Younger trend in acute myocardial infarction in China

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Abstract
There are more and more acute myocardial infarction (AMI). However, little is known about its age trend. Here, we report younger trend in AMI in China. To check literatures from PubMed according to keywords “AMI and Chin Med J (Engl)” and collect available data on ages from original research articles published in Chin Med J (Engl) from 1990 to 2019. Age groups were divided into 1990s, 1995s, 2000s, 2005s, 2010s, 2015s, and 2020s, respectively. Means of minimum ages of each group were about 55.0, 46.4, 48.2, 55.0, 47.1, 43.9, and 52.8 years old, respectively. The age curve showed younger trend in AMI due to unhealthy lifestyle related major risk factors. This novel classification of risk factors based “environment-sleep-emotion-exercise-diet” intervention [E(e)SEEDi] is beneficial to better control and prevent AMI in the globe.

Introduction
It is well known that more than 40% deaths each year are attributed to cardiovascular disease (CVD) in China. Acute myocardial infarction (AMI) is the leading cause of death in adults with CVD. It is also a major “killer” in younger adults. Mortality of AMI in both urban and rural population in China is more than 1.1‰. However, previous studies on trends in AMI focused mainly on its sex-specific or gender differences, risk factors and mortalities, little is known about data of evidence-based age trend in AMI in China.

Results
Data on ages of patients with acute myocardial infarction were collected from original research articles published in Chin Med J (Engl) during 1990 to 2019 (Table 1). Means of minimum ages of each group are about 55.0 (1990s), 46.4 (1995s), 48.2 (2000s), 55.0 (2005s), 47.1 (2010s), 43.9 (2015s), and 52.8 (2020s) years old, respectively. According to the curve on means of minimum ages of each group, it’s easy to find younger trend in AMI in China from 2003 to 2017 (Fig. 1). However, current data on ages of AMI in 2020s are incomplete.

Discussion
There were AMI patients aged 18 years enrolled in the VIRGO (Variation in Recovery: Role of Gender on Outcomes of Young AMI Patients) study. Of course, there is the geographical inequalities in incident AMI. Thus, there is arising need for control of AMI younger by more health coverage and essential health service since it is far from reality for poor and rural regions, and modifying unhealthy lifestyle and reducing unhealthy “environment-sleep-emotion-exercise-diet” intervention [E(e)SEEDi] based major risk factors.

Currently, younger trend in AMI could be due to unhealthy lifestyle and evidence-based major risk factors are highly associated with AMI onset (Table 2). First, abnormal external environment. There is increased
risk of AMI due to exposure to cold temperatures\textsuperscript{11}, radiation, traffic noises\textsuperscript{12}, dust\textsuperscript{13}, and air pollution (such as particulate matter exposure)\textsuperscript{14-17}; And abnormal internal environment, for example, inflammation & infection\textsuperscript{18,19}, acute infection including influenza epidemics\textsuperscript{20}. Previous studies showed that acute respiratory-tract infections are associated with an increased risk of first-time AMI\textsuperscript{21}, HIV infection also increases the risk of AMI\textsuperscript{22}. Serum triglyceride levels, familial-combined hyperlipidaemia\textsuperscript{23}, and type 2 diabetes (T2D) are traditional risk factors highly linked to AMI\textsuperscript{24}.

Second, bad sleep can induce AMI. Many young and middle-aged adults often stay up late, some work in shifts, and many adults suffer from insomnia or severe obstructive sleep apnea (OSA). Third, bad emotion, anxiety and depression. Physical exertion and anger or emotional upset are triggers associated with first AMI in all regions of the world, in men and women, and in all age groups\textsuperscript{25}. Screening for depression is necessary because patients with untreated depression are associated with increased long-term mortality of AMI\textsuperscript{26}. Self-reported symptoms of depression and anxiety, especially if recurrent, were also moderately associated with the risk of incident AMI\textsuperscript{27}. HIV-infected individuals with depression have a 30% increased risk for AMI than without depression\textsuperscript{28}. However, antipsychotic use is associated with a transient increase in risk for AMI.

Fourth, physical inactivity and long-term sitting linked to obesity and T2D may induce AMI due to popularization of cars, urban buses, subways, and elevators as well as lasting watching TV at home and mobile-phone entertainment. Lastly, there are unbalance of diet and nutrition including higher “salt, fat, and sugar” and inadequate water and fresh fruits intake\textsuperscript{29}, heavy alcohol consumption. But there is a protective role of Mg and low Ca:Mg ratio against coronary heart disease (CHD)\textsuperscript{30}. Tobacco use is one of the most important causes of AMI globally, especially in men\textsuperscript{31}. In contrast, smoking ban was associated with a reduction in AMI incidence\textsuperscript{32}.

In addition, the rates of awareness, treatment, and control of hypertension are still lower. Some drugs, e.g. cocaine abuse, oral contraceptive use, and post menopausal hormone replacement therapy may increase the risk of AMI\textsuperscript{33}. Incidence of AMI also associated with stopping evidence-based pharmacotherapy, e.g., statin, beta-blockers and clopidogrel\textsuperscript{34}. Early initiation of statin treatment and beta-blockers are underused for primary and secondary prevention of CHD before the first AMI.

So far, a number of risk factors have been identified to link with AMI and higher risk factor levels at younger ages link to the earlier age of AMI\textsuperscript{35,36}. The unhealthy E(e)SEEDi lifestyle results in not only CHD and C-type hypertension\textsuperscript{37}, but also AMI younger. Thus, a new program is indeed necessary for prevention and management of AMI. Without doubt, the published standardized comprehensive iRT-ABCDEF program for AMI is worthy of conduction in the globe\textsuperscript{38}. As a magic and novel “polypill” \textsuperscript{39}, healthy E(e)SEEDi lifestyle can help to halt AMI younger and reduce its morbidity and mortality due to better self-management of major risk factors.
Because the famous SPRINT (Systolic Blood Pressure Intervention Trial) found that a lower systolic blood-pressure is better for less AMI and other cardiovascular events, “clinical trial will change practice”\(^40\), it helps us to understand and support not only more aggressive treatment of hypertension but also the renewed AHA Guideline on a more strict definition of hypertension (130/80 mmHg). It can be said that more coverage by healthy E(e)SEEDi lifestyle and application of the iRT-ABCDEF program, more effectiveness in prevention of AMI younger.

Positive cardiovascular prevention will help reducing the first AMI among high risk individuals, new targets and treatments help to develop novel cardioprotective strategies\(^41-44\) and better biomarkers for screening, diagnosis or prognosis for patients with AMI. Since the China Acute Myocardial Infarction (CAMI) Registry is a good platform for evaluation, healthcare, investigation and prevention, it will help to improve quality of care (QOL) and better prevent AMI\(^45-46\). For example, invasive coronary angiography should be used rationally according to patients’ clinical presentation so as to get better diagnosis and care. With further understanding of cellular and molecular mechanisms on CVD (such as atherosclerosis, hypertension, heart failure, and stroke) and analysis of human atlases on cardiac cell and the adult heart\(^47-48\), new therapeutic targets and strategies will be developed for better control and prevention of AMI.

At the same time, to choose safer agents for anticoagulation therapy so as to improve AMI patients’ outcomes and QOL\(^49\). In addition, smoking ban linked to reduced hospitalization rates for AMI\(^50\). The iRT-ABCDEF program for management or self-management of AMI can help to control and prevent AMI so as to halt its younger trend, and improve QOL in patients with history of AMI. Herein, both the iRT-ABCDEF program and healthy E(e)SEEDi lifestyle\(^38,39\) are worthy of conduction in the globe, especially during the pandemic and post-COVID-19 era.

Data on ages of patients with AMI in this study were collected just only from original research articles published in \textit{Chin Med J (Engl)} during 1990 to 2019, which is highly authority and has a history of over a hundred and thirty years, and these papers were also finished by multi-centre clinical units in China. However, these data didn’t cover literatures published in other international journals. The curve on means of minimum ages of each group just showed younger trend in AMI in China from 2003 to 2017. they are still incomplete in 2020s. In addition, this study didn’t involve in data on patients’ gender, treatment and mortality.

In conclusion, there is indeed younger trend in AMI in China due to modern unhealthy E(e)SEEDi lifestyle and major risk factors. This novel classification of risk factors can help to prevent younger trend in AMI and improve QOL. Hence, it is worthy of conduction in the globe.

\textbf{Materials And Methods}

Literatures on AMI were checked from PubMed according to key words “AMI and \textit{Chin Med J (Engl)}” and to collect data on ages from original research articles on AMI published in \textit{Chin Med J (Engl)}. Data on
ages of patients with AMI were divided into seven groups: 1990s (1988-1992), 1995s (1993-1997), 2000s (1998-2002), 2005s (2003-2007), 2010s (2008-2012), 2015s (2013-2017), and 2020s (2018-2022), respectively, and recorded them in a table. The trend of ages in AMI was expressed with a curve on means of minimum ages of each group.

**Statistical analysis**

The results of original records were used. Data were statistically analyzed using the Statistical Package for the Social Sciences (SPSS version 17.0, SPSS Inc., Chicago, IL, USA) with t-test for comparisons between two groups. A $P$-value of $<$0.05 was considered statistically significant.

**Ethics statement**

The study was approved by Human Research Ethics Committee of the Nanchang University, Hospital of Nanchang University, Jiangxi Academy of Medical Science (approval 20120312). Data collection was followed by a study protocol that was approved by the local ethics committee. It was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2000, and all enrolled patients gave written informed consent. No potential sources of bias.

**Role of the funding source**

No funding for this study was received. All authors had full access to all study data, and the corresponding author had final responsibility for the decision to submit for publication.

**Reporting Summary.** Further information on research design is available in the Nature Research Reporting Summary linked to this article.

**Data availability**

The data that support the findings of this study are not publicly available but are available upon reasonable request from the corresponding author.

**Declarations**

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**Contributions**

CH drafted the manuscript and contributed to the critical revisions of the manuscript. CH is the corresponding author. All authors read and approved the final manuscript.

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Ethics declarations

Competing interests

The author declares no competing interests.

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Tables

Table 1. Ages of patients with AMI in China during 1990-2019.
| Time    | Literature on ages of patients with AMI                                                                 | Ages (yrs) | Mean of mini ages (yrs) |
|---------|--------------------------------------------------------------------------------------------------------|------------|-------------------------|
| 2020s   | **Chin Med J (Engl)**. 2019;132(9):1037-1044.                                                        | 56-74      | ≈52.8                   |
|         | Chin Med J (Engl). 2019;132(5):519-524.                                                               | 62.02±12.47|                         |
| 2015s   | **Chin Med J (Engl)**. 2017;130(13):1534-1539.                                                        | 44.4 ± 4.1 |                         |
|         | Chin Med J (Engl). 2017;130(5):542-548.                                                                | 62.86 ± 14.98|                      |
|         | Chin Med J (Engl). 2017;130(1):77-82.                                                                   | 38.68 ± 4.44|                         |
|         | Chin Med J (Engl). 2017;130(1):51-56.                                                                   | 58 ±12     |                         |
|         | **Chin Med J (Engl)**. 2016;129(5):518-22.                                                             | 61.5 ± 11.1|                         |
| 2010s   | Chin Med J (Engl). 2015;128(18):2415-9.                                                                | 53.78 ± 11.02| ≈43.9                  |
|         | Chin Med J (Engl). 2014;127(6):1008-11.                                                                | 62.1 ± 7.3 |                         |
|         | Chin Med J (Engl). 2013;126(21):4105-8.                                                                | 68.1 ± 8.5 |                         |
|         | Chin Med J (Engl). 2013;126(18):3481-5.                                                                | 58.2 ± 11.2|                         |
|         | Chin Med J (Engl). 2013;126(16):3079-86.                                                               | 62.8 ± 12.3|                         |
|         | Chin Med J (Engl). 2013;126(12):2281-5.                                                                | 61.8 ± 9.6 |                         |
|         | Chin Med J (Engl). 2013;126(3):464-70.                                                                 | 60.1 ± 14.4|                         |
| 2010s   | Chin Med J (Engl). 2012;125(8):1405-9.                                                                | 56 ± 12    |                         |
|         | Chin Med J (Engl). 2011;124(20):3275-80.                                                               | 60.5 ± 10.1|                         |
|         | Chin Med J (Engl). 2011;124(14):2083-8.                                                                | 62.1 ± 11.7|                         |
|         | Chin Med J (Engl). 2011;124(6):825-30.                                                                 | 59 ± 11.7  |                         |
|         | Chin Med J (Engl). 2010;123(20):2807-11.                                                               | 56.61 ± 11.44|                      |
|         | Chin Med J (Engl). 2010;123(14):1840-5.                                                                | 59 ± 12    |                         |
| 2010s   | Chin Med J (Engl). 2010;123(14):1833-9.                                                                | 57.8 ± 2.5 | ≈47.1                  |
|         | Chin Med J (Engl). 2009;122(22):2718-23.                                                                | 52 ± 11    |                         |
|         | **Chin Med J (Engl)**. 2009;122(14):1610-4.                                                             | 40-79      |                         |
|         | Chin Med J (Engl). 2009;122(6):665-9.                                                                  | 36–82      |                         |
|         | Chin Med J (Engl). 2009;122(6):636-42.                                                                  | 68.0 ± 10.6|                         |
|         | Chin Med J (Engl). 2008;121(23):2384-7.                                                                 | 60 ± 10    |                         |
|         | Chin Med J (Engl). 2008;121(9):771-5.                                                                   | 60.1 ± 12.1|                         |
|         | Chin Med J (Engl). 2007;120(14):1226-31.                                                                | 62.3 ± 9.3 |                         |
| Year   | Journal                                      | Median Age | Range | Notes                  |
|--------|----------------------------------------------|------------|-------|------------------------|
| 2005s  | Chin Med J (Engl). 2006;119(1):26-31.        | 62.3 ±11.3 |       | ≈55.0                  |
|        | Chin Med J (Engl). 2004;117(10):1443-8.      | 58±7       |       |                        |
| 2000s  | Chin Med J (Engl). 2002;115(2):163-5.        | 69 ±11     |       |                        |
|        | Chin Med J (Engl). 2001;114(7):698-702.      | 55 ±8.6    |       |                        |
|        | Chin Med J (Engl). 2000;113(8):733-6.        | 61.7 ±10.2 | ≈48.2 |                        |
|        | Chin Med J (Engl). 2000;113(8):702-5.        | 27-86      |       |                        |
|        | Chin Med J (Engl). 1999;112(1):18-21.       | 65 ±7      |       |                        |
| 1995s  | Chin Med J (Engl). 1997;110(11):839-42.      | 60 ±10.2   |       |                        |
|        | Chin Med J (Engl). 1997;110(11):834-8.       | 61.2 ±10.6 |       |                        |
|        | Chin Med J (Engl). 1997;110(3):184-6.        | 36-78      |       |                        |
|        | Chin Med J (Engl). 1997;110(1):56-8.        | 40-74      | ≈46.4 |                        |
|        | Chin Med J (Engl). 1997;110(1):50-2.        | 61.0 ±9.4  |       |                        |
|        | Chin Med J (Engl). 1995;108(7):501-5.       | 58 ±12     |       |                        |
|        | **Chin Med J (Engl).** 1993;106(6):410-4.    | 42         |       |                        |
| 1990s  | Chin Med J (Engl). 1990;103(7):541-5.       | 55         | =55.0 |                        |

**Notes:** Data of ages from original research articles published in *Chin Med J (Engl).*

**Table 2.** E(e)SEED related major risk factors of acute myocardial infarction
| E(e)SEED | AMI related risk factors | Notes |
|----------|--------------------------|-------|
| **External environment** | Abnormal climate and environment,\textsuperscript{10,11} e.g., cold temperatures\textsuperscript{11} traffic noise\textsuperscript{12} dust\textsuperscript{13} air pollution\textsuperscript{14-17} radiation socioeconomic factors | |
| **Internal environment** | Inflammation & infection\textsuperscript{18,19}, e.g., influenza epidemics\textsuperscript{20} acute respiratory-tract infections\textsuperscript{21} COPD/asthma HIV infection\textsuperscript{22} Coronary thrombosis Dyslipidemia, e.g., elevated apolipoprotein B/apolipoprotein A ratio serum triglyceride levels serum LDL-C levels familial-combined hyperlipidaemia\textsuperscript{23} Hypercoagulable state Diabetes\textsuperscript{24} Hypertension History of coronary heart disease (angina) Central obesity Family hereditary | Chronic obstructive pulmonary disease Human immunodeficiency virus |
| **Sleep** | Stay up late or work in shifts Insomnia OSA | Obstructive sleep apnea |
| Emotion | Physical exertion, anger or emotional upset\textsuperscript{25}  
|         | Stress at work or home  
|         | Anxiety and depression\textsuperscript{26-28} |
| Exercise | Physical inactivity |
| Diet | Inadequate daily intake of fresh fruits and vegetables\textsuperscript{29}  
|       | Low Mg and high Ca:Mg ratio\textsuperscript{30}  
|       | Se deficiency  
|       | Tobacco smoking\textsuperscript{31}  
|       | Heavy alcohol consumption  
| Drugs, e.g. | cocaine abuse  
| OC use | post menopausal hormone replacement therapy\textsuperscript{33}  
| Underuse or stopping evidence-based pharmacotherapy, e.g. | statin  
|       | clopidogrel\textsuperscript{34}  
|       | beta-blockers\textsuperscript{45} |

**Figures**

**Figure 1**

Curve on ages of patients with acute myocardial infarction (AMI) in China during 1990 to 2019 (1990s-2020s). It’s easy to find that ages of AMI decreased from 2005s to 2015s (2003 to 2017). Of course, data of 2020s (2018-2022) is not complete. This means that AMI patients are younger and younger since 2003.