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coronary angiography is critical to rule out the diagnosis of typical myocardial infarction and to allow for the arrival at the correct diagnosis of Takotsubo cardiomyopathy. On the other hand, emergency coronary angiography is more invasive for the patient undergoing emergency surgery. Especially in the patient who has a ruptured aortic aneurysm, oozing from the retroperitoneal small vessels injured by hematoma or surgical procedure is of concern because of the use of anticoagulants for catheterization. In our patient, despite a large blood transfusion including the platelet concentrates, platelet count on ICU admission was $6.0 \times 10^4/\mu L$. Therefore, we initially obtained transthoracic echocardiography by a cardiologist. According to the typical findings of Takotsubo cardiomyopathy revealed by echocardiography, normal creatine kinase MB fraction, and stable hemodynamic status, we selected careful observation.

We routinely perform preoperative coronary angiography to assess the risk of perioperative myocardial infarction. Although preoperative intact coronary angiography is also meaningful to avoid needless or harmful coronary angiography in the perioperative period, as in the case with our patient, preoperative screening for heart disease is often limited to an electrocardiogram in emergency cases. However, in a certain situation, Takotsubo cardiomyopathy could be diagnosed by integration of clinical noninvasive modalities.

We described the first case of Takotsubo cardiomyopathy after ruptured abdominal aortic aneurysm repair. We considered that diagnosis of this syndrome could be and should be made without invasive coronary angiography in certain situations to avoid further complications.

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Do statins delay the progression of aortic stenosis?

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Calcific aortic stenosis (AS) is the most common form of valvular heart disease in the Western world, and the only established therapy for patients with severe symptomatic AS is surgical valve replacement. There are currently no effective disease-modifying treatments, and the possibility of halting the disease process would represent a therapeutic advance.[1] Although some observational studies[2-4] demonstrated that statins (hydroxymethylglutaryl-coenzyme A reductase inhibitors) delayed the progression of AS, a randomized controlled trial[1] concluded that intensive lipid-lowering therapy with atorvastatin did not halt its progression. Furthermore, no meta-analysis of studies of statins for AS has been conducted to date. Therefore, the appropriate role of statins for AS remains unclear. We performed a meta-analysis of comparative studies of statins for the prevention of the progression of AS.

CLINICAL SUMMARY

All comparative studies of statins versus control (no statins or placebo) for AS were identified using a 2-level search strategy. First, a public domain database (MEDLINE) was searched using a Web-based search engine (PubMed). Second, relevant studies were identified through a manual search of secondary sources, including references of initially identified articles and a search of reviews and commentaries. The MEDLINE database was searched from January of 1966 to January of 2008. MeSH keywords included ''hydroxymethylglutaryl-CoA reductase inhibitors'' and ''aortic valve stenosis.'' Studies considered for inclusion met the following criteria: The design was a comparative study, and the study population comprised patients with AS. Patients were assigned to statins versus control (no statins or placebo), and the main outcomes included annualized changes of echocardiographic characteristics. Data regarding detailed

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Received for publication March 4, 2008; accepted for publication March 14, 2008.
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J Thorac Cardiovasc Surg 2009;137:e6-9
0022-5223/$36.00
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doi:10.1016/j.jtcvs.2008.03.018

TABLE 1. Baseline patient characteristics and outcomes

	Mohler and colleagues[5]	Moura and colleagues[2]	Cowell and colleagues[1]
Design	Prospective cohort	Prospective cohort	Randomized controlled
Statin type	NR	Rosuvastatin	Atorvastatin
Follow-up	1 y	18 mo (73 ± 24 wk)	≥2 y (median 25 [7–36] mo)
Statin	NR	NR	NR
No statin			
P value†			
Inclusion criteria	$0.7 \leq AVA \leq 2.0\ cm^2$	$1.0 \leq AVA \leq 1.5\ cm^2$	PAJV ≥ 2.5 m/sec
Patients (N)			
Statin	39	61	65
No statin	22	60	69
Age (y)			
Statin	69.5 ± 9.7	73.4 ± 8.5	68 ± 11
No statin	63.9 ± 10.1	73.9 ± 9.4	68 ± 10
P value†	NR	.749	NS
Baseline TC (mg/dL)			
Statin	174 ± 36	243.0 ± 40.5	220 ± 38
No statin	205 ± 28	192.0 ± 45.8	217 ± 34
P value†	NR	<.001	NS
Baseline PAJV (m/s)			
Statin	NR	3.65 ± 0.64	3.39 ± 0.62
No statin		3.62 ± 0.61	3.45 ± 0.67
P value†		.788	NS
Baseline AVA (cm^2)			
Statin	1.13 ± 0.27	1.23 ± 0.42	1.03 ± 0.4
No statin	1.22 ± 0.25	1.20 ± 0.35	1.02 ± 0.41
P value†	.18	.636	NS
Annualized increase in PAJV			
Statin	NR	0.04 ± 0.38 (m/s/y)	0.199 ± 0.210 (m/s/y)
No statin		0.24 ± 0.30 (m/s/y)	0.203 ± 0.208 (m/s/y)
P value†		.007	.95
Annualized decrease in AVA			
Statin	5.81 ± 14.5 (%/y)	0.05 ± 0.12 (cm^2/y)	0.079 ± 0.107 (cm^2/y)
No statin	–8.54 ± 29.1 (%/y)	0.10 ± 0.09 (cm^2/y)	0.083 ± 0.107 (cm^2/y)
P value†	.10	.041	.68

AS, Aortic stenosis; *AVA,* aortic valve area; *HC,* hypercholesterolemia; *IQR,* interquartile range; *MG,* mean gradient; *NR,* not reported; *NS,* not significant; *PAJV,* peak aortic jet velocity; *TC,* total cholesterol. Values are expressed as mean ± SD. *Value in 121 patients including 26 with aortic valve sclerosis (1.5 < PAJV < 2 m/s). †Value reported in each individual study.

inclusion criteria, statin type, duration of follow-up, and echocardiographic characteristics were abstracted (as available) from each individual study. We conducted a meta-analysis of summary statistics from the individual studies because detailed, patient-level data were not available for all studies. For each study, data regarding annualized ''increase'' in peak aortic jet velocity (PAJV) and annualized ''decrease'' in aortic valve area (AVA) in both the statin and control groups were used to generate standardized mean differences (SMDs) (<0 favors statins; >0 favors control) and 95% confidence intervals (CIs). Study-specific estimates were combined using both fixed- and random-effects models. Between-study heterogeneity was analyzed by means of standard chi-square tests. Where statistically significant heterogeneity was identified, the random-effects estimate was used preferentially as the summary measure. Publication bias was assessed mathematically using an adjusted rank-correlation test.

RESULTS

Our search identified 7 comparative studies[1-7] of statins versus control for AS. These included 1randomized

TABLE 1. Continued

Antonini-Canterin and colleagues[6]		Rosenhek and colleagues[3]	Bellamy and colleagues[4]	Novar and colleagues[7]
Retrospective cohort		Retrospective cohort	Prospective cohort	Retrospective cohort
Simvastatin		Simvastatin	Simvastatin	Simvastatin
Atorvastatin		Atorvastatin	Lovastatin, and so forth	Lovastatin
Pravastatin		Pravastatin, and so forth		Pravastatin
Fluvastatin				Atorvastatin
Cerivastatin				Fluvastatin
≥6 mo		≥6 (24 ± 18) mo	≥6 mo	≥12 (21 ± 7 [12–40]) mo
54 ± 34 mo		NR	3.7 ± 2.1 y	NR
50 ± 33 mo			3.7 ± 2.3 y	
.35			.94	
Mild AS	Moderate AS	PAJV > 2.5 m/sec	MG ≥ 10 mm Hg	1.0 ≤ AVA ≤ 1.8 cm^2
2 ≤ PAJV < 3 m/sec	3 ≤ PAJV < 4 m/sec		AVA ≤ 2.0 m^2	
63	32	50	38	57
63	32	161	118	117
67 ± 9*		72 ± 8	73 ± 11	71 ± 9
67 ± 9*		69 ± 11	78 ± 12	67 ± 13
NS		<.05	.03	.01
HC: 92%*		232 ± 48	246 ± 58	Median 210 (IQR, 193–241)
HC: 14%*		219 ± 41	214 ± 45	Median 208 (IQR, 186–227)
<.001		NS	<.01	.41
2.45 ± 0.66*		4.08 ± 0.86	2.8 ± 0.5	NR
2.44 ± 0.65*		3.92 ± 0.86	3.0 ± 0.8	
.95		NS	NR	
NR		0.82 ± 0.23	1.32 ± 0.29	1.2 (IQR, 1.0–1.4)
		0.84 ± 0.23	1.20 ± 0.35	1.2 (IQR, 1.0–1.4)
		NS	.04	.71
0.11 ± 0.25 (m/s/y)	0.23 ± 0.27 (m/s/y)	0.10 ± 0.41 (m/s/y)	5 ± 8 (%/y)	NR
0.10 ± 0.17 (m/s/y)	0.24 ± 0.23 (m/s/y)	0.39 ± 0.42 (m/s/y)	9 ± 12 (%/y)	
.79	.92	.0001	.03	
NR		NR	3 ± 10 (%/y)	0.06 ± 0.16 (cm^2/y)
			7 ± 13 (%/y)	0.11 ± 0.18 (cm^2/y)
			.04	NR

controlled trial,[1] 3 prospective cohort studies,[2,4,5] and 3 retrospective cohort studies.[3,6,7] The baseline patient characteristics and outcomes are summarized in Table 1. We did not pool annualized changes in peak and mean aortic valve pressure gradients because only 2 studies reported them. For annualized ''increase'' in PAJV, 2 studies by Moura and associates[2] and Rosenhek and colleagues[3] demonstrated a statistically significant benefit of statins over control. Pooled analysis (representing 812 patients) demonstrated a statistically significant reduction in annualized ''increase'' of PAJV with statins relative to control in the random-effects model (SMD, –0.28; 95% CI, –0.55 to –0.01; $P = .04$) (Figure 1, *A*). There was significant between-study heterogeneity of results ($P < .01$) but no evidence of significant publication bias ($P = .09$). For annualized ''decrease'' in AVA, the study by Moura and coworkers[2] demonstrated a statistically significant benefit of statins over control, but the study by Mohler and associates[5] demonstrated a statistically significant benefit of control over statins. Pooled analysis (representing 646 patients) demonstrated a statistically nonsignificant reduction in annualized ''decrease'' of AVA with statins relative to control in the random-effects model

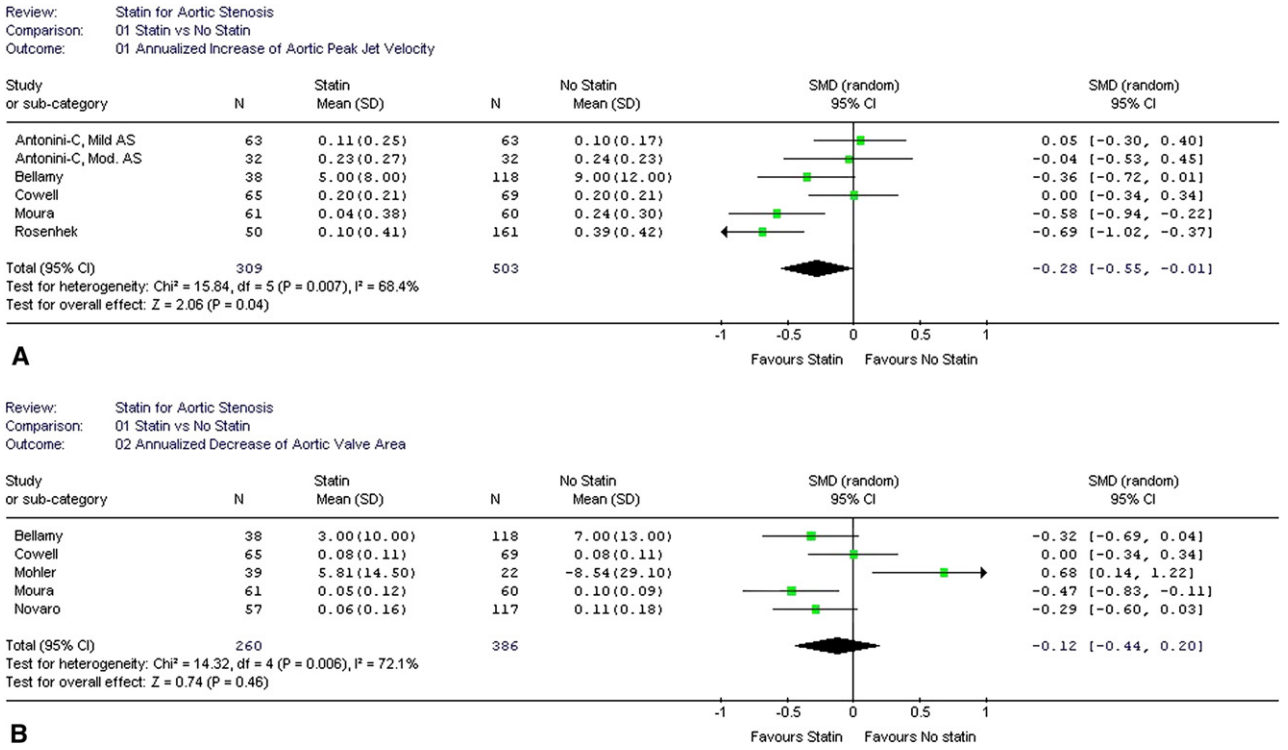

FIGURE 1. Outcomes and meta-analyses. A, Annualized ''increase'' in PAJV. B, Annualized ''decrease'' in AVA. *SD,* Standard deviation; *SMD,* standardized mean difference; *CI,* confidence interval.

(SMD, –0.12; 95% CI, –0.44 to 0.20; $P = .46$) (Figure 1, *B*). There was significant between-study heterogeneity of results ($P < .01$) but no evidence of significant publication bias ($P = 1.00$). For a sensitivity analysis, the study by Mohler and colleagues[5] was excluded, which only demonstrated a statistically significant benefit of control over statins; combining the remaining studies generated an attenuated and statistically significant result favoring statins (random-effects SMD, –0.26; 95% CI,–0.45 to –0.07; $P < .01$).

DISCUSSION

On the basis of the present meta-analysis, statins are likely to delay the progression of AS: reducing not ''decrease'' in AVA but ''increase'' in PAJV. These results should be interpreted with caution, because the design was nonrandomized observational in all studies but one in our meta-analysis, and there was qualitative heterogeneity in patient selection. The completion of ongoing randomized controlled trials[8,9] is expected to confirm the present results.

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