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Monocyte-to-high density lipoprotein cholesterol ratio as a predictor of mortality in patients with transcatheter aortic valve replacement

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Abstract. – OBJECTIVE: We aim to evaluate the prognostic value of monocyte-to-high density lipoprotein cholesterol ratio (MHR) in patients undergoing transcatheter aortic valve replacement (TAVR).

PATIENTS AND METHODS: This was a retrospective observational study and all patients who underwent TAVR for symptomatic and/or severe aortic stenosis between January 2014 and October 2019 were evaluated. Demographic characteristics, clinical features and laboratory data were retrieved from hospital electronic database and patient charts. We evaluated independent predictors of all-cause mortality with logistic regression test. *p*-value <0.05 was accepted as statistically significant.

RESULTS: A total of 145 patients (mean age 78.1±7.2 years, 49.7% female) who underwent TAVR were included in the study. The median MHR was 13.73 (interquartile range (IQR) 10.0-25.9). In correlation analysis, MHR positively correlated with only serum CRP level (R: 0.383, p=<0.001). The mortality rates during the observation period were 76.1% and 4.1% in patients who had MHT over and below the median MHR value, respectively (*p*<0.001). Based on the results of multivariate binary logistic regression analysis, MHR and presence of cerebrovascular accident emerged as independent predictors of all-cause mortality (OR: 1.514, 95% CI:1.231-1.862).

CONCLUSIONS: This is the first study of the independent predictive ability of MHR in TAVR patients. The strong independent predictive power of MHR possibly stems from the underlying coronary artery disease. Further studies particularly examining the predictive role of MHR on cardiovascular adverse events and cardiovascular death in TAVR patients are needed.

Key Words:

Aortic stenosis, Coronary artery disease, Monocyte-to-high density lipoprotein cholesterol ratio, Mortality, Transcatheter aortic valve replacement.

Introduction

Aortic stenosis (AS) is the most common valvular heart disease, and when symptomatic AS was left untreated, the mortality rate reaches 50% in two years[1]. Transcatheter aortic valve replacement (TAVR) is particularly helpful in elderly and frail patients with severe symptomatic AS and several comorbid conditions. Nowadays, TAVR is recommended by the ACC/AHA in patients who cannot proceed to surgical aortic valve replacement (SAVR) because of unacceptably high surgical risk and with at least 12 months survival expectation[2].

TAVR has a high technical success rate and is associated with increased quality of life, decreased left ventricular hypertrophy, reduced pulmonary artery pressure, and restored systolic function[3,4]. However, even after TAVR, mortality rates still remain high. In a meta-analysis, almost half of all deaths were caused by non-cardiovascular causes in the first 30 days post-procedure and thereafter. Heart failure emerged as the most frequent cause of death after TAVR[5]. Thus, preoperative left ventricular function and underlying coronary artery disease seems as crucial predictors of cardiovascular death after TAVR. In another meta-analysis, D'Ascenzo et al[6] reported that among all patients who had coronary artery disease who underwent TAVR, the presence of complex coronary disease (syntax score >22) was independently associated with higher mortality compared with other patients.

Inflammation is causally associated with both coronary artery disease and aortic stenosis. The aortic stenosis was considered as a static degenerative and calcific process. However, recently accruing evidence showed the contrary[7]. Apart from the role of inflammation in the pathogenesis of

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AS, some studies also showed that TAVR might be associated with increased inflammation[8,9]. Moreover, some other studies demonstrated that increased pre-TAVR inflammation (mainly C-reactive protein used as the inflammatory marker) was independently associated with increased mortality[10-12].

Recently novel inflammatory markers such as platelet-to-lymphocyte ratio, monocyte-to-lymphocyte ratio and platelet-to-lymphocyte ratio were seen to be independently associated with mortality after TAVR. These novel markers seemed to improve the predictive ability of CRP[13,14]. As a novel inflammatory marker, monocyte-to-HDL cholesterol ratio (MHR) is believed to reflect two important pathophysiologic aspects of atherosclerosis such as inflammation and dyslipidemia. MHR has been demonstrated as an independent prognostic factor in a number of settings, including patients with acute coronary syndrome[15], patients undergoing coronary bypass grafting[16], and patients with coronary artery disease who underwent percutaneous coronary intervention[17].

Considering the high frequency of coronary artery disease in patients undergoing TAVR and its impact on short- and long-term clinical outcomes in TAVR patients, implementing the predictive ability of novel inflammatory markers of adverse outcomes and mortality seems plausible. To the best of our knowledge, no study to date has attempted to evaluate the association of MHR with adverse outcomes in TAVR patients. Hence, the aim of the present study was to evaluate the predictive ability of MHR of all-cause mortality in TAVR patients.

Patients and Methods

Study Design and Patients

This is a retrospective observational study and all patients who underwent TAVR for symptomatic and/or severe aortic stenosis between January 2014 and October 2019 at cardiology department of Bağcılar Training and Research Hospital were evaluated. The end of the observation period was considered as January 2020. TAVR decision was reached by a cardiology team for each patient based on the data gathered from physical examination and transthoracic Doppler echocardiography. TAVR patients who had missing data and who were lost to follow up were excluded from the study. The study protocol was approved by the University Ethics Committee (2020.09.1.09.126) and was conducted in accordance with the Ethical principles put forward by the Declaration of Helsinki. The Ethics Committee approved the design of the present study. Informed consent was waived due to the retrospective design of the study.

Data Collection

Demographic characteristics, clinical features, and laboratory data were retrieved from hospital electronic database and patient charts. Transthoracic echocardiography was performed by an experienced cardiologist before and one week after the TAVR procedure. Ejection fraction and pulmonary artery pressure were measured and recorded in each echocardiography. Monocyte-to-HDL cholesterol ratio (MHR) was calculated as dividing peripheral blood monocyte count by HDL cholesterol level.

TAVR Procedure and Postoperative Follow-Up

Patients who underwent TAVR received most commonly the Edwards-SAPIEN-XT (Edwards Lifesciences Corp., One Edwards Way Irvine, CA, USA) and The St. Jude Medical (St. Jude Medical, Inc., St. Paul, MN, USA) prostheses. A computed tomographic angiogram performed before the procedure was used to determine the valve size for the proper prosthesis placement. Acetylsalicylic acid and clopidogrel were commenced before the procedure and were continued for at least 3 months after the TAVR procedure.

Outcome Measures

The outcome measure of the present study was all-cause mortality. The survival status of the study participants was ascertained from the patient charts and by means of telephone calls. The goal of the current study was to evaluate the impact of MHR on all-cause mortality.

Statistical Analysis

The Shapiro–Wilk test was used to check the normality assumptions of the data. Only age, hemoglobin, albumin, and uric acid variables were normally distributed. These normally distributed variables were presented as mean ± standard deviation (SD), whereas non-normally distributed variables were given as median and interquartile range. The Independent samples *t*-test and the Mann-Whitney U test were used for normally distributed and non-normally distributed numerical variables in two group comparisons, respective-

ly. To compare the categorical variables between the groups, the Chi-square test and Fisher's exact test were used. In addition, the study group was divided into two according to the MHR median value. Correlation between normally distributed numerical variables was evaluated with the Pearson correlation analysis, whereas the Spearman correlation was used for non-normally distributed numerical variables. The point biserial correlation was used when evaluating the correlation between dichotomous and numeric variables.

To determine the independent risk factors of mortality risk after TAVR we conducted binary logistic regression analysis. Initially, individual variables were evaluated in univariate analysis; then, the variables that had a p-value <0.05 were included in the multivariate analysis. Only one of the variables that showed a strong correlation with each other was selected to be included in the regression model. Clinical judgment was also used when selecting variables for the regression model. We included albumin, MHR, CRP, GFR, use of calcium channel blocker, and presence of cerebrovascular accident, and heart failure in the model. Although there was a strong correlation between CRP and MHR, we kept CRP in the model since it was an established cardiovascular risk factor. We excluded postoperative ejection fraction and pulmonary artery pressure variables since there were a significant number of missing values in the dataset. Because MHR included the HDL cholesterol value, we did not use dyslipidemia in the model as a separate variable, either. The SPSS 25.0 software package (IBM Corp., Armonk, NY, USA) was used to analyze the data of the study. A p-value <0.05 was accepted as statistically significant.

Results

Clinic-Demographic and Laboratory Characteristics of the Participants

A total of 145 patients (49.7% female) who underwent TAVR was included in the study. The mean age of the study cohort was 78.1±7.2 (range: 50-93) years. The most common chronic medical condition among the patients was hypertension (87.6%), followed by coronary artery disease (80.7%) and chronic obstructive pulmonary disease (58.6%). Acetylsalicylic acid (74.5%) and ACE inhibitors (73.1%) or angiotensin receptor blockers were the most used drugs (Table I). The median MHR was 13.73 (interquartile range (IQR) 10.0-25.9). The median serum creatinine value increased from 1.0 mg (IQR 0.8-1.2) to 1.2 mg (IQR 0.9-1.8) after TAVR. The median glomerular filtration rate was calculated as 60 mL/minute (IQR 45-77). Other laboratory values, including blood white cell counts, C-reactive protein, albumin, and uric acid are shown in Table I.

Comparison of Patients with MHR Values Over and Below the Median

We divided the whole study group into two based on the median value of MHR (Table II). There was no age of sex difference between the groups with higher and lower MHR. Cerebrovascular accident and heart failure were more frequent in the higher MHR group compared with the lower MHR group (p=0.025, p=0.008, respectively). On the other hand, hyperlipidemia was more frequent among the patients with lower MHR than patients with higher MHR (p<0.001). Contrast nephropathy development after TAVR was also significantly more common among patients with higher MHR compared to patients with lower MHR (52.1% *vs.* 29.7%, p=0.007). CCB use was significantly more common among patients with lower MHR (p=0.022).

As expected, median monocyte count was significantly higher (p<0.001), and HDL cholesterol level was lower (p<0.001) in patients with higher MHR compared to patients with lower MHR. In addition, patients with higher MHR had significantly higher serum creatinine, lower hemoglobin, and lower lymphocyte counts compared to patients with lower MHR (p<0.001, p=0.002, p=0.001, respectively) (Table II).

Patient Survival

The median follow-up duration was 28.0 months (range: 2.7-74.1). We compared clinic-demographic features and laboratory and echocardiographic values of decedent and surviving patients (Table III). There was no difference between the decedent and survivor patients in terms of age and sex distribution. However, the rate of cerebrovascular accident, chronic obstructive pulmonary disease, hyperlipidemia, and heart failure were significantly more common among the decedents compared with the survivors (p<0.001, p=0.010, p<0.001, p=0.018, respectively). Contrast nephropathy was developed more frequently among the deceased compared to the surviving patients (p=0.003). As to cardiovascular drug use, only CCB use was significantly more common among the survivors (p=0.029).

Table I. Demographic characteristics, comorbid conditions, and laboratory values of the patients (n=145).

	Values (mean± SD or median (interquartile range))
Age (years)	78.1±7.2
Gender	
Female / Male	72 (49.7%) / 73 (50.3%)
Body mass index (kg/m^2)	25.7 (24.0-29.1)
Comorbidities n (%)	
Coronary artery disease	117 (80.7%)
Coronary artery bypass grafting	23 (15.9%)
Diabetes Mellitus	71 (49.0%)
Hypertension	127 (87.6%)
Cerebrovascular accident	14 (9.7%)
Pulmonary artery hypertension	56 (38.6%)
COPD	85 (58.6%)
Hyperlipidemia	80 (55.2%)
Malignancy	22 (15.2%)
Chronic kidney disease	22 (15.2%)
Atrial fibrillation (n=135)	24 (17.8%)
History of vascular surgery (n=134)	18 (13.4%)
Myocardial infarction (n=133)	3 (2.3%)
Heart failure (n=133)	32 (24.1%)
Smoking	75 (52.1%)
Contrast nephropathy	59 (40.7%)
Cardiovascular medications n (%)	
ACEIs-ARBs	106 (73.1%)
Statins	59 (40.7%)
Anticoagulants	19 (13.1%)
Acetyl salicylic acid	108 (74.5%)
Calcium Channel Blocker	46 (31.7%)
Beta Blocker	99 (68.3%)
Laboratory parameters	
White blood cell count (x10^3/μL)	7.1 (5.8-8.4)
Monocyte count (x10^3/μL)	0.6 (0.4-0.8)
Lymphocyte count (x10^3/μL)	1.6 (1.2-2.0)
Neutrophil count (x10^3/μL)	4.6 (3.7-5.7)
Platelet count (x10^3/μL)	217 (192-286)
HDL-cholesterol (mg/dL)	38 (31-47)
MHR	13.73 (10.0-25.9)
Hemoglobin (g/dL)	11.3±1.5
Albumin (g/dL)	3.81±0.48
Uric acid (mg/dL)	6.5±2.2
Creatinine (mg/dL)	1.0 (0.8-1.2)
Postop creatinine (mg/dL)	1.2 (0.9-1.8)
Glomerular filtration rate	60 (45-77)
C-reactive protein (mg/dL)	5.4 (3-15)
Echocardiographic measurements	
Preoperative EF (%)	55 (45-60)
Postoperative EF (%) (n=120)	55 (50-60)
Preoperative PAP (mmHg)	40 (35-45)
Postoperative PAP (mmHg) (n=71)	35 (30-40)
Length of CCU stay (days)	2 (2-3)
Survival status	
Decedents	
57 (39.3%)	

ACEI: Angiotensin receptor enzyme inhibitor, ARB: Angiotensin receptor blocker, CCU: coronary care unit, COPD: Chronic obstructive pulmonary disease, CRP: C-reactive protein, EF: Ejection fraction, MHR: Monocyte-to-High Density Lipoprotein cholesterol ratio, PAP: pulmonary artery pressure.

Monocyte-to-HDL cholesterol ratio was significantly higher in the deceased group compared to the surviving group (29.63 (IQR 23.57-39.15) *vs.* 12.34 (IQR 8.47-13.87), respectively, $p<0.001$) (Figure 1). Median values of lymphocyte count, albumin level, and glomerular filtration rate were significantly lower among the decedents compared with the survivors ($p=0.001$, $p=0.001$, $p=0.015$, respectively). In contrast, C-reactive protein was higher in the former ($p<0.001$). Median pre-TAVR ejection value was lower in the deceased patients compared with the survivors ($p=0.029$) (Table III). In correlation analysis, MHR positively correlated with only serum CRP level (R: 0.383, $p<0.001$).

Independent Predictors of All-Cause Mortality

Based on the results of univariate and multivariate binary logistic regression analyses, only MHR and the presence of cerebrovascular accident (CVA) emerged as the independent predictors of all-cause mortality in patients who underwent TAVR (Table IV). However, there was only one patient with CVA among the surviving patients. The confidence interval value was too large and the odds ratio for mortality was too disproportionately high. Thus, we advise caution when interpreting this result. Every 1 unit increase in MHR ratio was associated with approximately a 50% increase in the risk of death in patients who underwent TAVR.

Discussion

The most salient finding of the present study was that the monocyte-to-high density lipoprotein cholesterol ratio (MHR) was an independent predictor of all-cause mortality among the patients who underwent TAVR. The mean age of our patient cohort was 78.1±7.2 years.

Efforts to better prognosticate the post-TAVR patients are of crucial importance because these patients are quite older with a high burden of chronic medical conditions, including coronary artery disease. Actually, almost 50% of patients who underwent TAVR due to severe symptomatic aortic stenosis (AS) had underlying coronary artery disease[18]. Even if the TAVR procedure goes smoothly, these patients still succumb to other diseases. The rate of coronary artery disease was quite high in the present study. Eight out of every 10 patients in our study population had underlying coronary artery disease.

Recent years witnessed the emergence of inflammation as a pathogenic factor in the development and progression of aortic stenosis[7]. Imai et al[10] found that patients with severe AS had higher serum CRP values compared with mild-to-moderate AS. CRP was an independent predictor of the development of severe AS. In addition, in a subgroup in which AS progressed rapidly had higher serum CRP levels compared with other patients. Serum CRP was also shown to be associated with clinical outcomes in patients undergoing SAVR operation. In patients with high CRP/albumin ratio, morbidity and perioperative complications were higher compared with patients who had lower ratios[11]. The median CRP values were significantly higher in the deceased patients in our study.

In addition to the fact that AS is associated with increased mortality per se, the procedure of aortic valve replacement be it surgical or transcatheter,

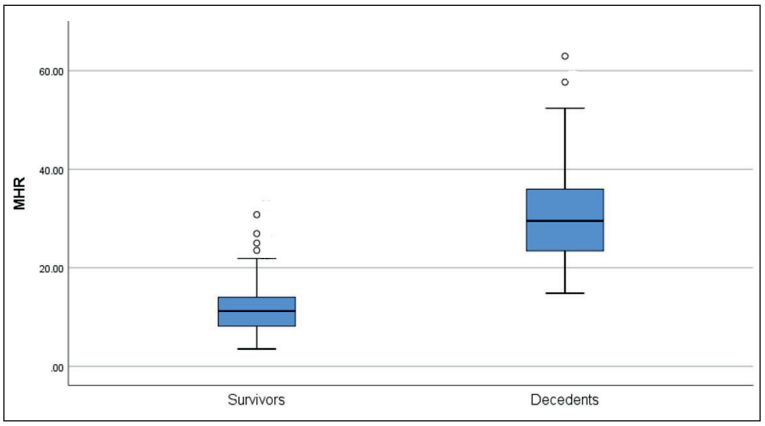

Figure 1. Box-plot showing monocyte-to-High Density Lipoprotein cholesterol ratio (MHR) in patients who survived and died.

Table II. Comparison of the patients according to the median value of monocyte to HDL ratio MHR) in terms of the demographic characteristics, comorbid conditions, and laboratory values.).

	Patients with MHR below median (n=74)	Patients with over median value (n=71)	MHR *p*-value
Age (years)	78.4±7.2	77.9±7.4	0.575
Gender			
Female / Male	41 (55.4%) / 33 (44.6%)	31 (43.7%) / 40 (56.3%)	0.185
Body mass index (kg/m^2)	25.0 (23.4-29.3)	26.0 (24.8-29.1)	
Comorbidities n (%)			
Coronary artery disease	55 (74.3%)	62 (87.3%)	0.059
Coronary artery bypass grafting	11 (14.9%)	12 (16.9%)	0.822
Diabetes Mellitus	35 (47.3%)	36 (50.7%)	0.741
Hypertension	65 (87.8%)	62 (87.3%)	1.000
Cerebrovascular accident	3 (4.1%)	11 (15.5%)	**0.025**
Pulmonary artery hypertension	25 (33.8%)	31 (43.7%)	0.237
COPD	38 (51.4%)	47 (66.2%)	0.092
Hyperlipidemia	53 (71.6%)	27 (38.0%)	**<0.001**
Malignancy	12 (16.2%)	10 (14.1%)	0.818
Chronic kidney disease	9 (12.2%)	13 (18.3%)	0.358
Atrial fibrillation (n=135)	9 (12.9%)	15 (23.1%)	0.176
History of vascular surgery (n=134)	9 (12.9%)	9 (14.1%)	1.000
Myocardial infarction (n=133)	2 (2.7%)	1 (1.7%)	1.000
Heart failure (n=133)	11 (14.9%)	21 (35.6%)	**0.008**
Smoking (n=144)	33 (45.2%)	42 (59.2%)	0.099
Contrast nephropathy	22 (29.7%)	37 (52.1%)	**0.007**
Cardiovascular medications n (%)			
ACEIs-ARBs	54 (73.0%)	52 (73.2%)	1.000
Statins	31 (41.9%)	28 (39.4%)	0.866
Anticoagulants	9 (12.2%)	10 (14.1%)	0.808
Acetyl salicylic acid	59 (79.7%)	49 (69.0%)	0.182
Calcium Channel Blocker	30 (40.5%)	16 (22.5%)	**0.022**
Beta Blocker	53 (71.6%)	46 (64.8%)	0.476
Laboratory parameters			
White blood cell count (x10^3/μL)	7.35 (6.33-8.65)	6.60 (5.50-7.80)	0.265
Monocyte count (x10^3/μL)	0.500 (0.400-0.500)	0.800 (0.700-1.000)	**<0.001**
Lymphocyte count (x10^3/μL)	1.85 (1.53-2.08)	1.30 (1.10-1.80)	**0.001**
Neutrophil count (x10^3/μL)	4.80 (3.39-5.93)	4.50 (3.40-5.60)	0.834
Platelet count (x10^3/μL)	229 (194-306)	209 (169-251)	0.420
HDL-cholesterol (mg/dL	45 (38-51)	30 (26-32)	**<0.001**
Hemoglobin (g/dL)	11.3±1.7	11.3±1.3	**0.002**
Albumin (g/dL)	1 (0.8-1.2)	1.1 (0.9-1.4	0.213
Uric acid (mg/dL)	6.29±1.86	6.84±2.58	0.052
Creatinine (mg/dL)	0.95 (0.8-1.18)	1.1 (0.9-1.5)	**<0.001**
Postop creatinine (mg/dL)	1.0 (0.9—1.3)	1.5 (1.1-2.1)	0.265
Glomerular filtration rate (mL/min)	65 (48.5-78.7)	52 (44-75)	0.061
C-reactive protein (mg/dL)	3.8 (2.2-11.00)	6.3 (4.2-21.6)	<0.001
Echocardiographic measurements			
Preoperative EF (%)	60 (48.5-60)	50 (40-60)	0.140
Postoperative EF (%)	60 (50-60)	55 (45-60)	0.080
Preoperative PAP (mmHg)	38 (35-43.8)	40 (35-55)	0.942
Postoperative PAP (mmHg)	35 (30-40)	36.5 (30-50)	0.383
Length of CCU stay (days)	2 (2-3)	2 (2-3)	0.037
Survival status n (%)			
Decedent	3 (4.1%))	54 (76.1%)	**<0.001**

ACEI: Angiotensin receptor enzyme inhibitor, ARB: Angiotensin receptor blocker, CCU: coronary care unit, COPD: Chronic obstructive pulmonary disease, CRP: C-reactive protein, EF: Ejection fraction, GFR: glomerular filtration rate, MHR: Monocyte-to-High Density Lipoprotein cholesterol ratio, PAP: pulmonary artery pressure.

Table III. Comparison of demographic characteristics, comorbid conditions, and laboratory values of the deceased and survivor patients.

	Decedents (n=57)	Survivors (n=88)	*p*-value
Age (years)	78.2±8.1	78.1±6.8	0.264
Gender			
Female / Male	23 (40.4%) / 34 (59.6%)	49 (55.7%) / 39 (44.3%)	0.089
Body mass index (kg/m^2)	26.6 (25-29.3)	24.9 (23.4-27.6)	0.423
Comorbidities n (%)			
Coronary artery disease	50 (87.7%)	67 (76.1%)	0.091
Coronary artery bypass grafting	8 (14%)	15 (17%)	0.652
Diabetes Mellitus	30 (52.6%)	41 (46.6%)	0.501
Hypertension	48 (84.2%)	79 (89.8%)	0.440
Cerebrovascular accident	13 (22.8%)	1 (1.1%)	**<0.001**
Pulmonary artery hypertension	27 (47.4%)	29 (33.0%)	0.116
COPD	41 (71.9%)	44 (50.0%)	0.010
Hyperlipidemia	16 (28.1%)	64 (72.7%)	**<0.001**
Malignancy	9 (15.8%)	13 (14.8%)	1.000
Chronic kidney disease	13 (22.8%)	9 (10.2%)	0.057
Atrial fibrillation (n=135)	12 (22.2%)	12 (14.8%)	0.358
History of vascular surgery (n=134)	8 (15.7%)	10 (12.0%)	0.606
Myocardial infarction (n=133)	1 (2.2%)	2 (2.3%)	1.000
Heart failure (n=133)	17 (37%)	15 (17.2%)	**0.018**
Smoking (n=144)	32 (56.1%)	43 (49.4%)	0.496
Contrast nephropathy	32 (56.1%)	27 (30.7%)	**0.003**
Cardiovascular medications n (%)			
ACEIs-ARBs	43 (75.4%)	63 (71.6%)	0.703
Statins	23 (40.4%)	36 (40.9%)	1.000
Anticoagulants	7 (12.3%)	12 (13.6%)	1.000
Acetyl salicylic acid	38 (66.7%)	70 (79.5%)	0.083
Calcium Channel Blocker	12 (21.2.%)	34 (38.6%)	**0.029**
Beta Blocker	37 (64.9%)	62 (70.5%)	0.584
Laboratory parameters			
White blood cell count (x10^3/μL)	6.80(6.25-7.95)	7.30 (5.68-8.43)	0.585
Monocyte count (x10^3/μL)	0.90 (0.70-1.10)	0.50 (0.40-0.60)	**<0.001**
Lymphocyte count (x10^3/μL)	1.30 (1.10-1.85)	1.75 (1.38-2.03)	**0.001**
Neutrophil count (x10^3/μL)	4.80 (3.40-5.95)	4.60 (3.78-5.48)	0.517
Platelet count (x10^3/μL)	209 (169-267)	225 (198-297)	0.218
HDL-cholesterol (mg/dL)	30 (27-35)	44(34-49)	**<0.001**
MHR	29.63 (23.57-39.15)	12.34 (8.47-13.87)	**<0.001**
Hemoglobin (g/dL)	11.3±1.4	11.3±1.7	0.678
Albumin (g/dL)	3.65±0.54	3.89±0.43	**0.001**
Uric acid (mg/dL)	6.99±2.82	6.29±1.80	0.151
Creatinine (mg/dL)	1.05 (0.90-1.50)	1.0 (0.80-1.20)	**0.016**
Postop creatinine (mg/dL)	1.50 (1.05-2.15)	1.1 (0.90-1.50)	**<0.001**
Glomerular filtration rate (mL/min)	52.0 (44.5-77.0)	63.5 (46.8-77.3)	**0.015**
C-Reactive protein (mg/dL)	12.4 (5.4-23.7)	3.80 (2.18-9.00)	**<0.001**
Echocardiographic measurements			
Preoperative EF (%)	45 (39-60)	60 (50-60)	**0.029**
Postoperative EF (%)	50 (43-60)	60 (52-60)	**0.004**
Preoperative PAP (mmHg)	40 (36-53)	38 (35-45)	0.429
Postoperative PAP (mmHg)	40 (34-53)	35 (30-40)	**0.005**
Length of CCU stay (days)	3 (2-3)	2 (2-3)	**0.014**

ACEI: Angiotensin receptor enzyme inhibitor, ARB: Angiotensin receptor blocker, CCU: coronary care unit, COPD: Chronic obstructive pulmonary disease, EF: Ejection fraction, MHR: Monocyte-to-High Density Lipoprotein cholesterol ratio, PAP: pulmonary artery pressure.

Table IV. Univariate and multivariate binary logistic regression analysis to determine the independent predictors of the survival after TAVI (Hosmer and Lemeshow test, p=0.607).

		Univariate LR		Multivariate LR		
Variables		**OR 95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Age	1.028	0.979-1.079	0.264	-	-	-
Sex	1.857	0.945-3.651	0.073	-	-	-
Albumin	0.296	0.135-0.650	0.002	0.639	0.061-6.660	0.708
Calcium channel blocker use	0.424	0.197-0.913	0.028	0.508	0.033-7.773	0.627
C-reactive protein (CRP)	1.103	1.054-1.155	<0.001	1.042	0.916-1.186	0.528
Glomerular filtration rate (GFR)	0.976	0.959-0.994	0.009	0.993	0.944-1.045	0.789
Heart failure	2.814	1.243-6.371	0.013	1.536	0.175-13.504	0.699
MHR	1.407	1.256-1.577	<0.001	1.514	1.231-1.862	<0.001
Cerebrovascular accident	25.705	3.257-202.894	0.002	111.996	1.611-7785.685	0.029
Contrast nephropathy	2.892	1.447-5.777	0.003	2.815	0.409-19.379	0.293
Preoperative EF	0.965	0.935-0.995	0.025	0.950	0.864-1.044	0.288
Preoperative PAP	1.011	0.986-1.036	0.393	1.011	0.956-1.069	0.706
Length of CCU stay	1.203	1.008-1.436	0.040	0.989	0.569-1.720	0.970

CI: Confidence interval, CCU: Coronary care unit, EF: Ejection fraction, LR: logistic regression, OR: Odds ratio, MHR: Monocyte-to-High Density Lipoprotein cholesterol ratio, PAP: Pulmonary artery pressure.

is also associated with a further increase in inflammation[8]. On the other hand, compared with SAVR, the magnitude of inflammatory reaction was smaller in TAVR patients[9].

Sexton et al[19] showed that thromboinflammatory changes, including decreased platelet number, increase in white blood cell number, and increased inflammatory markers, were associated with adverse clinical outcomes and death in patients undergoing TAVR. More recently, Kalinczuk et al[20] confirmed the findings of the latter study. Hioki et al[12] demonstrated that baseline serum CRP value was an independent predictor of mortality after TAVR.

Lately, MHR has emerged as a novel inflammatory marker that can predict adverse clinical outcomes independent of other established cardiovascular risk factors and CRP. This ratio brings the predictive ability of both monocyte count and low HDL cholesterol together in patients with cardiovascular disease. Severe AS has been shown to be related to increased numbers of circulating intermediate monocytes. Pre-intervention numbers of intermediate monocytes reduced both with TAVR and SAVR, though the decline was more rapid in the former[21]. Neuser et al[22] prospectively evaluated 57 patients who underwent elective transfemoral TAVR. The authors showed that the number of circulating intermediate monocytes was associated with left ventricular function both before and 3 months after the procedure. Higher monocyte numbers were again related to worse functional outcomes post-TAVR. The median number of circulating monocytes was significantly higher among the deceased TAVR patients and among patients with higher MHR values in the present study.

The impact of dyslipidemia on clinical outcomes in patients AS also has been extensively investigated. HDL cholesterol was significantly lower in patients with AS compared with control subjects[23]. In another study, the total cholesterol/HDL cholesterol ratio could predict annual AS progression[24]. HDL2 subtype of HDL cholesterol showed a positive correlation with the progression of AS[25]. On the other hand, a large study utilizing two-sample Mendelian randomization did not show an association between HDL cholesterol and the presence of AS in contrast to LDL and triglycerides concentrations[26]. Our results also showed that median serum HDL cholesterol concentration was significantly lower among the deceased compared with the surviving patients.

Duran et al[27] compared MHR between patients with bicuspid aortic valve AS (70 patients) and tricuspid-valve AS (140 patients). Monocyte counts were significantly increased, and HDL cholesterol level was significantly decreased in bicuspid aortic valve AS compared with tricuspid-valve AS. Efe et al[28] found that patients with calcific AS had significantly lower values of lymphocyte/monocyte ratio. The ratio was positively correlated with the severity of AS. However, to our knowledge, there is no study in the literature evaluating the impact of MHR on mortality in patients who underwent TAVR. Our study, for the first time,

demonstrated that MHR was an independent predictor of mortality in these patients.

Limitations

Some limitations of the present study deserve mention. First, our sample size is not large enough to detect subtle impacts of risk factors on the outcome measure. Second, we assessed mortality as the all-cause mortality since data were lacking regarding the precise causes of death of the deceased study patients. Thirdly because of the low data quality and missing information, partly due to the retrospective design, we did not include postoperative complications and nonfatal cardiovascular outcomes in outcome measures in this study.

Conclusions

Despite the above-mentioned limitations, this is the first report of the independent predictive ability of MHR in TAVR patients. The median age of the patients was quite high, and the comorbidity burden was fairly heavy in this patent cohort. It was also notable that 80.7% of the study participants had coronary artery disease. Although the patients were freed from the stenotic aortic valve by TAVR, they still had coronary artery disease that is closely related to inflammation. The strong independent predictive power of MHR possibly stems from the underlying coronary artery disease. Further studies, particularly examining the predictive role of MHR on cardiovascular adverse events and cardiovascular death in TAVR patients, are needed.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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