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Clinical Outcomes of Primary Angioplasty in ST Elevation Myocardial Infarction Patients With Antecedent Hypertension During Hospital Stay and Follow-up

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Abstract

Hypertension is a known risk factor for coronary artery disease. However, the number of studies focusing on the events following ST elevation myocardial infarction (STEMI) in patients with an antecedent hypertension is limited. Our aim is to evaluate the clinical outcomes of primary angioplasty in STEMI patients with antecedent hypertension during hospital stay and follow-up. A total of 373 patients (177 of whom had antecedent hypertension) who were treated by primary angioplasty because of STEMI were included in this study. All parameters were compared between the groups with and without hypertension. Hypertensive patients who received primary angioplasty were older (59.9 ± 12.6 vs. 52 ± 12.3 , $P < .001$) and had higher rates of in-hospital mortality and major adverse cardiac events than patients without hypertension. Among STEMI patients, only history of hypertension for more than 10 years was a predictor of in-hospital mortality (odds ratio: 4.374, 95% CI 1.017–18.822, $P = .04$). Patients with an antecedent hypertension have higher initial risk profiles and show more negative outcomes during a 6-month follow-up period.

Keywords: hypertension, mortality, primary angioplasty, prognosis, ST elevation myocardial infarction

INTRODUCTION

Hypertension is a risk factor for coronary artery disease (CAD), which leads to ischemia by increasing the need for oxygen and plaque rupture. Hypertension markedly elevates cardiovascular mortality in the presence of coexisting risk factors (1). There are many studies in the literature that focus on the evaluation of the clinical prognosis of myocardial infarction patients with antecedent hypertension (2–11). While elevated levels of heart failure, stroke, cranial hemorrhage, and mortality risk have been shown in patients with antecedent hypertension receiving thrombolytic therapy (6,9–11), the number of studies assessing clinical prognosis in patients treated by primary angioplasty is inadequate and the outcomes obtained from those studies differ (2,8,12).

In this study, we aim to evaluate the clinical events encountered in patients with antecedent hypertension who received primary angioplasty for ST elevation myocardial infarction (STEMI) during hospital stay and the follow-up (6-month) period.

PATIENTS AND METHODS

Patient Population

We prospectively evaluated 373 consecutive patients with STEMI who were admitted to the emergency department of our hospital and treated by urgent cardiac catheterization procedures between December 2009 and June 2010. Patients fulfilling the following criteria were included in the study: (i) presentation within 12 hours from the onset of symptoms (typical chest pain lasting for >30 minutes); (ii) ST-segment elevation of ≥ 2 mm in at least two contiguous electrocardiography (ECG) leads or new onset of complete left bundle branch block; and (iii) treatment with primary angioplasty. The exclusion criteria were as follows: no indication for angioplasty, treatment with coronary bypass surgery, and the presence of advanced valve disease. The study protocol was approved by the Local Ethics Committee.

Data Sources

Demographic data and the clinical history concerning risk factors such as age, sex, diabetes mellitus (DM),

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hypertension, hyperlipidemia, smoking, family history of CAD, myocardial infarction, angioplasty or bypass surgery, and earlier drug use were obtained from the patients and their medical records. *Chest pain to reperfusion time*, door-to-balloon time, and duration of hypertension were recorded. Moreover, heart rate, blood pressure, waist circumference, and body mass index (BMI) were measured at initial presentation. Physical examination was also performed. Blood values were determined at initial presentation (before catheterization procedures) and on a daily basis during the hospital stay. A 12-lead electrocardiogram was carried out in each patient just after hospital admission. Transthoracic ECG was performed by using a system V (Vingmed, GE, Horten, Norway) with a 2.5-MHz phased-array transducer. Recordings were acquired from patients in the left lateral decubitus position. The left ventricular ejection fraction was measured using a modified Simpson's rule (13).

Coronary Angiography, Primary Angioplasty, and Stent Implantation

All patients received chewable aspirin (300 mg, unless contraindicated) and clopidogrel (300 mg, loading dose) before coronary angiography. Angiographic data of the patients were obtained from the cardiac catheterization laboratory records. Emergency coronary angiography was performed by percutaneous femoral approach. In all cases, nonionic low-osmolality contrast media were used. The first injection was given through the contralateral artery. Infarct-related artery (IRA) was graded according to the thrombolysis in myocardial infarction (TIMI) classification (14). Heparin (10 000 U) was administered after determination of the coronary anatomy. A coronary artery stenosis more than 50% was considered clinically significant. Occlusion of the IRA was crossed by using a 0.014-inch guidewire. Primary angioplasty including balloon angioplasty and/or stent implantation was performed only for IRA based on the lesion anatomy. For each procedure, interventional success at the acute phase was defined as reduction of the stenosis or obstruction to less than 50% with TIMI grade 2 or 3 flows after primary angioplasty.

After angioplasty, all patients were admitted to the coronary care unit, where 500 U/hour of intravenous heparin or 1 mg/kg/day of subcutaneous low molecular weight heparin was administered, whereas aspirin (100 mg) and clopidogrel (75 mg) were continued in all patients. The use of tirofiban was left to the discretion of the physician.

Definitions

Hypertension was defined as the presence of hypertension for more than 1 year and/or the use of antihypertensive drugs as per the recommendation of a physician (6–8). In our study, 87.5% of the hypertensive patients were observed to use antihypertensive drugs

and these drugs were beta-blockers (30.3%), diuretics (1.3%), angiotensin-converting enzyme/angiotensin receptor blockers (55.4%), and calcium channel blockers (12.9%). Diabetes mellitus was considered to be present in patients with diabetes controlled by diet, oral hypoglycemic agents, or insulin, as well as in patients discharged from the hospital with a diagnosis of diabetes and/or prescription of hypoglycemic agents. Hyperlipidemia was defined as the presence of use of lipid-lowering agents, a serum cholesterol level >240 mg/dL, or a serum triglyceride level >200 mg/dL. *Chest pain to reperfusion time* was defined as the interval from the onset of chest pain symptoms to the first balloon inflation. Door-to-balloon time was defined as the time between hospital admission and balloon inflation. Admission anemia was defined as a baseline hemoglobin concentration <13 mg/dL in men and <12 mg/dL in women (World Health Organization). Cardiogenic shock was defined as marked and persistent (>30 minutes) hypotension with a systolic arterial pressure lower than 80 mm Hg, in combination with signs of hypoperfusion due to left ventricular dysfunction, right ventricular infarction, and mechanical complications. Patients were also evaluated according to the Killip classification (15). Multivessel disease was defined as the presence of a stenosis greater than 50% in three major epicardial coronary arteries.

Positive family history of CAD was defined as a documented evidence of CAD in a parent or sibling before 60 years of age. Acute stent thrombosis was defined as an abrupt onset of cardiac symptoms (i.e., an acute coronary syndrome) along with elevated biomarker levels or electrocardiographic evidence of myocardial injury after stent deployment within the first 24 hours, accompanied by angiographic evidence of a flow-limiting thrombus near a previously placed stent. Cardiovascular mortality was defined as unexpected sudden death or mortality associated with acute myocardial infarction, heart failure, or arrhythmia. Reinfarction was described as elevation of the serum creatine kinase myocardial band enzyme levels by twice the upper limit of normal values and ST-segment re-elevations. Target-vessel revascularization (TVR) was defined as an angioplasty or a coronary artery bypass surgery due to restenosis or reocclusion in the IRA. Major adverse cardiac events (MACEs) were defined as cardiovascular mortality, reinfarction, and repeat TVR (percutaneous or surgical).

Follow-up

Serious ventricular arrhythmias (ventricular tachycardia and/or fibrillation), stroke, cardiopulmonary resuscitation, *temporary* pace intervention, intra-aortic balloon pump, atrial fibrillation, acute stent thrombosis, mortality, dialysis, cardiogenic shock, and MACE were evaluated during the hospital stay. Follow-up data were obtained from hospital records or by interviewing

patients (directly or by telephone), their families, or their personal physicians.

Statistical Analysis

Quantitative variables were expressed as mean value \pm SD, and qualitative variables were expressed as percent (%). The characteristics of the groups were compared by using analysis of variance for continuous variables and by using chi-square statistic for categorical variables. Backward stepwise multivariate logistic regression analysis that included variables with $P < .1$ was performed to identify independent predictors of in-hospital mortality. The cumulative survival curves for mid-term cardiovascular mortality were constructed using the Kaplan–Meier method, with differences assessed with the log-rank test. Gender, age, DM, hypertension, anemia, multivessel disease, post procedure TIMI grade III, family history, *chest pain to reperfusion time*, Killip, hypertension duration ≥ 10 years, and admission creatinine were entered into the model. A P value of $<.05$ was considered statistically significant. All statistical studies were carried out with the SPSS program (version 15.0, SPSS Inc., Chicago, IL, USA).

RESULTS

Clinical and Demographic Characteristics

Clinical and demographic characteristics of the patients are shown in Table 1. When the two groups were compared (177 patients with antecedent hypertension and 196 patients with no history of hypertension), hypertensive patients were found to be older (mean age: 59.9 ± 12.6 vs. 52 ± 12.3 years, $P < .001$). While the history of stroke, hyperlipidemia, and DM as well as waist circumference and BMI were higher in the hypertensive group, the nonhypertensive group had more smokers and males. The hypertensive group had significantly higher rates of aspirin, oral anti-diabetic drugs, insulin, or statin use at initial presentation. No significant difference was observed between the two groups with regard to infarct location (particularly anterior wall infarction), history of infarction, history of revascularization, systolic blood pressure levels at first presentation, door-to-balloon time, and *chest pain to reperfusion time*.

Biochemical Parameters

Biochemical parameters are shown in Table 2. At first presentation, creatinine levels were higher and anemia was more common in the hypertensive group compared with the nonhypertensive group. While hemoglobin A1c (HbA1c) was higher in the hypertensive group, glucose levels at first presentation did not show any significant difference between the two groups.

Table 1. Baseline characteristics of study patients

	HT (–) (<i>n</i> = 196)	HT (+) (<i>n</i> = 177)	<i>P</i> value
Age, y	52 (12.3)	59.9 (12.6)	<.001
Male	182 (92.9)	136 (76.8)	<.001
Anterior MI	97 (49.5)	76 (42.9)	.21
Hyperlipidemia	41 (20.9)	76 (42.9)	<.001
DM	22 (11.2)	43 (24.3)	.001
Current smoker	152 (77.6)	100 (56.5)	<.001
Stroke history	1 (0.5)	9 (5.1)	.006
Family history for CAD	86 (43.9)	77 (43.5)	.94
Heart rate, beats/min	78 (13.1)	77.4 (13.1)	.66
SBP, mm Hg	123.8 (22.6)	127.6 (25.6)	.13
Killip class >1	11 (5.6)	9 (5.1)	.92
Bypass	5 (2.6)	8 (4.5)	.3
PCI	13 (6.6)	16 (9)	.39
MI history	23 (11.7)	23 (13)	.71
Waist circumference, cm	93.3 (9.5)	97.4 (12.2)	<.001
BMI, kg/m ²	27.3 (3.9)	28.8 (4.6)	.001
Chest pain to reperfusion time, min	231.3 (152.3)	231.7 (170.3)	.98
Door-to-balloon time, min	30 (26)	35 (23)	.78
Prior aspirin use	22 (11.2)	41 (23.2)	.002
Prior insulin use	3 (1.5)	12 (6.8)	.01
Prior oral anti-diabetic use	13 (6.6)	28 (15.8)	.005
Prior β -blocker use	13 (6.6)	47 (26.6)	<.001
Prior diuretic use	0 (0)	2 (1.1)	.14
Prior statin use	7 (3.6)	19 (10.7)	.007
Prior ACE/ARB use	9 (4.6)	86 (48.6)	<.001
Prior CCB	3 (1.5)	20 (11.3)	<.001

Mean values (SD) and % (*n*) are reported for continuous and categorical variables, respectively.

Abbreviations: ACE/ARB – angiotensin-converting enzyme/angiotensin receptor blocker; BMI – body mass index; CAD – coronary artery disease; CCB – calcium channel blocker; HT – hypertension; MI – myocardial infarction; PCI – percutaneous coronary intervention; SBP – systolic blood pressure.

Angiographic and Procedural Characteristics

Angiographic and procedural characteristics for both the groups are shown in Table 3. There was no significant difference between the two groups in terms of culprit lesion, pre procedure TIMI grade, post procedure TIMI grade stent use, stent type, tirofiban use, and procedural success.

In-hospital and Follow-up Outcomes

In-hospital outcomes are shown in Table 4. Seventeen of the STEMI patients who received primary angioplasty demonstrated cardiovascular mortality. Cardiovascular mortality rate was 6.8% ($n = 12$) in the hypertensive patients and 2.6% ($n = 5$) in the nonhypertensive patients. MACE rate was higher in the hypertensive group. Outcomes determined at 6-month follow-up assessments are shown in Table 5. While cardiovascular mortality and MACE were higher particularly at 6 months (8.5% vs. 3%, $P = .02$ and 27.1% vs.

Table 2. Laboratory findings of patients

	HT (-) (n = 196)	HT (+) (n = 177)	P value
HbA1c, %	6.1 (1.4)	6.4 (1.2)	.04
Admission creatinine, mg/dL	0.84 (0.2)	0.96 (0.4)	<.001
Admission creatinine (≥1.5 mg/dL)	3 (1.5)	12 (6.8)	.01
Peak CK-MB, U/L	178.6 (163.2)	180.8 (145.1)	.9
Total cholesterol, mg/dL	197.9 (46.8)	196.1 (48)	.71
LDL-cholesterol, mg/dL	126.2 (36.4)	122.4 (41.1)	.34
HDL-cholesterol, mg/dL	39.9 (10.3)	42.1 (11.1)	.05
Triglycerides, mg/dL	159.3 (95.4)	160.6 (93.3)	.89
Admission glucose, mg/dL	156.7 (70)	170.2 (81.3)	.09
Admission anemia	11 (5.6)	21 (11.9)	.03

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively.

Abbreviations: CK-MB – creatine kinase myocardial band; HbA1c – hemoglobin A1c; HDL – high-density lipoprotein; HT – hypertension; LDL – low-density lipoprotein.

16.8%, $P = .02$, respectively), other parameters demonstrated similar values (e.g., TVR and reinfarct). Mid-term survival curves for both the groups are shown in Figure 1.

Multivariate Predictors of In-Hospital Mortality

Independent predictors of in-hospital mortality are shown in Table 6. High Killip class or creatinine levels at first presentation, presence of multivessel disease, and a history of hypertension for longer than 10 years were determined to be the independent predictors of in-hospital mortality. History of hypertension longer than 10 years was found to solely elevate in-hospital mortality (odds ratio: 4.374, 95% CI 1.017–18.822, $P = .04$).

DISCUSSION

The principal clinical events that occurred during hospital stay and at mid-term follow-up assessment in STEMI patients with hypertension who received primary angioplasty were summarized. First, STEMI patients with antecedent hypertension were older and had higher rates for the presence of coexisting diseases (e.g., DM and hyperlipidemia) compared with the nonhypertensive group. Second, in-hospital mortality and MACE rates were higher than those of the other group. Finally, cardiovascular mortality was still present at mid-term follow-up assessment.

Consistent with the studies investigating the effects of hypertension after myocardial infarction, our study demonstrated higher rates of comorbidities (DM, hyperlipidemia, stroke, obesity, and advanced age) accompanying hypertensive patients treated by primary

Table 3. Angiographic and procedural characteristics of patients

	HT (-) (n = 196)	HT (+) (n = 177)	P value
Culprit lesion			.34
LAD	99 (50.5)	79 (44.6)	
CX	31 (15.8)	25 (14.1)	
RCA	65 (33.2)	73 (41.2)	
Others	1 (0.5)	0 (0)	
Number of diseased vessels			.07
1	111 (56.6)	79 (44.6)	
2	50 (25.5)	59 (33.3)	
3	35 (17.9)	39 (22.1)	
Pre procedure TIMI grade			.42
0/1	192 (98)	176 (99.4)	
2	3 (1.5)	1 (0.6)	
3	1 (0.5)	0 (0)	
Post procedure TIMI grade			.27
0/1	3 (1.5)	6 (3.4)	
2	11 (5.6)	15 (8.5)	
3	182 (92.9)	156 (88.1)	
Stent	151 (77)	134 (75.7)	.9
Stent length, mm	18.2 (4.8)	18.3 (5.5)	.76
Stent diameter, mm	3.1 (0.37)	3.08 (0.34)	.66
Stent type			.22
BMS	147 (97.4)	133 (99.3)	
PES	2 (1.3)	1 (0.7)	
SES	2 (1.3)	0 (0)	
Proximal location of the lesion	133 (67.9)	129 (72.9)	.29
LVEF, %	45.4 (7.9)	43.8 (8.1)	.06
Tirofiban	77 (39.3)	71 (40.1)	.87
Success of procedure	185 (94.4)	163 (92.1)	.67

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively.

Abbreviations: BMS – bare metal stent; CX – circumflex; HT – hypertension; LAD – left anterior descending; LVEF – left ventricular ejection fraction; PES – paclitaxel eluting stent; RCA – right coronary artery; SES – sirolimus eluting stent; TIMI – thrombolysis in myocardial infarction.

angioplasty, whereas the number of males and smokers was higher in the nonhypertensive group (2,6,7,12). Moreover, similar to the data in the literature, our study showed statistically significantly higher rates for use of aspirin and statins as a primary or secondary precautionary measure in the hypertensive group (8). While previous studies had higher rates of history of revascularization (primary angioplasty and bypass) and blood pressure at first presentation, our study did not show any significant difference in terms of these two parameters (7,8).

Parallel to the previous studies (2,6,7), creatinine level at first presentation was significantly higher in the hypertensive group (0.96 ± 0.4 vs. 0.84 ± 0.2 , $P < .001$) and it was determined to be the strongest indicator of in-hospital mortality (odds ratio: 8.22, 95% CI 1.776–38.093, $P = .007$). This may be a result of the potential impact of renal dysfunction in the hypertensive group, accompanying comorbid conditions such as DM.

Table 4. In-hospital cardiac events and complications

	HT (-) (n = 196)	HT (+) (n = 177)	P value
In-hospital mortality	5 (2.6)	12 (6.8)	.05
Reinfarction	1 (0.5)	5 (2.8)	.08
TVR	1 (0.5)	2 (1.1)	.5
MACE	6 (3.1)	17 (9.6)	.009
Stroke	0 (0)	1 (0.6)	.29
Serious ventricular arrhythmia	19 (9.7)	14 (7.9)	.55
Cardiopulmonary resuscitation	10 (5.1)	11 (6.2)	.64
Cardiogenic shock	9 (4.6)	9 (5.1)	.82
Intra-aortic balloon pump	2 (1)	5 (2.8)	.23
Renal failure requiring dialysis	0 (0)	2 (1.1)	.14
New atrial fibrillation	6 (3.1)	6 (3.4)	.86
Complete atrioventricular block requiring temporary pacemaker	5 (2.6)	8 (4.5)	.3
Acute stent thrombosis	3 (1.5)	4 (2.3)	.6
Time of hospital stay, days	6.6 (4.6)	6.3 (3.4)	.47

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively.

Abbreviations: HT – hypertension; MACEs, – major adverse cardiac events (cardiovascular death, reinfarction, and TVR); TVR – target-vessel revascularization.

Table 5. Six-month follow-up outcomes

	HT (-) (n = 196)	HT (+) (n = 177)	P value
All-cause mortality	6 (3)	15 (8.5)	.02
Cardiac death	6 (3)	15 (8.5)	.02
Non-cardiac death	0	0	–
Fatal reinfarction	0 (0)	2 (1.1)	.14
Non-fatal reinfarction	18 (9.2)	20 (11.3)	.5
TVR	25 (12.8)	33 (18.6)	.12
MACE	33 (16.8)	48 (27.1)	.02
Stroke	1 (0.5)	1 (0.6)	.94
HF requiring hospitalization	2 (1)	2 (1.1)	.92

Mean values (SD) and % (n) are reported for continuous and categorical variables, respectively.

Abbreviations: HF – heart failure; HT – hypertension; MACEs – major adverse cardiac events (cardiovascular death, reinfarction, and TVR); TVR – target-vessel revascularization.

There are many studies in the literature focusing on the effects of hypertension on in-hospital mortality following myocardial infarction, which show varying results (2,7,8,10,12); however, the characteristics of the patients included in those studies are not similar. Thus, the number of studies investigating STEMI patients treated only by primary angioplasty is not much (2,12). This may explain the reason why previous studies produced differing outcomes on in-hospital

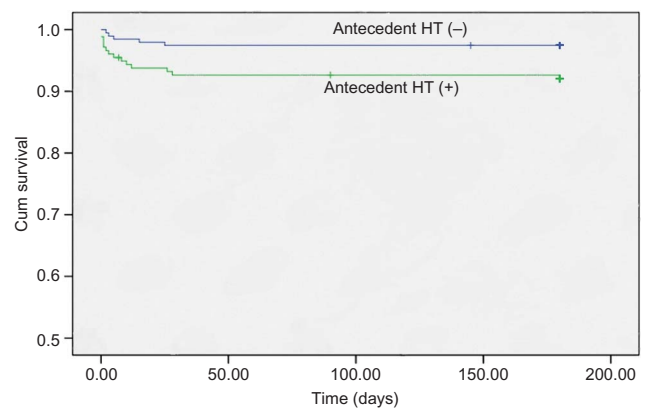


Figure 1. Kaplan–Meier curve for cardiovascular mortality of patients with and without antecedent hypertension at midterm. Abbreviation: HT – hypertension.

Table 6. Multivariate predictors of in-hospital mortality

Variables	Wald	OR	95% CI	P value
Killip	22.6	4.996	2.573–9.703	<.001
Admission creatinine	7.3	8.226	1.776–38.093	.007
Multivessel disease	4.9	7.186	1.257–41.077	.03
HT duration ≥10 y	3.9	4.374	1.017–18.822	.04

Gender, age, DM, hypertension, family history, chest pain to reperfusion time, anemia, admission glucose, and post-TIMI III flow were also in the regression model.

Abbreviations: CI – confidence interval; HT – hypertension; OR – odds ratio; DM – diabetes mellitus; TIMI – thrombolysis in myocardial infarction.

mortality. Abrignani et al. (8) are one of the investigator groups that found lower in-hospital mortality in the hypertensive group and they associated this finding with higher diastolic blood pressure increasing the coronary perfusion, greater number of non-STEMI patients with elevated coronary collateral flow, and smaller infarct formation (compared with the transmural infarct) in non-STEMI due to subendocardial ischemia. Majahalme et al. (7) observed the acute mortality rates to be similar in both groups and explained this result with ineffectiveness of long-term antihypertensive drug use. Similar to the study of Rembek et al. (2), we found high in-hospital mortality rates among the hypertensive patients, which was still present at the mid-term follow-up assessment. In-hospital mortality may be associated with frequency of the accompanying comorbidities (e.g., advanced age, DM, hyperlipidemia, and obesity), elevated HbA1c (16) and creatinine levels as well as anemia (17) being more common at presentation, higher rates for the presence of multivessel disease, reduced coronary flow reserve, elevated sympathetic tonus, insulin resistance, and coronary vascular resistance (6,18). The duration of hypertension may be associated with the mortality as well, because as shown by our study, persistence of hypertension for more than 10 years is an independent predictor of mortality (odds

ratio: 4.374, 95% CI 1.017–18.822, $P = .04$). As mentioned by Parodi et al. (12), cardiovascular mortality observed at mid-term follow-up assessment may be due to sudden cardiac death arising from impaired coronary flow and hypertension rather than loss of contractile tissue.

Limitations of the Study

Several limitations should be considered while evaluating the results of our study. First, since we included hypertension patients based on the history, there may be patients that we excluded despite the presence of hypertension; therefore, we may have underestimated the prevalence of antecedent hypertension. However, the prevalence of hypertensive patients that we enrolled in the study (47.4%) is consistent with those of the previous studies (2,6,8). Second, we do not know the level of blood pressure control in hypertensive patients within a period of 6 months. Finally, the follow-up period in our study was limited to 6 months. A longer follow-up period may have provided additional data.

Clinical Implications

As shown in our study, STEMI patients with antecedent hypertension who are treated by primary angioplasty show high mid-term cardiovascular mortality. Therefore, hypertensive individuals should be treated by first reducing the accompanying risk factors and then applying aggressive treatment.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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