative HDL-C levels in the Low ratio group tended to be higher than those in the High ratio group. These results may suggest that risk for later cardiovascular events could be reduced even in patients with low preoperative HDL-C levels, i.e., those at high risk for later cardiovascular events. Preoperative HDL-C level is indeed a strong predictor for later cardiovascular events as shown in the previous report,\(^{10}\) but the high risk could be modified depending on postoperative management. For that purpose, intensive control of lipid levels would be necessary that can achieve the lowered LDL-C/HDL-C ratio as low as less than 1.5.

These results indicate that the ratio of LDL-C/HDL-C could be employed as a beneficial index during the follow-up for patients having undergone AAA repair, aiming at a target value of LDL-C/HDL-C ratio less than 1.5. The introduction of endovascular repair (EVAR) was associated with an increasing incidence of intact AAA repair and improvement in operative mortality; a greater number of patients with AAA may receive postoperative long-term follow-up.\(^{25}\) Since cerebral and cardiovascular diseases are responsible for approximately two-thirds of late deaths in patients receiving AAA repair, decrease in the cardiovascular events by adequate control of lipid levels may contribute to improvement of prognosis and late survival in these patients.\(^{17–22}\)

Regarding the relationship between the statin treatment and later cardiovascular events occurrence, the statin treatment itself did not reduce the prevalence of later cardiovascular events in this study. As statins would be given to those with dyslipidemia exhibiting a high serum level of LDL-C or low level of HDL-C, there would be many patients at high risk for developing cardiovascular events in the patient group receiving statins. Development of side effects by statins may vary from patient to patient; thus, an adequate lipid level may not be obtained in patients who developed some side effects like myalgia or liver dysfunction. Cardiovascular events occurrence depended much on whether adequate lipid levels were obtained or not, rather than the presence or absence of statin treatment in our study. Probably, aggressive lipid-modifying therapy, including drug, diet, and exercise therapy, aiming at a clearly targeted value of LDL-C/HDL-C ratio would be necessary to reduce the incidence of cardiovascular events occurrence.

There are some limitations in this study. In our study design, patients with AAA were retrospectively examined and divided into the two groups based on the postoperative LDL-C/HDL-C ratio, as a single center experience. Lipid-modifying therapy was not given to all patients after surgery based on the condition of patients. Ideally, a randomized prospective study is required to
determine the value of predictor with a larger number of patients. Second, the findings of our study were limited to those aged <70 at surgery, thus, the value of LDL-C/HDL-C ratio in patients with age older than the present study group is unknown. Since the majority of subjects were male patients, we can draw no conclusions on the association of lipids with cardiovascular events in women. Third, the follow-up period is relatively short in some patients, thus, the short follow-up period may influence on the incidence of cardiovascular events. Although there are many limitations, our study results may help to understand the predictive value of serum lipid levels and to prognosticate the outcome at least in part of patients with AAA.

In conclusion, our study indicated that lowered postoperative LDL-C/HDL-C ratio <1.5 can decrease in the risk for later cardiovascular events after AAA surgery. These results may support the rationale for postoperative aggressive lipid-modifying therapy in patients undergoing AAA repair.

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