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Original Research

Impact of Helicopter Transport on Reperfusion Times and Long-Term Outcomes in Acute Myocardial Infarction Patients in Rural Areas: A Report From the Mie Acute Coronary Syndrome Registry

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A B S T R A C T

Objective: Helicopter emergency medical services (HEMS) are effective for time-sensitive conditions, such as stroke and trauma. However, prognostic data on helicopter transport for acute myocardial infarction (AMI) patients are insufficient.

Methods: We registered 2,681 AMI patients in the Mie Acute Coronary Syndrome Registry and enrolled 163 patients from rural areas to HEMS base hospitals with HEMS or ground emergency medical services (GEMS). They were categorized into 4 groups according to the transportation method for interhospital transfer (direct HEMS: n = 52, direct GEMS: n = 54, interhospital HEMS: n = 32, and interhospital GEMS: n = 25). The primary end point was the emergency medical services (EMS) call-to-balloon time. The secondary end point was 2-year major adverse cardiac and cerebrovascular events.

Results: The direct HEMS group was younger than the direct GEMS group ($P = .029$). The EMS call-to-balloon time was shorter in the direct HEMS and interhospital HEMS groups than in each GEMS group ($P = .015$ and $P = .046$). The incidence of 2-year major adverse cardiac and cerebrovascular events tended to be lower in both HEMS groups than in each GEMS group.

Conclusion: Direct HEMS for AMI in rural areas shortens the time from the EMS call to reperfusion when the transport distance is expected to exceed 30 km, which may result in a better patient prognosis. In addition, prehospital diagnostic modalities, such as 12-lead electrocardiography and echocardiography, may shorten the duration from the EMS call to reperfusion.

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Reperfusion therapy by primary percutaneous coronary intervention (PCI) for patients with acute myocardial infarction (AMI) needs to be performed as soon as possible to shorten the onset-to-balloon time (OBT) for a better prognosis.^{1,2} However, residents in rural areas generally have more limited access to health care resources than urban residents, and differences in health outcomes have been reported between urban and rural residents.³⁻⁵ A previous study demonstrated an increased in-hospital mortality rate in AMI patients in rural areas who were transported to hospitals with a low primary PCI volume.⁶ In addition, direct transfer to a PCI-capable hospital was

shown to be very important for minimizing OBT in AMI patients from rural areas and was suggested to improve outcomes.³

Mortality rates in patients with major traumatic injuries and stroke were previously shown to be significantly lower with helicopter emergency medical services (HEMS) than with ground emergency medical services (GEMS).^{7–11} HEMS for AMI patients in rural areas as a transportation system shortened OBT in cases when the PCI-capable hospital was far from the scene of onset or when the condition of the patient was severe. However, it currently remains unclear whether HEMS improves the short- and long-term prognosis of AMI patients.^{12–20}

HEMS with a critical care doctor on board has been available in Japan since 2001; however, only a few studies have been conducted on HEMS for AMI patients.^{21–23} Factors related to the usefulness of HEMS are regional circumstances, including the size and distribution of the population, the locations of HEMS base hospitals, the number of ground ambulances, emergency medical service (EMS) centers at which ground ambulances are on standby, the functions of receiving hospitals, the distance between the scene of onset and the hospital, and road conditions. The present study was conducted in Mie Prefecture, which is located on the Kii Peninsula in the middle of Japan; it is a long-shaped prefecture from north to south and has many intricate coastlines and remote islands. Therefore, GEMS may take an unexpected amount of time to transport AMI patients to PCI-capable hospitals. A previous study reported that AMI patients in Mie Prefecture had a longer time delay from onset to reperfusion and a higher prevalence of interhospital transfer than those in Tokyo, the capital of Japan.³ Therefore, the present study investigated the impact of HEMS on EMS calls for reperfusion and its prognostic importance for AMI patients compared with GEMS in Mie Prefecture, Japan.

Methods

Study Population

We consecutively registered 2,681 AMI patients with primary PCI between January 2013 and December 2017 using data from the Mie Acute Coronary Syndrome Registry, a prospective and multicenter registry of Mie in Japan.^{3,24,25} There were 520 AMI patients in rural areas in which HEMS is used for AMI patients in Mie Prefecture (Figs. 1 and 2), and 163 patients who arrived at 2 HEMS base/PCI-capable hospitals (Mie University Hospital and Ise Red Cross Hospital) during the daytime were included in this analysis. AMI patients who arrived at these PCI-capable hospitals during the night were excluded because HEMS was unavailable. Patients who did not use EMS were also excluded. We divided patients into 4 groups based on the transport mode and admission route to PCI-capable hospitals (direct

HEMS, direct GEMS, interhospital HEMS, and interhospital GEMS) and then examined the impact of HEMS on reperfusion times and the prognosis of patients in comparison with GEMS in each direct transfer and interhospital transfer group. The diagnosis of AMI was based on the third universal definition of myocardial infarction (MI).²⁶

This registry was approved by the Institutional Review Board of the Mie University Graduate School of Medicine and each participating institutional ethics committee (reference number 2881). We provided patients with the opportunity to opt out of the study (<https://www.hosp.mie-u.ac.jp/ethics/web/wp-content/uploads/2881optout-2.pdf>). The trial was registered at <https://www.umin.ac.jp/ctr/index-j.htm> (unique identifier: UMIN 000036020).^{3,24,25}

GEMS

GEMS staff make first contact with patients suspected of AMI at the scene and record blood pressure and electrocardiography (NASA and CM5 leads). Most GEMS in rural areas are not equipped with the 12-lead electrocardiographic (ECG) transmission system. If patients in rural areas have ST-segment changes in electrocardiography and are far from a PCI-capable hospital, GEMS staff call for HEMS. GEMS staff are skilled at interpreting ECG readings. However, if HEMS are not available, GEMS staff transfer the patient to the nearest hospital. In addition, when patients show ST-segment changes, GEMS staff transmit this information to the hospital. Staff at the emergency room in the PCI-capable hospital inform the attending cardiologist to prepare for PCI. Furthermore, specially trained paramedics are capable of performing venous access with epinephrine and tracheal intubation under specific instructions by the critical care doctor in the GEMS unit.

HEMS

Mie Prefecture has 1 helicopter and 2 HEMS base hospitals (Fig. 2). Patients may make EMS calls by dialing 1-1-9 but cannot directly request HEMS. The fire department receiving the emergency call assesses the need for HEMS when acute coronary syndrome is suspected. Indications for helicopter transfer are judged by the fire department, ground ambulance staff, or a doctor at a non-PCI-capable hospital. HEMS may be unavailable because of bad weather, when the fire service for helicopters is closed (8:30–17:00), or when the helicopter has been dispatched to transport other patients.

Fentanyl, morphine, adrenaline, lidocaine, atropine, nifekalant, and amiodarone may be intravenously administered by the critical care doctor in the HEMS unit. Oral medication with aspirin and nitrates is also available. The critical care doctor in the HEMS unit may also perform portable echocardiography. If the findings obtained

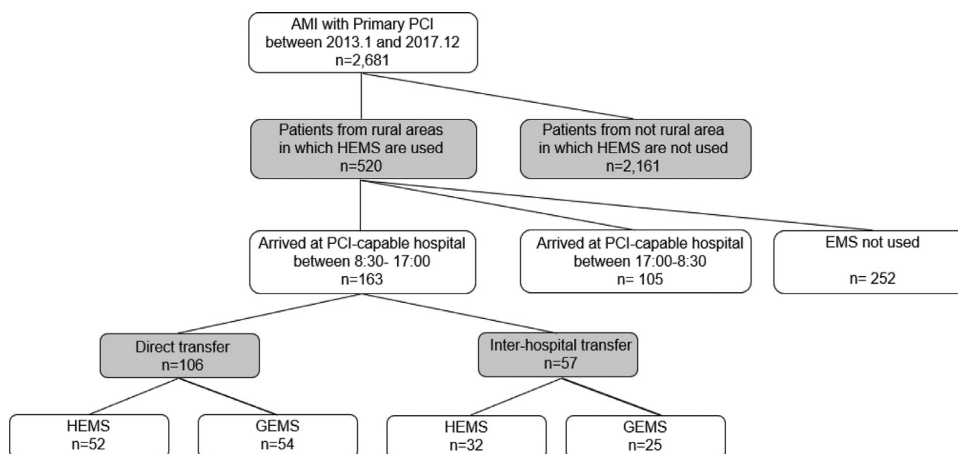


Figure 1. A flowchart of patient enrollment.

Mie Prefecture in Japan



Figure 2. A map of Mie Prefecture in Japan with 2 helicopter base hospitals. The areas colored in gray are the rural areas in which helicopters operate. Concentric circles of 30 km from each helicopter base hospital are shown.

indicate AMI, HEMS staff transmit this information to the PCI-capable hospital.

Patient Outcomes

Outcome data were collected via patient interviews at the outpatient clinic, hospital chart reviews, or telephone interviews with the patient or close relatives, and clinical events were recorded in a Web system. Major adverse cardiac or cerebrovascular events (MACCEs) as the secondary end point were defined as cardiovascular death, non-fatal MI, unstable angina pectoris requiring admission, heart failure admission, and stroke admission during the follow-up. The follow-up rate was 100% in this study population.

Definitions of Distance and Transport Time

The scene of onset was defined as the place at which a patient or witness calls EMS. Ground driving distances from the scene of onset to a PCI-capable hospital (direct) or via a non-PCI-capable hospital to a PCI-capable hospital (indirect) were calculated from the Google Maps website (<https://www.google.co.jp/maps/>, October 15, 2020). The helicopter transport distance was calculated as the ground route from the scene of onset to the PCI-capable hospital. In the interhospital HEMS group, the transport distance via the non-PCI-capable hospital was calculated. We used official activity reports by EMS and evaluated the EMS call-to-balloon time. The balloon time was defined as the time when the first device was used or balloon inflation was conducted. Door time was defined as the arrival time at the emergency room of the hospital at which primary PCI was performed. The time from the EMS call-to-balloon time was defined as the primary end point.

Statistical Analysis

Continuous variables with normal distributions were expressed as the mean \pm standard deviation, and those without normal distributions were expressed as the median and interquartile range. Categorical variables were expressed as a number and percentage. The chi-square test or Mann-Whitney *U* test was used for comparisons of categorical variables according to a nominal or ordinal scale. The Student *t*-test or Wilcoxon rank sum test was used for continuous variables where appropriate. The significance of differences was defined as $P < .05$. Statistical analyses were performed using SPSS Version 25.0 (IBM Corp, Armonk, NY).

Results

Baseline Patient Characteristics

Baseline patient characteristics are summarized in Table 1. The median age of 163 patients was 72 years, and 71.8% were male. A significant difference was observed in age between the direct HEMS and direct GEMS groups ($P = .029$). A significant difference was also noted in the proportion of ST-elevation MI between the interhospital HEMS and interhospital GEMS groups. The Killip classification at arrival was similar in each group. Differences in prehospital medical practices are summarized in Table 2. The 12-lead ECG transmission system was used on 5.8% of patients in the direct HEMS group and 20.4% in the direct GEMS group ($P = .027$). However, the prevalence of peripheral venous access and echocardiography during transmission was higher in the direct HEMS group than in the direct GEMS group ($P < .001$).

Angiographic Findings and In-Hospital Outcomes

Angiographic characteristics are shown in Table 3. No significant differences were observed in culprit lesions or the prevalence of multivessel disease between the HEMS and GEMS groups in each direct transfer and interhospital transfer group. More than 90% of patients with primary PCI achieved postprocedural TIMI flow III. The left ventricular ejection fraction was higher in the direct HEMS group than in the direct GEMS group. The in-hospital mortality rate was 4.8% among all patients and was slightly lower in the HEMS groups than in the GEMS groups in each direct transfer and interhospital transfer group. No significant differences were noted in the lengths of hospital stays in both transfer groups between the HEMS and GEMS groups.

Time Elements and Transport Distances

Time elements are summarized in Figure 3. EMS call-to-balloon times were significantly shorter in the direct HEMS group than in the direct GEMS group due to slightly shorter EMS call-to-door times and significantly shorter door-to-balloon times. Furthermore, EMS call-to-balloon times were shorter in the interhospital HEMS group than in the interhospital GEMS group. In terms of door-to-balloon times, a significant difference was observed between the direct HEMS group and direct GEMS group. In addition, a significant difference was noted in EMS call-to-door times between the interhospital HEMS group and the interhospital GEMS group.

Table 1
Baseline Patient Characteristics

	All Patients (N = 163)	Direct		P Value	Interhospital (Indirect)		P Value
		HEMS (n = 52)	GEMS (n = 54)		HEMS (n = 32)	GEMS (n = 25)	
Age, years	72 (65-79)	68 (64-77)	76 (67-82)	.029	71 (63-78)	74 (71-78)	.212
Male, n (%)	117 (71.8)	45 (86.5)	41 (75.9)	.216	19 (59.4)	12 (48)	.432
BMI, kg/m ²	22.9 (20.7-25.3)	23.5 (21.7-24.9)	23.2 (20.8-25.6)	.710	22.9 (20.7-25.6)	21.2 (19.8-24.5)	.096
Diagnosis							
STEMI, n (%)	137 (84.0)	43 (82.7)	46 (85.2)	.730	30 (93.8)	18 (72.0)	.030
NSTEMI, n (%)	26 (16.0)	9 (17.3)	8 (14.8)		2 (6.2)	7 (28.0)	
Killip 1, n (%)	109 (66.9)	41 (78.8)	30 (55.6)	.071	22 (68.8)	16 (64.0)	.760
2/3, n (%)	34 (20.9)	5 (9.6)	14 (25.9)		8 (25)	7 (28.0)	
4, n (%)	20 (12.2)	6 (11.5)	10 (18.5)		2 (6.2)	2 (8.0)	
Out-of-hospital cardiac arrest, n (%)	8 (4.9)	5 (9.6)	1 (1.9)	.109	2 (6.2)	0 (0)	.499
Hypertension, n (%)	110 (67.4)	33 (63.5)	33 (61.1)	.843	25 (78.1)	19 (76.0)	1.0
Diabetes mellitus, n (%)	30 (18.4)	8 (15.1)	13 (23.6)	.332	5 (15.6)	4 (16.0)	1.0
Dyslipidemia, n (%)	71 (43.5)	21 (40.4)	25 (46.2)	.562	16 (50.0)	9 (36.0)	.420
Prior myocardial infarction, n (%)	11 (6.7)	1 (1.9)	5 (9.3)	.206	2 (6.2)	3 (12.0)	.645
Prior PCI, n (%)	16 (9.8)	3 (5.8)	8 (14.8)	.202	3 (9.4)	2 (8.0)	1.0
Prior CABG, n (%)	2 (1.2)	0 (0)	1 (1.9)	1.0	0 (0.0)	1 (4.0)	.439
Prior cerebral infarction, n (%)	10 (6.1)	5 (9.6)	3 (5.6)	.484	2 (6.2)	1 (4.0)	1.0

BMI = body mass index; CABG = coronary artery bypass grafting; GEMS = ground emergency medical services; HEMS = helicopter emergency medical services; NSTEMI = non-ST-elevated myocardial infarction; PCI = percutaneous coronary intervention.

Data are shown as means (standard deviations), medians (interquartile ranges), or numbers (percentages).

Table 2
Medical Practices in Direct Helicopter Emergency Medical Services (HEMS) and Direct Ground Emergency Medical Services (GEMS)

	Direct		P Value
	HEMS (n = 52)	GEMS (n = 54)	
12-lead ECG transmission, n (%)	3 (5.8)	11 (20.4)	.027
Peripheral venous access, n (%)	43 (83)	1 (1.9)	<.001
Adrenaline, n (%)	0	1 (1.9)	.326
Aspirin, n (%)	16 (31)	0	<.001
Nitroglycerin, n (%)	21 (40.4)	0	<.001
Echocardiography during transmission, n (%)	38 (73)	0	<.001

ECG = electrocardiographic.

Data are shown as numbers (percentages).

Transport distances are summarized in [Figure 4](#). No significant difference was found in transport distances from the scene of onset to a PCI-capable hospital between the HEMS and GEMS groups in each direct transfer and interhospital transfer group.

Long-Term Outcome Data

During the follow-up duration of 730 days (2 years), MACCEs occurred in 22 of 165 patients (13%), including 6 with cardiovascular

death, 2 with non-fatal MI, 4 with unstable angina requiring revascularization, 3 with HF requiring hospitalization, and 7 with stroke requiring hospitalization ([Table 4](#)). MACCE rates in the direct HEMS and interhospital HEMS groups were 5.8% and 15.6%, respectively, which were approximately one half of each GEMS group, respectively, and this difference was not significant ([Fig. 5](#), left panel). All-cause mortality rates in the direct HEMS group and interhospital HEMS group were 5.8% and 6.2%, respectively, which were

Table 3
Angiographic and In-Hospital Outcomes

	All Patients (N = 163)	Direct		P Value	Interhospital		P Value
		HEMS (n = 52)	GEMS (n = 54)		HEMS (n = 32)	GEMS (n = 25)	
Angiographic data							
Culprit artery							
LMT, n (%)	2 (1.2)	1 (1.9)	1 (1.9)	1.0	0 (0)	0 (0)	—
LAD, n (%)	71 (43.6)	23 (44.2)	22 (40.7)	.844	16 (50.0)	10 (40.0)	.593
RCA, n (%)	68 (41.7)	23 (44.2)	26 (48.1)	.702	14 (43.8)	5 (35.7)	.794
LCX, n (%)	17 (10.4)	6 (11.5)	5 (9.3)	.759	1 (3.1)	5 (20.0)	.077
Multivessel disease, n (%)	53 (32.5)	19 (36.5)	16 (29.6)	.583	9 (28.1)	9 (34.1)	.575
Final TIMI flow grade 3, n (%)	152 (93.2)	49 (94.2)	50 (92.6)	1.0	30 (93.8)	23 (92.0)	1.0
Level of peak CPK, IU/L	2362 (863-3996)	2327 (864-3653)	1836 (817-3595)	.897	2681 (1165-5197)	1741 (749-4201)	.292
Left ventricular ejection fraction, %	61.2 (52.9-67.5)	65.2 (58.0-69.3)	58.0 (47.0-64.0)	.002	61.7 (57.9-65.8)	63.7 (51.7- 69.0)	.980
Duration of hospital stay, days	12 (9-18)	11 (9-15)	13 (9-19)	.387	15 (11-20)	13 (9-17)	.407
In-hospital mortality, n (%)	8 (4.8)	1 (1.9)	4 (7.3)	.363	1 (3.1)	2 (8.0)	.576

CPK = creatinine phosphokinase; GEMS = ground emergency medical services; HEMS = helicopter emergency medical services; LAD = left anterior descending artery; LCX = left circumflex artery; LMT = left main trunk; RCA = right coronary artery; TIMI = Thrombolysis in Myocardial Infarction trial.

Data are shown as means (standard deviations), medians (interquartile ranges), or numbers (percentages).

Time elements and transport form

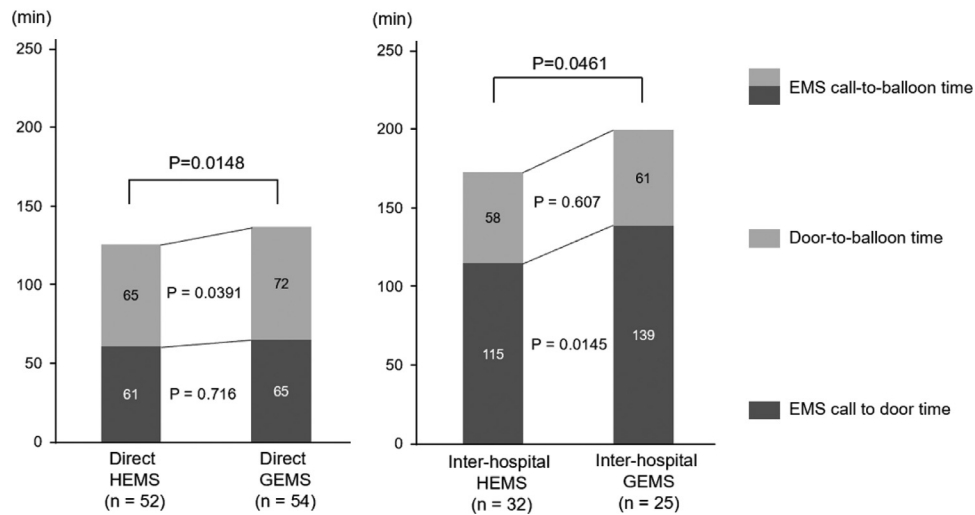


Figure 3. The time elements and transport forms.

approximately two thirds and one third of each GEMS group, respectively, without a significant difference (Fig. 5, right panel).

Discussion

The present results demonstrated that the EMS call-to-balloon time was shorter with HEMS than with GEMS in AMI patients who were referred to PCI-capable hospitals either directly from the scene of onset or through interhospital transfers. Furthermore, 2-year MAC-CEs and all-cause mortality rates were slightly lower in patients who were transported with HEMS than with GEMS from rural areas in Mie Prefecture. These results confirmed the clinical usefulness of HEMS for AMI patients in rural areas of Mie Prefecture, Japan.

The prognosis of AMI patients has been improved by primary PCI over the past few decades.^{27,28} However, further improvements in the prehospital management of AMI are needed to reduce the time to

PCI. A previous study demonstrated that the shortening of OBT improved the prognosis of AMI patients.²⁹ Masuda et al³ also reported that AMI patients in rural areas were less likely to be transported directly to PCI-capable hospitals than those in urban areas, resulting in a time delay to primary PCI. Matsuzawa et al⁶ showed that a low population density was associated with in-hospital mortality in AMI patients, suggesting a worse prognosis in rural areas than in urban areas. Therefore, the present study investigated whether HEMS shortened the EMS call-to-balloon time, which may improve the prognosis of patients in rural areas.

Previous studies investigated the effectiveness of HEMS for AMI patients. Funder et al¹⁷ reported that the time from diagnostic electrocardiography to PCI-capable hospital arrival in eastern Denmark was shorter with HEMS than with GEMS, with no significant differences in 30-day mortality rates between the 2 groups. Homma et al²³

Comparison of transport distance

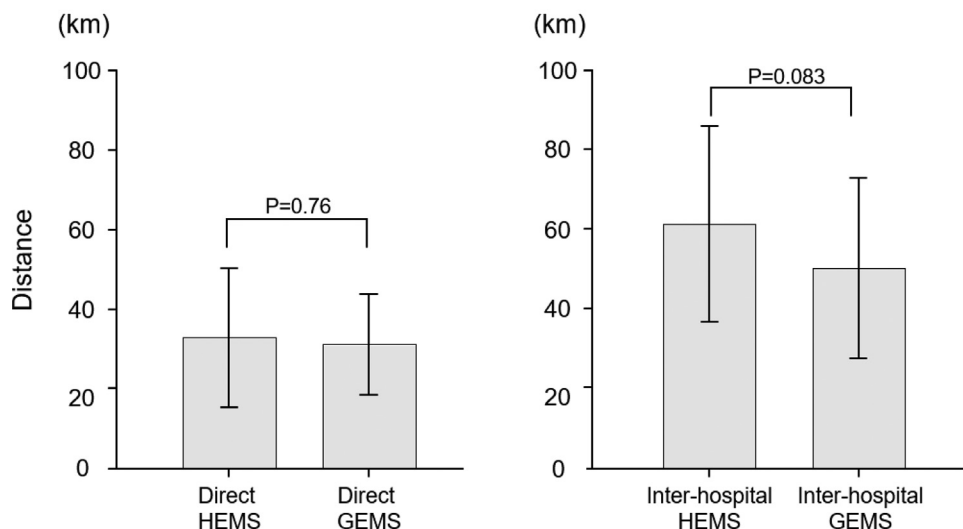


Figure 4. A comparison of transport distances by different transport forms.

Table 4
Outcome Data

	All patients (N = 163)	Direct		P Value	Interhospital (indirect)		P Value
		HEMS (n = 52)	GEMS (n = 54)		HEMS (n = 32)	GEMS (n = 25)	
Follow-up period, days (median)	751 (390-865)	751 (543-881)	765 (390-918)	.933	772 (484-853)	738 (240-797)	.31
All-cause mortality, n (%)	15 (9.2)	3 (5.8)	5 (9.3)	.716	2 (6.2)	5 (20.0)	.221
MACCEs, n (%)	21 (12.9)	3 (5.8)	6 (11.5)	.488	5 (15.6)	7 (30.4)	.208
Cardiovascular death, n (%)	6 (3.7)	1 (1.9)	2 (3.7)	1.0	1 (3.1)	2 (8.0)	.576
Nonfatal myocardial infarction, n (%)	2 (1.2)	0 (0)	1 (1.8)	1.0	0 (0)	1 (4.0)	.439
Unstable angina pectoris requiring revascularization, n (%)	4 (2.5)	1 (1.9)	2 (3.7)	1.0	1 (3.1)	0 (0)	1.0
Heart failure requiring hospitalization, n (%)	3 (1.8)	1 (1.9)	0 (0)	.491	1 (3.1)	1 (4.0)	1.0
Stroke requiring hospitalization, n (%)	6 (3.7)	0 (0.0)	1 (1.9)	1.0	2 (6.2)	3 (12.0)	.645

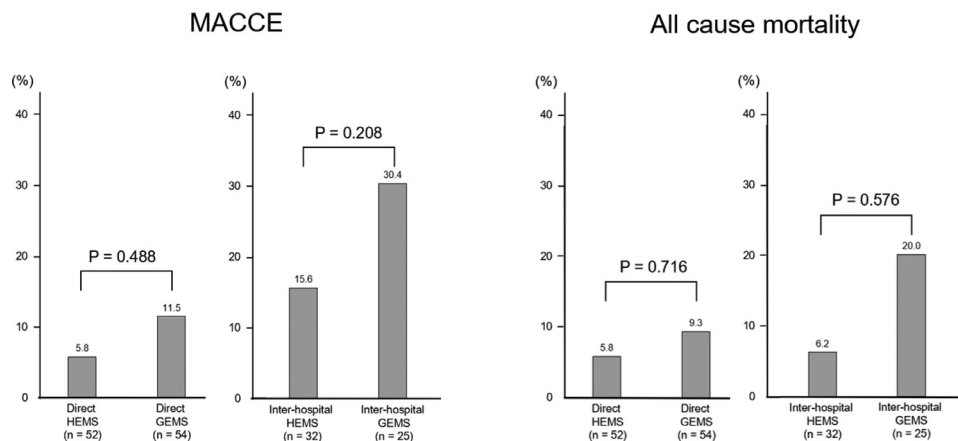
GEMS = ground emergency medical services; HEMS = helicopter emergency medical services; MACCEs = major adverse cardiac and cerebrovascular events. Data are shown as medians (interquartile ranges) or numbers (percentages).

also demonstrated that the EMS call-to-balloon time was shorter with HEMS than with GEMS in Hokkaido, Japan, without improvements in-hospital mortality rates. These findings were consistent with the present results showing that direct HEMS shortened the EMS call-to-balloon time but did not improve in-hospital mortality rates. However, Hakim et al³⁰ found that HEMS did not effectively shorten the transfer time from a distance of less than 50 km in the Centre-Val de Loire region in France. In our analysis, direct HEMS was used for a distance of approximately 30 km, which is shorter than in previous studies. Because of the geographic features of rural areas in Mie Prefecture, which include mountains, intricate coastlines, and remote islands, HEMS effectively reduced the EMS call-to-balloon time within a short distance, whereas GEMS may take an unexpected amount of time to transport AMI patients to PCI-capable hospitals. Because the usefulness of HEMS may be affected by geographic features, the management systems and implementation strategies of individual local governments, and interhospital locations, difficulties are associated with generalizing the effectiveness of HEMS.

The door-to-balloon time was significantly shorter in the direct HEMS group than in the direct GEMS group. Prehospital information provided by doctors in the helicopter may shorten preparation times by catheter laboratories. Furthermore, EMS call-to-balloon times were significantly shorter in the direct HEMS and interhospital HEMS groups than in each GEMS group. HEMS transfer may accelerate the decision-making process because the emergency physician at the scene or in transit actively evaluates and communicates with interventional cardiologists.

In the present study, the in-hospital mortality rate was 4.8% among all patients and was slightly lower in the HEMS groups than in the GEMS groups in each direct transfer and interhospital transfer group. Furthermore, 2-year MACCE rates in the direct HEMS group and interhospital HEMS group were approximately one half of each GEMS group, respectively. Two-year all-cause mortality rates in the direct HEMS group and the interhospital HEMS group were also approximately two thirds and one third of each GEMS group, respectively. Although no significant differences were observed, presumably because of the small patient population, the shorter EMS call-to-balloon time provided by HEMS may contribute to a better long-term prognosis. In addition, to improve the prognosis of patients, it may be useful to construct a system that transmits information obtained using 12-lead electrocardiography to doctors in PCI-capable hospitals at the time GEM staff initially reach the patient; therefore, AMI patients may be transported directly and rapidly to appropriate hospitals.^{31,32} In a rural regional ST-elevation MI network, prehospital electrocardiography decreased the time from first medical contact to reperfusion by 50%, which may be attributed to non-PCI-capable hospitals being bypassed in favor of direct transport to a PCI-capable facility, and was associated with excellent clinical outcomes at 1 year.³³ The 12-lead ECG transmission system is currently used by only a few ambulances in Mie Prefecture. Although the rate of 12-lead electrocardiography was lower in HEMS than in GEMS, echocardiography during transmission was performed more frequently in HEMS than in GEMS, which may have led to the earlier and more accurate diagnosis of AMI and faster treatment.

Outcome data by transport form

**Figure 5.** Outcome data by transport forms.

Limitations

The present study was not randomized and only included a small number of patients. The final decision to call HEMS is left to EMS staff at the scene even though they follow a specific protocol in principle. A multivariate analysis was not used to clarify whether HEMS contributed to a better prognosis because of the small number of events examined. Furthermore, the transport distance for HEMS was calculated as the ground route from the scene to a PCI-capable hospital and thus did not represent the exact transport distance for HEMS.

Conclusion

Direct HEMS for AMI patients in rural areas shortens the time from the EMS call to reperfusion when the transport distance is expected to exceed 30 km, which may improve patient outcomes. In addition, the widespread use of prehospital diagnostic modalities, such as the 12-lead ECG transmission system and echocardiography, may shorten the time for the EMS call to reperfusion by directly activating cardiac catheter laboratories and bypassing emergency rooms.

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