ESC HEART FAILURE
ESC Heart Failure 2015; **2**: 46–49
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI:** 10.1002/ehf2.12036

EDITORIAL

Heart failure in Southeast Asia: facts and numbers

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Abstract

Southeast Asia is home to a growing population of >600 million people, the majority younger than 65 years, but among whom, rapid epidemiological transition has led to high rates of premature death from non-communicable diseases (chiefly cardiovascular disease) (up to 28% in the Philippines vs. 12% in UK). There is a strikingly high prevalence of stage A heart failure (HF) risk factors in Southeast Asia, particularly hypertension (>24% in Cambodia and Laos vs. 13–15% in UK and USA), tobacco smoking (>36% in Indonesia), physical inactivity (>50% in Malaysia) and raised blood glucose (10–11% in Brunei, Malaysia, Singapore and Thailand) in spite of a low prevalence of overweight/obesity (21–26% in Southeast Asia vs. 67–70% in UK and USA). Accordingly, the prevalence of symptomatic HF appears to be higher in Southeast Asian countries compared with the rest of the world. Epidemiologic trends in Singapore showed a sharp 38% increase in age-adjusted HF hospitalizations (from 85.4 per 10 000 in 1991 to 110.3 per 10 000 in 1998) with notable ethnic differences (hospitalization rates ~35% higher in Malays and Indians vs. Chinese; mortality 3.5 times higher in Malays vs. Indians and Chinese). Furthermore, Southeast Asian patients present with acute HF at a younger age (54 years) compared with USA patients (75 years) but have more severe clinical features, higher rates of mechanical ventilation, longer lengths of stay (6 vs. 4.2 days) and higher in-hospital mortality (4.8 vs. 3.0%). Finally, there is under-usage of guideline-recommended HF medical therapies (prescribed in 31–63% of patients upon discharge) and device therapies in Southeast Asia. Large gaps in knowledge that need to be addressed in Southeast Asia include the prevalence of HF with preserved ejection fraction, clinical outcomes, barriers to recommended therapies and their cost-effectiveness, as well as possible ethnicity-specific pathophysiologic mechanisms.

Keywords Heart failure; Southeast Asia; Epidemiology; Ethnicity

Received: 23 March 2015; Accepted: 23 March 2015
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Southeast Asia refers to the geographic sub-region of Asia south of China, east of India, west of New Guinea and north of Australia and includes the states of the Association of Southeast Asian Nations (Brunei, Cambodia, Indonesia, Laos, Malaysia, Myanmar, Philippines, Singapore, Thailand and Vietnam) (*Table 1*). The region is notable for its unique history and sociocultural heterogeneity and is home to a rapidly growing population of >600 million people, the majority of whom are younger than 65 years. Recent globalisation and development have led to a rapid epidemiological transition in the region, as evidenced by a reduction in deaths from communicable diseases, an increase in average life expectancy, and an epidemic rise in non-communicable diseases, chief among which is cardiovascular disease. In fact, according to the World Health Organization 2014 global status report, the probability of premature death from non-communicable diseases far exceeds that of the UK (12.0%) in many countries in Southeast Asia, with more than double the risk in the Philippines (27.9%), Myanmar (24.3%) and Laos (24.2%). The risk of premature death from non-communicable diseases is also high in Indonesia (23.1%), Malaysia (19.6%), Cambodia (17.7%), Vietnam (17.4%), Brunei (16.8%) and Thailand (16.2%); with Singapore (10.2%) being the only exception with comparable risk with the UK.

Risk factors for heart failure in Southeast Asia

The cardiovascular risk factors in *Table 1* represent the population with Stage A HF; according to current international HF guidelines.[1] In this context, striking features of Southeast Asian patients at risk of progression to symptomatic HF are observed. Firstly, the prevalence of hypertension in Southeast

Table 1. Prevalence of Stage A HF cardiovascular risk factors in Southeast Asian nations compared with the United Kingdom and United States of America (from the World Health Organization Global Status Report 2014)

		Prevalence in population aged 18+ years (crude adjusted estimates with 95% Confidence Interval)				
Country	World Bank Income Group Classification	insufficient physical activity	Current tobacco smoking[a]	Overweight[b]	Raised blood glucose[c]	Raised blood pressure[d]
Brunei	High	—	15.8 (6.7–26.6)	47.8 (40.7–54.3)	11.2 (5.1–17.1)	19.3 (12.4–26.3)
Cambodia	Low	9.7 (8.7–10.8)	21.3 (16.0–27.5)	16.4 (12.7–20.2)	6.8 (3.6–10.3)	24.4 (17.8–30.9)
Indonesia	Lower middle	22.8 (18.0–28.1)	36.5 (29.9–45.3)	24.4 (19.9–28.9)	8.0 (4.0–11.8)	23.3 (17.7–29.1)
Laos	Lower middle	9.0 (7.4–10.8)	—	16.6 (13.1–20.6)	6.4 (3.4–9.4)	24.1 (18.3–30.4)
Malaysia	Upper middle	51.6 (46.3–56.8)	23.6 (17.2–30.7)	37.3 (31.9–42.6)	9.9 (5.5–14.2)	22.1 (16.4–27.8)
Myanmar	Low	9.0 (7.4–10.9)	22.6 (15.6–29.7)	17.4 (13.4–21.2)	6.3 (2.8–9.5)	23.7 (17.7–30.4)
Philippines	Lower middle	14.4 (3.3–42.2)	27.0 (21.5–32.3)	22.3 (18.1–26.6)	6.0 (2.7–9.2)	22.1 (16.2–28.2)
Singapore	High	33.7 (31.3–36.1)	15.6 (12.6-19.6)	34.6 (30.1–38.9)	9.8 (6.1–13.9)	14.1 (10.0–17.9)
Thailand	Upper middle	14.6 (13.4–16)	—	31.6 (26.7–36.7)	10.9 (6.3–15.5)	21.3 (15.8–26.9)
Vietnam	Lower middle	23.6 (16.2–32.5)	24.3 (19.8–29.5)	20.4 (16.2-24.6)	6.0 (3.1–8.9)	22.2 (16.3–28.3)
United Kingdom	High	40.0 (38.6–41.4)	19.9 (16.2–23.5)	66.7 (63.4–70.3)	10.1 (6.9–13.7)	15.2 (11.9–18.6)
United States of America	High	35.0 (32.5–37.6)	18.0 (14.9–21.1)	69.6 (66.0–73.5)	10.5 (6.6–13.9)	13.4 (10–17.1)

[a]In the population aged 15+ years.
[b]Body mass index ≥25 kg/m^2.
[c]Fasting glucose ≥7.0 mmol/L or on medications for raised blood glucose or with history of diabetes.
[d]Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg.

Asians is high (>24% in Cambodia and Laos) compared with the UK (15.2%) or USA (13.4%). Secondly, in spite of a much lower prevalence of overweight/obesity (21.6–26.2% in Southeast Asia vs. 66.7% in UK and 69.6% in USA), raised blood glucose/diabetes is a notable risk factor among Southeast Asians, reaching similarly high prevalence in Brunei, Malaysia, Singapore and Thailand compared with the UK and USA. Finally, the high prevalence of smoking is of concern, with smoking rates much higher in Southeast Asian countries (up to 36.5% in Indonesia) than UK or USA, except in Brunei and Singapore. This adverse lifestyle habit, coupled with physical inactivity particularly in Malaysia (51.6%), may contribute to the high premature mortality from cardiovascular diseases in these Southeast Asian countries.

These data have important implications for (1) a high population attributable risk of hypertension for the development of HF in Southeast Asia; (2) a strong cardiometabolic basis for HF in a unique 'lean diabetic' Southeast Asian phenotype, distinct from HF in Western patients where diabetes is closely linked to obesity; (3) public health preventive strategies that are urgently needed to reduce smoking and promote physical activity in Southeast Asia.

Epidemiology of clinical heart failure in Southeast Asia

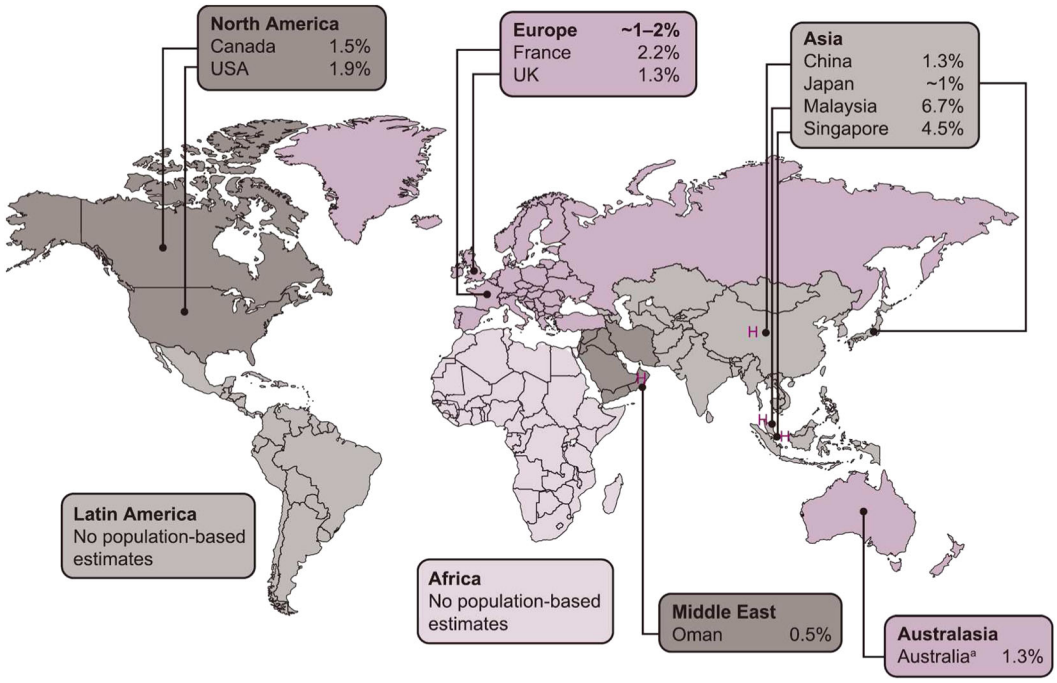
In sharp contrast to the wealth of epidemiologic data on HF in Western populations, reliable population-based data on the incidence, prevalence and secular trends of clinical (Stage C) HF are scarce in Southeast Asia. Limited single-centre data in Malaysia and Singapore suggest that the prevalence of HF in Southeast Asian countries is higher compared with countries in the rest of the world (4.5–6.7% vs. 0.5–2% respectively) (*Figure 1*).[2] In an epidemiologic survey of HF hospitalizations among the elderly (≥65 years old) in Singapore from 1991–1998 (*n*=15 774; 77% Chinese, 14% Malay and 10% Indians),[3] a 38% increase in age-adjusted HF hospitalization rates was clearly demonstrated (from 85.4 per 10 000 in 1991 to 110.3 per 10 000 in 1998), whereas mortality decreased by 20% (from 7.3 per 10 000 in 1991 to 6.1 per 10 000 in 1998). Interestingly, significant ethnic differences were observed, wherein HF hospitalization rates were ~35% higher in Malays and Indians compared with Chinese; and mortality was 3.5 times higher in Malays compared with both Indians and Chinese, with mortality rates climbing over 1991–1998 only among the Malays (but declining in Indians and Chinese). More contemporary (2002–2004) data from two centres in Singapore (*n*=668; 72% Chinese, 17% Malay and 11% Indian)[4] confirmed higher HF readmission rates in Indians and Malays, as well as higher mortality rates in Malays. Whereas greater prevalence of diabetes and atherosclerotic vascular disease explained the higher event rates among Indians, the reasons for poorer prognosis among Malays remained unclear.

Unique characteristics of Southeast Asian patients with symptomatic heart failure

To date, the best available published data allowing comparisons of Asian to Western patients hospitalized with acute HF are from the Acute Decompensated Heart Failure Registry (ADHERE) International-Asia Pacific study that included the Southeast Asian countries of Indonesia, Philippines, Singapore

DOI: 10.1002/ehf2.12036

Figure 1 Proportion of the population living with heart failure in individual countries across the globe. H: Estimates based on a single centre. Reproduced from Ponikowski et al.[2] under the terms of its CC-BY-NC-ND license.



and Thailand.[5] In the overall cohort, Asian Pacific patients were younger (median age 67 years vs. 75 years), but yet had more severe clinical features and higher rates of mechanical ventilation, compared with patients in the parallel US-based ADHERE registry.[6] Specifically among Southeast Asian patients in the ADHERE-Asia Pacific study, the mean age at presentation was even younger (54 years).[7] Despite the younger age of patients, length of stay was longer (6 vs. 4.2 days), and in-hospital mortality higher (4.8 vs. 3.0%), in ADHERE Asia-Pacific compared with ADHERE US.[6] Of note, ADHERE Asia-Pacific (2006–2008) was not performed contemporaneously with ADHERE US (2005–2006), did not include long term follow-up and was limited by missing data particularly with respect to echocardiographic and electrocardiographic data. Their limitations are being addressed in the ongoing simultaneous parallel multi-centre studies in Singapore (Singapore Heart Failure Outcomes and Phenotypes Study) and New Zealand (Outcome in Patients with Heart Failure with Preserved Left Ventricular Ejection Fraction [PEOPLE] Study).[8]

Medical therapy of heart failure in Southeast Asia

Under-usage of disease-modifying HF therapies was reported in the ADHERE Asia-Pacific cohort, with angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers prescribed upon discharge in 63%, beta-blockers in 41% and mineralocorticoid receptor antagonists in 31% of patients. The frequency of use of these HF therapies appeared to be even lower among the Southeast Asian subset of patients.[7] Key gaps in knowledge include reasons for under-treatment of patients as well as the tolerability and effective HF drug doses in Southeast Asian patients, in whom smaller body sizes may impact the maximum tolerated doses or prescription habits of doctors.

Heart failure with preserved ejection fraction in Southeast Asia

The high prevalence of hypertension and rapidly ageing societies in Southeast Asia portend a large increase in heart failure with preserved ejection fraction (HFpEF). Currently, very little is known regarding the prevalence and outcome of patients with HFpEF from Southeast Asia. Retrospective single-centre studies have reported prevalences of HFpEF ranging from 17–38%.[4,9,10] Most recently, the 2-year mortality in 751 patients with HFpEF from Singapore was found to be 26.6% (compared with 37.1% in patients with reduced ejection fraction [HR 0.618; 95% CI 0.508–0.753]), with no ethnic differences.[10]

Advanced heart failure therapies in Southeast Asia

Data are scarce regarding the use of advanced HF therapies, such as device therapy (implantable cardiac defibrillators,

cardiac resynchronization therapy and left ventricular assist devices) and cardiac transplantation, in Southeast Asia. Small single-centre studies have described marked under-usage of device therapies in guideline-indicated cases[11] and conflicting efficacy data in Asian patients.[12,13] Important gaps in knowledge include real world rates of key clinical events (such as sudden cardiac death) in Southeast Asian HF patients, cost-effectiveness of device therapy within the varied healthcare systems of Southeast Asia and sociocultural barriers to device therapy. These issues are being assessed prospectively in the ongoing Asian Sudden Cardiac Death in Heart Failure (ASIAN-HF) Registry [ClinicalTrials.gov Identifier: NCT01633398].[14]

Conclusions

The facts and figures show that HF is a bourgeoning problem in Southeast Asia, fueled by a rapidly growing population with Stage A HF risk factors particularly hypertension, diabetes, in spite of relative lack of obesity, and smoking. Limited data in symptomatic Stage C HF patients from Southeast Asia indicate that HF hospitalizations are on the rise, and that compared with Western counterparts, HF decompensation occurs at a younger age and yet is characterized by more severe clinical features and worse outcomes in Southeast Asian patients. Important inter-ethnic differences exist, wherein Malay patients appear to fare worse than Indian or Chinese patients, for reasons that are poorly understood. Under-usage of disease-modifying HF therapies has been reported among Southeast Asian patients. There are large gaps in knowledge pertaining to the prevalence of HFpEF, clinical outcomes, barriers to recommended therapies and their cost-effectiveness in Southeast Asia, as well as possible ethnicity specific pathophysiologic mechanisms. These gaps will hopefully be addressed in ongoing studies (SHOP,[8] PEOPLE,[8] ASIAN-HF[14]).

References

1. Hunt SA, Baker DW, Chin MH, Cinquegrani MP, Feldman AM, Francis GS, Ganiats TG, Goldstein S, Gregoratos G, Jessup ML, Noble RJ, Packer M, Silver MA, Stevenson LW, Gibbons RJ, Antman EM, Alpert JS, Faxon DP, Fuster V, Gregoratos G, Jacobs AK, Hiratzka LF, Russell RO, Smith SC Jr. American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure); International Society for Heart and Lung Transplantation; Heart Failure Society of America. ACC/AHA Guidelines for the Evaluation and Management of Chronic Heart Failure in the Adult: Executive Summary A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1995 Guidelines for the Evaluation and Management of Heart Failure): Developed in Collaboration With the International Society for Heart and Lung Transplantation; Endorsed by the Heart Failure Society of America. *Circulation* 2001;**104**: 2996–3007.
2. Ponikowski P, Anker SD, AlHabib KF, Cowie MR, Force TL, Hu SS, Jaarsma T, Krum H, Rastogi V, Rohde LE, Samal UC, Shimokawa H, Siswanto BB, Sliwa K, Filippatos G. Heart failure: preventing disease and death worldwide. *ESC Heart Failure* 2014;**1**:4–25.
3. Ng TP, Niti M. Trends and ethnic differences in hospital admissions and mortality for congestive heart failure in the elderly in Singapore, 1991 to 1998. *Heart* 2003;**89**:865–870.
4. Lee R, Chan SP, Chan YH, Wong J, Lau D, Ng K. Impact of race on morbidity and mortality in patients with congestive heart failure: a study of the multiracial population in Singapore. *Int J Cardiol* 2009;**134**:422–425.
5. Atherton JJ, Hayward CS, Wan Ahmad WA, Kwok B, Jorge J, Hernandez AF, Liang L, Kociol RD, Krum H. ADHERE International-Asia Pacific Scientific Advisory Committee. Patient characteristics from a regional multicenter database of acute decompensated heart failure in Asia Pacific (ADHERE International-Asia Pacific). *J Card Fail* 2012;**18**:82–88.
6. Yancy CW, Lopatin M, Stevenson LW, De Marco T, Fonarow GC. Clinical presentation, management, and in-hospital outcomes of patients admitted with acute decompensated heart failure with preserved systolic function: a report from the Acute Decompensated Heart Failure National Registry (ADHERE) Database. *J Am Coll Cardiol* 2006;**47**:76–84.
7. Callender T, Woodward M, Roth G, Farzadfar F, Lemarie JC, Gicquel S, Atherton J, Rahimzadeh S, Ghaziani M, Shaikh M, Bennett D, Patel A, Lam CS, Sliwa K, Barretto A, Siswanto BB, Diaz A, Herpin D, Krum H, Eliasz T, Forbes A, Kiszely A, Khosla R, Petrinic T, Praveen D, Shrivastava R, Xin D, MacMahon S, McMurray J, Rahimi K. Heart failure care in low- and middle-income countries: a systematic review and meta-analysis. *PLoS Med* 2014;**11**:e1001699.
8. Santhanakrishnan R, Ng TP, Cameron VA, Gamble GD, Ling LH, Sim D, Leong GK, Yeo PS, Ong HY, Jaufeerally F, Wong RC, Chai P, Low AF, Lund M, Devlin G, Troughton R, Richards AM, Doughty RN, Lam CS. The Singapore Heart Failure Outcomes and Phenotypes (SHOP) study and prospective evaluation of outcome in patients with heart failure with preserved left ventricular ejection fraction (PEOPLE) study: rationale and design. *J Card Fail* 2013;**19**:156–162.
9. Leong KT, Goh PP, Chang BC, Lingamanaicker J. Heart failure cohort in Singapore with defined criteria: clinical characteristics and prognosis in a multi-ethnic hospital-based cohort in Singapore. *Singapore Med J* 2007;**48**:408–414.
10. Yap J, Sim D, Lim CP, Chia SY, Go YY, Jaufeerally FR, Sim LL, Liew R, Ching CK. Predictors of two-year mortality in Asian patients with heart failure and preserved ejection fraction. *Int J Cardiol* 2015;**183C**:33–38.
11. Lee E, Chen R, Aziz S, Tan PT, Seow YH, Toon WL, Chai P, Wong R, Seow SC, Lam C. Socio cultural barriers to device therapy among Asian patients with heart failure. *Eur J Heart Fail* 2012;**11** (suppl 1):S268.
12. Tanno K, Miyoshi F, Watanabe N, Minoura Y, Kawamura M, Ryu S, Asano T, Kobayashi Y, Katagiri T. MADIT II. The Multicenter Automtic Defibrillator Implantation Trial. Are the MADIT II criteria for ICD implantation appropriate for Japanese patients? *Circ J* 2005;**69**:19–22.
13. Siu CW, Pong V, Ho HH, Liu S, Lau CP, Li SW, Tse HF. Are MADIT II criteria for implantable cardioverter defibrillator implantation appropriate for Chinese patients? *J Cardiovasc Electrophysiol* 2010;**21**:231–235.
14. Lam CS, Anand I, Zhang S, Shimizu W, Narasimhan C, Park SW, Yu CM, Ngarmukos T, Omar R, Reyes EB, Siswanto B, Ling LH, Richards AM. Asian Sudden Cardiac Death in Heart Failure (ASIAN-HF) registry. *Eur J Heart Fail* 2013;**15**:928–936.