

1 **Supplementary Files** for the article entitled “**Nitroglycerin use and adverse clinical**
2 **outcomes in elderly patients with acute coronary syndrome**” by **Komaki et al.**
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4 **TABLE OF CONTENTS**

5 **Supplementary Methods S1:** Design and study population - geographic characteristics of
6 hospital location..... **p 2**

7 **Supplementary Methods S2:** Definitions of coronary risk factors..... **p 2**

8 **Supplementary Methods S3:** PCI procedures.....**p 3**

9 **Supplementary Table S1:** Demographics in patients with ACS with/without GTN use.... **p 8**

10 **Supplementary Table S2:** Characteristics of ACS and PCI procedures in the GTN and non-
11 GTN groups.....**p 9**

12 **Supplementary Table S3:** Baseline characteristics of the GTN group with and without the
13 incidence of MACE **p 11**

14 **Supplementary Table S4:** Demographics in elderly and non-elderly patients with ACS
15 with/without GTN use..... **p 13**
16

17 **Supplementary Methods**

18 **S1: Design and study population - geographic characteristics of hospital location**

19 Miyazaki Prefectural Nobeoka Hospital is the only regional hospital that plays a central role
20 in acute intensive care and is the only facility in Nobeoka City with a cardiac catheterization
21 laboratory where percutaneous coronary intervention can be performed (1,2). The nearest
22 facility with a catheter laboratory is approximately 60 km from our hospital in another
23 prefecture. The second nearest facility with a catheter laboratory is approximately 90 km
24 from our hospital in another city in Miyazaki prefecture. Therefore, it is highly unlikely that
25 patients with acute coronary syndrome (ACS) in Nobeoka City were transported by
26 ambulance to facilities other than ours. These features of our hospital allowed us to calculate
27 the accurate clinical outcomes of patients hospitalized for ACS in Nobeoka City.

28 **S2: Definitions of coronary risk factors**

29 In accordance with the Japanese Society of Hypertension 2009 Guidelines, hypertension was
30 defined as a systolic blood pressure of 140 mmHg or more, a diastolic blood pressure of 90
31 mmHg or more, or receiving pharmacological treatment (3). Moreover, in accordance with
32 the Japanese Atherosclerosis Society 2012 Guidelines, dyslipidemia was defined as when
33 total cholesterol was 220 mg/dL or more, low-density lipoprotein cholesterol was 140 mg/dL
34 or more, high-density lipoprotein cholesterol was less than 40 mg/dL, triglycerides were 150
35 mg/dL or more, or patients were receiving pharmacological treatment (4). Diabetes mellitus

36 was defined when the fasting plasma glucose level was 126 mg/dL or more, the casual
37 plasma glucose level was 200 mg/dL or more, the HbA1c was 6.5% or more, the 2-hour
38 plasma glucose level after 75 g glucose loading was 200 mg/dL or more, or the patient was
39 receiving oral hypoglycemic agents and insulin.

40 **S3: PCI procedures**

41 All patients received aspirin, a P2Y12 inhibitor (clopidogrel or prasugrel), and weight-
42 adjusted intravenous heparin before primary percutaneous coronary intervention (PCI) (5-9).
43 Patients had a bolus injection of intravenous unfractionated heparin at a dose of 70 to 100
44 units/kg and maintenance of activated coagulation time at 250 seconds or longer. Invasive
45 coronary angiography was performed with standard techniques. At least two different views
46 were obtained for each main vessel. The extent of stenosis of each lesion was evaluated and
47 recorded based on the visual assessment. The interventional cardiologist judged the indication
48 of revascularization for culprit lesions. In primary PCI, the efficacy of revascularization of
49 the culprit artery was comprehensively evaluated for improvement in angiographic findings,
50 symptom relief, hemodynamic and electrical stabilization, and resolution of ST-segment
51 elevation by electrocardiogram (ECG). Door-to-balloon time was measured as an index of
52 early reperfusion in primary PCI for acute coronary syndrome (ACS) and aimed for a door-
53 to-balloon time shorter than 90 minutes in accordance with the guideline (10). Successful
54 reperfusion was defined as an acquisition of TIMI 3 flow after PCI.

55 All patients with ACS after PCI were immediately and comprehensively treated in the
56 coronary care unit while monitoring their ECG and vital signs. Cardiac rehabilitation was
57 performed at an individually appropriate timing in reference to peak creatinine kinase level or
58 the presence/absence of complications after ACS in the coronary care unit (11).

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Table S1: Demographics in patients with ACS with and without GTN use

	Total (n = 947)	GTN group (n = 289)	Non-GTN group (n = 658)	p-value
Height (cm)	161.8 (154.0-168.0)	162.0(156.0-168.0)	161.2 (153.0-168.0)	0.334
Body weight (kg)	60.7 (52.9-69.5)	62.0 (54.0-70.2)	60.3 (52.0-68.5)	0.052
BMI (kg/m ²)	23.4 (21.4-26.0)	23.7 (21.4-26.3)	23.4 (21.4-25.8)	0.114
Past history				
PCI, n (%)	140 (14.7)	52 (17.9)	88 (13.3)	0.065
CABG, n (%)	6 (0.6)	3 (1.0)	3 (0.4)	0.298
MI, n (%)	93 (9.8)	34 (11.7)	59 (8.9)	0.183
Stroke, n (%)	87 (9.1)	29 (10.0)	58 (8.8)	0.549
Antihypertensive therapy before ACS	501 (52.9)	151 (52.2)	350 (53.1)	0.789
Calcium channel blocker, n (%)	381 (40.2)	117 (40.4)	264 (40.1)	0.916
ACEi/ARB, n (%)	298 (31.4)	84 (29.0)	214 (32.5)	0.291
β blocker, n (%)	61 (6.4)	18 (6.2)	43 (6.2)	0.860
diuretic, n (%)	52 (5.4)	18 (6.2)	34 (4.9)	0.509
Antithrombotic drug use before ACS				
Aspirin, n (%)	147 (15.5)	60 (20.7)	87 (12.7)	0.003
Clopidogrel, n (%)	27 (2.8)	5 (1.7)	22 (3.2)	0.170
Prasugrel, n (%)	2 (0.2)	1 (0.3)	1 (0.1)	0.549
Warfarin, n (%)	11 (1.1)	7 (2.4)	4 (0.5)	0.016
Direct oral anticoagulants, n (%)	13 (1.3)	7 (2.4)	6 (0.8)	0.066

91 Data are presented as medians (interquartile ranges) or numbers (percentages).

92 ACEi, angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; ARB,
93 angiotensin II receptor blocker; BMI, body mass index; CABG, coronary artery bypass graft;

94 GTN, nitroglycerin; MI, myocardial infarction; PCI, percutaneous coronary intervention.

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Table S2: Characteristics of ACS and PCI procedures

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in the GTN and non-GTN groups

	Total (n = 947)	GTN group (n = 289)	Non-GTN group (n = 658)	p-value
PCI approach vessel, n (%)				
Radial artery	796 (84.0)	251 (86.8)	545 (82.8)	0.348
Brachial artery	86 (9.0)	23 (7.9)	63 (9.5)	
Femoral artery	65 (6.8)	15 (5.1)	50 (7.5)	
PCI lesion, n (%)				
LMT	36 (3.8)	10 (3.4)	26 (3.9)	0.108
LAD	403 (42.5)	126 (43.5)	277 (42.0)	
LCX	137 (14.4)	54 (18.6)	83 (12.6)	
RCA	370 (39.0)	98 (33.9)	272 (41.3)	
SVG	1 (0.1)	1 (0.3)	0 (0.0)	
Culprit lesion RCA, n (%)	370 (39.0)	98 (33.9)	272 (41.3)	0.031
Multivessel coronary artery disease, n (%)	388 (40.9)	122 (42.2)	266 (40.4)	0.606
Killip Classification, n (%)				
1	594 (62.7)	183 (63.3)	411 (62.4)	0.927
2	164 (17.3)	45 (15.5)	119 (18.0)	
3	60 (6.3)	22 (7.6)	38 (5.7)	
4	129 (13.6)	39 (13.4)	90 (13.6)	
PCI procedure, n (%)				
Drug-eluting stents	805 (85.0)	239 (82.6)	566 (86.0)	0.241
Bare metal stents	74 (7.8)	22 (7.6)	52 (7.9)	
POBA, only	53 (5.5)	21 (7.2)	32 (4.8)	
Aspiration, only	15 (1.5)	7 (2.4)	8 (1.2)	
Peak CK level, (units/L)	1762.0 (724.7-3458.5)	1740.0 (736.5-3512.0)	1824.0 (713.0-3459.0)	0.920
Door-to-balloon time, (min)	73.0 (58.0-102.0)	73.0 (58.0-95.0)	73.0 (58.0-106.0)	0.245
Use of imaging device, n (%)	934 (98.6)	283 (97.9)	651 (98.9)	0.218
Cardiac and respiratory assist devices, n (%)	164 (17.3)	41 (14.1)	123 (18.6)	0.092
IABP, n (%)	95 (10.0)	31 (10.7)	64 (9.7)	0.637
ECMO, n (%)	26 (2.7)	7 (2.4)	19 (2.8)	0.687
Temporary pacing, n (%)	87 (9.1)	17 (5.8)	70 (10.6)	0.020
NPPV or ventilator, n (%)	80 (8.4)	18 (6.2)	62 (9.4)	0.104
PCI Failure, n (%)	5 (0.5)	1 (0.3)	4 (0.6)	0.609
Antithrombotic medication at discharge				
Aspirin, n (%)	937 (98.9)	284 (98.2)	653 (99.2)	0.179
Clopidogrel, n (%)	369 (38.9)	106 (36.6)	263 (39.9)	0.428
Prasugrel, n (%)	565 (59.6)	176 (60.8)	389 (59.1)	0.563
Warfarin, n (%)	22 (2.3)	10 (3.4)	12 (1.8)	0.283
Direct oral anticoagulants, n (%)	59 (6.2)	23 (7.9)	36 (5.4)	0.145

98 Data are presented as medians (interquartile ranges) or numbers (percentages).



99 CK, creatine kinase; ECMO, extracorporeal membrane oxygenation; GTN, nitroglycerin; IABP,
100 intra-aortic balloon pumping; LAD, left anterior descending artery; LCX, left circumflex
101 artery; LMT, left main coronary trunk; NPPV, non-invasive positive airway pressure
102 ventilation; PCI, percutaneous coronary intervention; POBA, percutaneous old balloon
103 angioplasty; RCA, right coronary artery; STEMI, ST-elevation myocardial infarction; SVG,
104 saphenous vein graft.
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Table S3: Baseline characteristics of the GTN group

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with and without the incidence of MACE

	GTN group with MACE (n = 56)	GTN group without MACE (n = 233)	p-value
Age (years)	77.0 (68.2-86.0)	68.0 (60.0-78.0)	< 0.001
Elderly (≥ 75 years), n (%)	33 (58.9)	79 (33.9)	< 0.001
Male, n (%)	38 (67.8)	177 (75.9)	0.212
Height (cm)	159.0 (153.5-165.0)	163.0 (156.9-168.0)	0.030
Body weight (kg)	56.6 (49.2-68.0)	62.6 (55.3-71.0)	0.015
BMI (kg/m ²)	23.0 (21.2-25.8)	23.9 (21.4-26.4)	0.240
Waist circumference (cm)	90.0 (82.0-97.0)	87.5 (82.0-94.0)	0.446
Systolic blood pressure (mmHg)	130.0 (95.0-141.0)	132.0 (113.0-146.0)	0.011
Diastolic blood pressure (mmHg)	76.5 (57.7-91.2)	84.0 (70.0-95.0)	0.011
Previous/current smoking, n (%)	22 (39.2)	117 (50.2)	0.142
Hypertension, n (%)	47 (83.9)	192 (82.4)	0.786
Dyslipidemia, n (%)	40 (71.4)	182 (78.1)	0.287
Diabetes mellitus, n (%)	25 (44.6)	75 (32.1)	0.079
Metabolic syndrome, n (%)	13 (23.2)	99 (42.4)	0.005
Hemodialysis, n (%)	4 (7.1)	6 (2.5)	0.093
TG (mg/L)	93.0 (72.5-132.0)	107.0 (72.0-154.0)	0.429
HDL-C (mg/L)	42.5 (38.2-52.7)	50.0 (42.5-59.0)	0.001
LDL-C (mg/L)	110.0 (87.0-140.2)	124.0 (99.5-155.0)	0.034
HbA1c (%)	6.30 (5.60-7.55)	5.90 (5.60-6.50)	0.068
eGFR (mL/min per 1.73 m ²)	45.6 (29.4-63.5)	63.8 (52.2-75.2)	< 0.001
LVEF (%)	45.8 (35.5-52.7)	58.0 (53.0-62.8)	< 0.001
Past history			
PCI, n (%)	13 (23.2)	39 (16.7)	0.257
CABG, n (%)	1 (1.7)	2 (0.8)	0.539
MI, n (%)	13 (23.2)	21 (9.0)	0.003
Stroke, n (%)	10 (17.8)	19 (8.1)	0.030
Antihypertensive therapy before ACS, n (%)	27 (48.2)	124 (53.2)	0.501
Calcium channel blocker, n (%)	20 (35.7)	97 (41.6)	0.418
ACEi/ARB, n (%)	13 (23.2)	71 (30.4)	0.283
β blocker, n (%)	7 (12.5)	11 (4.7)	0.031
Diuretic, n (%)	7 (12.5)	11 (4.7)	0.031
Antithrombotic drug use before ACS			
Aspirin, n (%)	14 (25.0)	46 (19.7)	0.384
Clopidogrel, n (%)	0 (0)	5 (2.1)	0.269
Prasugrel, n (%)	0 (0)	1 (0.4)	0.623
Warfarin, n (%)	1 (1.7)	6 (2.5)	0.730
Direct oral anticoagulants, n (%)	3 (5.3)	4 (1.7)	0.112

STEMI, n (%)	45 (80.3)	181 (77.6)	0.663
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108 Data are presented as medians (interquartile ranges) or numbers (percentages).

109 ACEi, angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; ARB,
110 angiotensin II receptor blocker; BMI, body mass index; CABG, coronary artery bypass graft;
111 eGFR, estimated glomerular filtration rate; GTN, nitroglycerin; HDL-C, high-density
112 lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVEF, left-ventricular
113 ejection fraction; MACE, major adverse cardiovascular events; MI, myocardial infarction; PCI,
114 percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; TG,
115 triglyceride.

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Table S4: Baseline characteristics in elderly and non-elderly patients with ACS

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with/without GTN use

	Elderly (≥ 75 years) (n = 378)			Non-elderly (< 75 years) (n = 569)		
	GTN group (n = 112)	Non-GTN group (n = 266)	p-value	GTN group (n = 177)	Non-GTN group (n = 392)	p-value
Age (years)	82.0 (78.2-86.0)	82.0 (78.0-86.0)	0.951	64.0 (56.0-69.0)	64.0 (57.2-70.0)	0.296
Male, n (%)	64 (57.1)	136 (51.1)	0.285	151 (85.3)	327 (83.4)	0.569
Height (cm)	155.0 (146.8-162.0)	154.0 (146.8-161.1)	0.871	165.5 (160.0-170.0)	165.0 (159.7-169.0)	0.303
Body weight (kg)	55.0 (46.1-61.3)	54.0 (45.9-60.9)	0.464	66.3 (59.0-74.3)	64.6 (57.6-72.7)	0.096
BMI (kg/m ²)	22.4 (20.3-26.0)	22.8 (20.2-24.8)	0.715	24.5 (22.3-26.4)	23.8 (21.8-26.2)	0.135
Waist circumference (cm)	84.7 (78.6-91.0)	85.0 (80.0-93.0)	0.632	89.5 (83.0-96.0)	87.5 (82.0-93.0)	0.034
Systolic blood pressure (mmHg)	132.0 (100.0-143.0)	134.0 (113.7-157.0)	0.007	132.0 (119.0-144.0)	133.0 (112.0-157.0)	0.511
Diastolic blood pressure (mmHg)	74.0 (64.0-87.0)	75.0 (64.0-86.2)	0.868	84.0 (69.0-97.0)	87.0 (73.0-98.0)	0.380
Previous/current smoking, n (%)	28 (25.0)	74 (27.8)	0.573	111 (62.7)	252 (64.2)	0.718
Hypertension, n (%)	96 (85.7)	210 (78.9)	0.126	143 (80.7)	268 (68.3)	0.002
Dyslipidemia, n (%)	86 (76.7)	160 (60.1)	0.002	136 (76.8)	275 (70.1)	0.099
Diabetes mellitus, n (%)	29 (25.8)	69 (25.9)	0.992	71 (40.1)	131 (33.4)	0.122
Metabolic syndrome, n (%)	24 (21.4)	61 (22.9)	0.802	88 (49.7)	157 (40.0)	0.070
Hemodialysis, n (%)	2 (1.7)	6 (2.2)	0.772	8 (4.5)	13 (3.3)	0.481
TG (mg/L)	89.0 (69.0-128.0)	84.0 (62.0-123.5)	0.220	117.0 (84.0-169.7)	126.0 (85.0-207.0)	0.053
HDL-C (mg/L)	49.0 (41.2-62.5)	49.0 (41.0-60.7)	0.643	48.0 (41.0-58.0)	47.0 (39.0-55.5)	0.190
LDL-C (mg/L)	117.5 (94.2-141.0)	112.0 (89.0-140.0)	0.389	127.0 (99.0-160.0)	129.0 (102.0-159.0)	0.892
HbA1c (%)	5.80 (5.50-6.40)	5.80 (5.40-6.20)	0.514	6.00 (5.63-7.07)	5.90 (5.53-6.78)	0.109
eGFR (mL/min per 1.73 m ²)	52.0 (36.2-63.6)	52.7 (40.2-64.4)	0.224	66.7 (55.0-81.0)	65.0 (54.0-77.6)	0.231
LVEF (%)	54.5 (45.8-61.4)	55.7 (47.4-61.5)	0.579	57.4 (51.7-62.6)	57.4 (50.0-62.7)	0.661
Past history						
PCI, n (%)	21 (18.7)	39 (14.6)	0.321	31 (17.5)	49 (12.5)	0.111
CABG, n (%)	2 (1.7)	2 (0.7)	0.370	1 (0.5)	1 (0.2)	0.563
MI, n (%)	15 (13.3)	26 (9.7)	0.302	19 (10.7)	33 (8.4)	0.375
Stroke, n (%)	18 (16.0)	36 (13.5)	0.520	11 (6.2)	22 (5.6)	0.776
Antihypertensive therapy before ACS, n (%)	71 (63.3)	182 (68.4)	0.343	80 (45.1)	168 (42.8)	0.602
Calcium channel blocker, n (%)	55 (49.1)	137 (51.5)	0.670	62 (35.0)	127 (32.3)	0.537
ACEi/ARB, n (%)	36 (32.1)	107 (40.2)	0.139	48 (27.1)	107 (27.2)	0.965
β blocker, n (%)	8 (7.1)	20 (7.5)	0.899	10 (5.6)	23 (5.8)	0.918
Diuretic, n (%)	12 (10.7)	19 (7.1)	0.248	6 (3.3)	15 (3.8)	0.798
Antithrombotic drug use before ACS						
Aspirin, n (%)	28 (25.0)	44 (16.5)	0.056	32 (18.0)	43 (10.9)	0.020
Clopidogrel, n (%)	3 (2.6)	9 (3.3)	0.721	2 (1.1)	13 (3.3)	0.132
Prasugrel, n (%)	0 (0)	1 (0.3)	0.516	1 (0.5)	0 (0)	0.136
Warfarin, n (%)	2 (1.7)	4 (1.5)	0.841	5 (2.8)	0 (0)	<0.001
Direct oral anticoagulants, n (%)	5 (4.4)	5 (1.8)	0.153	2 (1.1)	1 (0.2)	0.182

STEMI, n (%)	88 (78.5)	206 (77.4)	0.810	138 (77.9)	316 (80.6)	0.467
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119 Data are presented as medians (interquartile ranges) or numbers (percentages).

120 ACEi, angiotensin-converting enzyme inhibitor; ACS, acute coronary syndrome; ARB,
121 angiotensin II receptor blocker; BMI, body mass index; CABG, coronary artery bypass graft;
122 eGFR, estimated glomerular filtration rate; GTN, nitroglycerin; HDL-C, high-density
123 lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; LVEF, left-ventricular
124 ejection fraction; MACE, main adverse cardiac events; MI, myocardial infarction; PCI,
125 percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction; TG,
126 triglyceride.