Age-Specific Incidence Rates of Acute Coronary Syndrome in Japan

— A Special Gift From a Collaboration of Cardiologists and Epidemiologists —

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Researchers in the MONICA study attempted to answer the question of whether differences in the incidence rate of coronary artery disease (CAD) existed between countries by using the unified criteria of acute myocardial infarction (AMI) and by evaluating the age-adjusted incidence rates using the WHO standard population.¹ They found very high incidence rates of first-ever AMI in Finland (600 per 100,000 person-years in males) and very low rates in China (<100 per 100,000 person-years in males). Unfortunately, data for Japan were not included in the study and Professor Ueshima later added it (based on Isomura's report²) to the results of the MONICA project and low incidence rates of AMI in Japan were revealed.³ However, these data were obtained more than 20 years ago and the current age distributions are very different from that time.

Japan is the most rapidly aging country in the world and the proportion of elderly people is very high. There should be a relatively large number of elderly people with AMI in Japan now; however, most previous studies in Japan have only addressed age-adjusted incidence rates of AMI or provided age-specific incidence rates of AMI only in middle-aged people (shown in the **Supplementary Table**). Thus, it

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would be interesting to know the incidence rates of CAD in all age categories, but there have been very few studies that provided age-specific incidence rates of acute coronary syndrome (ACS) or AMI, probably due to difficulties in conducting appropriate studies on age-specific incidence rates of CAD. Nielsen et al described 4 methodological problems for the determination of the incidence rate of ACS: (1) selection biases of the patients included in the study, (2) lack of identification and control of the background population, (3) uncertainties and inconsistencies in the use of diagnostic criteria, and (4) missing data.⁴

Table 1 shows studies conducted in Western countries that provided comprehensive age-specific incidence rates of CAD (AMI, ACS with/without sudden cardiac death (SCD)).^{4–6} Both the prospective study in Denmark⁴ and the comprehensive registry study in Canada⁶ provided similar age-specific incidence rates of AMI in middle-aged people and these incidence rates are also similar to the incidence rates in Western European nations in the WHO MONICA project.¹ On the other hand, Canadian researchers showed

Table 1. Studies Assessing Age-Specific Incidence Rates of ACS/AMI in Western Countries

Study name (published year) Reference	Study design	Analytical method	Subjects	Outcomes	Age-specific incidence rates (95% CI)
Göteborg/Sweden (1997) ⁵	The Myocardial Infarction Register in Göteborg (n=450,000 inhabitants)	Age-specific crude incidence rates	Women 35–44 years old	The MONICA criteria: non-fatal AMI + fatal AMI	14
			Women 45–54 years old		55
			Women 55–64 years old		194
	Non-fatal AMI in hospital records SCD among all persons living in Göteborg, Sweden, aged 35–64 years were included	Age-specific crude incidence rates	Men 35–44 years old	The MONICA criteria: non-fatal AMI + fatal AMI	62
			Men 45–54 years old		272
			Men 55–64 years old		687

(Table 1 continued the next page.)

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Study name (published year) Reference	Study design	Analytical method	Subjects	Outcomes	Age-specific incidence rates (95% CI)
Aarhus/Denmark (2007) ⁴	Prospective cohort of residents of the municipality of Aarhus, Denmark, aged 30–69 years (n=138,290) Observation period: April 2000 to March 2002	Age-specific crude incidence rates	Women 30–39 years old	Definite AMI + unstable angina + SCD	25
			Women 40–49 years old		73
			Women 50–59 years old		157
			Women 60–69 years old		437
			Women age-adjusted 30–69 years old		137
		Age-specific crude incidence rates	Men 30–39 years old	Definite AMI + unstable angina + SCD	39
			Men 40–49 years old		156
			Men 50–59 years old		472
			Men 60–69 years old		1,106
			Men age-adjusted 30–69 years old		331
Canadian Cardiovascular Outcomes Research (2009) ⁶	(1) Annual Canadian Mortality Database (n=18,102, 2,004 death certificates) (2) Canadian Institute for Health Information's Hospital Morbidity Database (n=56,759, 2,004 in-hospital records) (n=180,102 in-hospital patients and death certificates) Observation period: 1994–2004	Crude annual incidence rate (per 100,000 person-years) = total annual no. of cases of AMI as numerator/annual population of Canada National Census as denominator Direct age-adjustment was performed using the 1991 Canadian population census as the standard	Women 20–49 years old	Death certificates (D) + in-hospital records of patients with AMI (H)	1.4 (death); 15.7 (in-hospital)
			Women 50–64 years old		18.6 (D); 125.4 (H)
			Women 65–74 years old		90.6 (D); 374.8 (H)
			Women ≥75 years old		524.5 (D); 1,009.6 (H)
			Women overall		64.2 (D)
			Men 20–49 years old	Death certificates (D) + in-hospital records of patients with AMI (H)	7.2 (D); 66.9 (H)
			Men 50–64 years old		69.6 (D); 422.2 (H)
			Men 65–74 years old		212.2 (D); 764.3 (H)
			Men ≥75 years old		743.9 (D); 1,509.4 (H)
			Men overall		86.7 (D)

ACS, acute coronary syndrome; AMI, acute myocardial infarction; SCD, sudden cardiac death.

Table 2. Studies Assessing Age-Specific Incidence Rates of ACS/AMI in Japan

Study name (published year) Reference	Study design	Analytical method	Subjects	Outcomes	Age-specific incidence rates (95% CI)
Hiroshima/Nagasaki study (1990) ⁷	Hiroshima and Nagasaki Prefecture prospective cohorts Observation period: 1958–1984 (n=20,141) 360 cases of AMI (definite and possible)	Average age-adjustment was performed using the age distribution of the cohort study	Women 30–39 years old	The MONICA criteria: definite and probable AMI not including SCD	0.3
			Women 40–49 years old		8.7
			Women 50–59 years old		30.9
			Women 60–69 years old		132.2
			Women 70–79 years old		345.7
			Women ≥80 years old		557.2
			Women age-adjusted		78.8
			Men 30–39 years old	The MONICA criteria: definite and probable AMI not including SCD	5.1
			Men 40–49 years old		34.8
			Men 50–59 years old		136.1
			Men 60–69 years old		419.1
			Men 70–79 years old		683.4
			Men ≥80 years old		908.7
			Men age-adjusted		204.9
JMS cohort (2008) ⁸	12 areas and area-related rural hospital-based prospective cohorts 10.7 years follow-up period (1992–) (n=12,490) in-hospital records (n=92 consecutive patients with 1st-ever AMI) not including SCD	Direct age-adjustment was performed using the 1985 Japan population census as the standard	Women ≤39 years old	The MONICA criteria In-hospital records of patients with AMI not including SCD	0.0
			Women 40–49 years old		0.0
			Women 50–59 years old		25.5
			Women 60–69 years old		45.8
			Women ≥70 years old		217.1
			Women age-adjusted		34.2
			Men ≤39 years old	The MONICA criteria In-hospital records of patients with AMI not including SCD	19.1
			Men 40–49 years old		16.8
			Men 50–59 years old		80.2
			Men 60–69 years old		202.1
			Men ≥70 years old		424.3
			Men age-adjusted		123.7

(Table 2 continued the next page.)

Study name (published year) Reference	Study design	Analytical method	Subjects	Outcomes	Age-specific incidence rates (95% CI)
Yamagata (2016) ⁹	Multicenter-hospital-based Inhospital records (n=5,325 consecutive patients with 1st-ever AMI not including cardiac death) Study period: 1994–2010	Crude annual incidence rate (per 100,000 person- years)=total annual no. of cases of AMI as numerator/annual population of each area as denominator Direct age-adjustment was performed using the 2005 Japan population census as the standard	Women ≤64 years old	The MONICA criteria	4.0 (3.5–4.6)
			Women 65–74 years old	Inhospital records of patients with AMI not including SCD	44.1 (39.3–49.1)
			Women ≥75 years old		101.1 (92.2–110.0)
			Women age-adjusted		20.3 (18.4–22.3)
			Men ≤64 years old	The MONICA criteria	23.4 (21.5–25.3)
			Men 65–74 years old	Inhospital records of patients with AMI not including SCD	131.1 (122.0–140.1)
			Men ≥75 years old		178.1 (162.8–193.4)
			Men age-adjusted		45.6 (43.1–48.1)
Takashima (2008) ¹⁰	Population-based, data from all hospitals (3 hospitals inside the area and a Shiga University Hospital), county ambulance records and county death certificates (cross-checked by epidemiologists and cardiologists) were certificated by epidemiologists in Shiga University of Medical Science (total population=55,451; census 2000) Observation period: 1990–2001	Crude annual incidence rate (per 100,000 person- years)=total annual number of cases of AMI as numerator/ annual population of the study area as denominator	Women 45–54 years old	The MONICA criteria: definite AMI including SCD	0
			Women 55–64 years old		27.2 (7.4–71.9)
			Women 65–74 years old		78.7 (34.9–154.1)
			Women 75–84 years old		92.2 (34.7–201.2)
			Women ≥85 years old		121.5 (22.9–381.2)
			Men ≤35 years old	The MONICA criteria: definite AMI including SCD	2.9 (0.2–12.6)
			Men 35–44 years old		33.9 (11.2–80.2)
			Men 45–54 years old		88.2 (41.5–166.1)
			Men 55–64 years old		84.1 (41.4–153.2)
			Men 65–74 years old		135.4 (66.7–246.8)
			Men 75–84 years old		283.8 (145.5–503.0)
			Men ≥85 years old		428.6 (115.9–1,131.2)
Iwate (2017) ¹¹	Population-based, data from all hospitals with a catheterization laboratory (2 hospitals (Kuji and Ninohe prefectural hospitals) inside the study area and Iwate Medical University Hospital, Hachinohe Redcross Hospital, Hachinohe Municipal Hospital and Aomori Rosai Hospital) and small hospitals and clinics (4 institutes) were certificated by epidemiologists in Iwate Medical University (total population=116,004; census 2014) Observation period: 2012–2014	Crude annual incidence rate (per 100,000 person- years)=total annual number of cases of AMI as numerator/ annual population of the study area as denominator	Women 30–39 years old	The MONICA criteria: definite AMI including SCD	5.7 (1.9–12.3)
			Women 40–49 years old		4.7 (1.3–10.9)
			Women 50–59 years old		11.8 (5.8–20.3)
			Women 60–69 years old		24.4 (15.3–35.7)
			Women 70–79 years old		67.5 (52.3–85.6)
			Women 80–89 years old		204.5 (177.4–234.5)
			Men 30–39 years old	The MONICA criteria: definite AMI including SCD	11.2 (5.4–19.6)
			Men 40–49 years old		56.4 (42.3–72.7)
			Men 50–59 years old		78.3 (61.6–97.3)
			Men 60–69 years old		146.4 (123.2–171.6)
			Men 70–79 years old		239.5 (210.1–271.8)
			Men 80–89 years old		420.2 (380.7–462.1)

ACS, acute coronary syndrome; AMI, acute myocardial infarction; SCD, sudden cardiac death.

very high incidence rates of in-hospital AMI in elderly people, both female (1,009.6 per 100,000 person-years) and male (1,509.4 per 100,000 person-years).⁶

Table 2 shows studies that provided age-specific incidence rates of CAD in Japan, including 2 prospective cohort studies,^{7,8} a multihospital-based registry study,⁹ and 2 population-based registry studies.^{10,11} The incidence rates in middle-aged individuals in the 2 prospective cohort studies^{10,11} were higher than the rates in the report by Isomura.² Age-specific incidence rates in elderly people in the JMS cohort,⁸ Takashima AMI registry¹⁰ and Northern Iwate Registry¹¹ were similar, but the rates in the Yamagata AMI registry⁹ were lower than in those studies. Collecting patients' data from tertiary referral hospitals would definitely contribute to a selection bias. Very old patients and patients with very serious conditions such as malnutrition are not likely to be transported to the tertiary referral hospitals because of their very low chance of recovery. Moreover, cases of SCD attributable to ACS were not included in the Yamagata registry.⁹ These might be reasons for the underestimation of incidence rates, especially in elderly people. Although prospective studies can provide reliable data for the incidence rates of CAD, the study design requires a large-scale sample and an observation period of 10 years or longer.

In an inventory survey of CAD, the most formidable challenge is how to handle SCD. Because it has been shown that CAD accounts for more than 75% of the total number of SCDs,¹² much effort was made in previous studies to recruit patients with AMI who died out of hospital. Researchers in the Takashima AMI registry¹⁰ and Northern Iwate Heart Disease registry¹¹ consisted of not only cardiologists but also epidemiologists and the collaboration of these 2 teams almost completed inventory surveys including SCD, whereas tertiary referral hospital-based registries such as the Yamagata AMI registry⁹ and the Miyagi AMI registry¹³ showed relatively low incidence rates probably due to underestimation. Researchers in the Yamagata AMI registry recently published a study that addressed out-of-hospital cardiac arrest (OHCA).¹⁴ Surprisingly, they showed that more than 50% of the total cases of AMI were attributed to OHCA. If they re-estimated the age-specific incidence rates of AMI using data that included cases of OHCA, the results would be different from the previously published data.

In this issue of the Journal, Ogata et al¹⁵ report on their attempt to reveal accurate age-specific incidence rates of AMI and ACS including SCD by bringing together cardiologists and epidemiologists. They show not only comprehensive age-specific incidence rates of AMI, but also age-specific incidence rates of ACS, including fatal/non-fatal AMI, unstable angina and SCD. They utilized data from the Nobeoka Medical Control Consultative Committee for Emergency Transportation and found cases of highly suspected CAD-related SCD among cases of OHCA. This achievement should be warmly praised.

However, all the studies (Takashima, Iwate and Nobeoka) were conducted in rural areas and there have been no studies on age-specific incidence rates of CAD in urban areas of Japan. We hope that a further collaboration of cardiologists and epidemiologist will conduct a com-

plete inventory survey in an urban area of Japan. That team would certainly give us a special gift.

Conflicts of Interest

None declared.

References

1. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project: Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation* 1994; **90**: 583–612.
2. Isomura K. Study on the development of the community-based long-term follow-up system for cardio-cerebrovascular diseases in 1993 Annual Report of the Cardiovascular Diseases. National Cardiovascular Center: Suita 1994 (in Japanese).
3. Ueshima H. Explanation for the Japanese paradox: Prevention of increase in coronary heart disease and reduction in stroke. *J Atheroscler Thromb* 2007; **14**: 278–286.
4. Nielsen KM, Foldspang A, Larsen ML, Gerdes LU, Rasmussen S, Faergeman O. Estimating the incidence of the acute coronary syndrome: Data from a Danish cohort of 138 290 persons. *Eur J Cardiovasc Prev Rehabil* 2007; **14**: 608–614.
5. Wilhelmsen L, Rosengren A, Johansson S, Lappas G. Coronary heart disease attack rate, incidence and mortality 1975–1994 in Goteborg, Sweden. *Eur Heart J* 1997; **18**: 572–581.
6. Tu JV, Nardi L, Fang J, Liu J, Khalid L, Johansen H. National trends in rates of death and hospital admissions related to acute myocardial infarction, heart failure and stroke, 1994–2004. *CMAJ* 2009; **180**: E118–E125.
7. Kodama K, Sasaki H, Shimizu Y. Trend of coronary heart disease and its relationship to risk factors in a Japanese population: A 26-year follow-up, Hiroshima/Nagasaki study. *Jpn Circ J* 1990; **54**: 414–421.
8. Ishikawa S, Kayaba K, Gotoh T, Nago N, Nakamura Y, Tsutsumi A, et al. Incidence of total stroke, stroke subtypes, and myocardial infarction in the Japanese population: The JMS Cohort Study. *J Epidemiol* 2008; **18**: 144–150.
9. Wanezaki M, Watanabe T, Nishiyama S, Hirayama A, Arimoto T, Takahashi H, et al. Trends in the incidences of acute myocardial infarction in coastal and inland areas in Japan: The Yamagata AMI Registry. *J Cardiol* 2016; **68**: 117–124.
10. Rumana N, Kita Y, Turin TC, Murakami Y, Sugihara H, Morita Y, et al. Trend of increase in the incidence of acute myocardial infarction in a Japanese population: Takashima AMI Registry, 1990–2001. *Am J Epidemiol* 2008; **167**: 1358–1364.
11. Nakamura M, Tanaka F, Segawa T, Takahashi T, Matsuura Y, Sakai T, et al. Temporal trends in the incidence and clinical features of acute myocardial infarction in a Japanese rural area from 2006 to 2014. *Circ J* 2017; **81**: 1854–1861.
12. Hayashi M, Shimizu W, Albert CM. The spectrum of epidemiology underlying sudden cardiac death. *Circ Res* 2015; **116**: 1887–1906.
13. Cui Y, Hao K, Takahashi J, Miyata S, Shindo T, Nishimiya K, et al. Age-specific trends in the incidence and in-hospital mortality of acute myocardial infarction over 30 years in Japan: Report from the Miyagi AMI Registry Study. *Circ J* 2017; **81**: 520–528.
14. Toshima T, Hirayama A, Watanabe T, Goto J, Kobayashi Y, Otaki Y, et al. Unmet needs for emergency care and prevention of prehospital death in acute myocardial infarction. *J Cardiol* 2021; **77**: 605–612.
15. Ogata S, Marume K, Nakai M, Kaichi R, Ishii M, Ikebe S, et al. Incidence rate of acute coronary syndrome including acute myocardial infarction, unstable angina, and sudden cardiac death in Nobeoka City for the super-aged society of Japan. *Circ J* 2021; **85**: 1722–1730.

Supplementary Files

Please find supplementary file(s);
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